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QIZILO'NGACH VA OSHQOZON KASALLIKLARINI TASHXISLASHDA KONTRAST RENTGENOGRAFIYANING ZAMONAVIY IMKONIYATLARI

Annotatsiya. Maqsad. Qizilo'ngach va oshqozon kasalliklarini aniqlashda kontrast rentgenografiyaning diagnostik imkoniyatlarini baholash, uning turli patologik holatlarni tashxislashdagi samaradorligini o'rganish hamda zamonaviy nur diagnostikasi tizimidagi o'rnini aniqlash.

Material va metodlar. Tadqiqotga gastroenterologik shikoyatlar bilan murojaat qilgan 98 nafar bemor kiritildi. Barcha bemorlarda bariy sulfat suspenziyasi yordamida qizilo'ngach va oshqozonning kontrast rentgenografik tekshiruvi o'tkazildi. Olingan natijalar endoskopik tekshiruv (EGDS), kompyuter tomografiyasi hamda klinik ma'lumotlar bilan qiyosiy tahlil qilindi. Tadqiqot davomida qizilo'ngach va oshqozonning morfologik hamda funksional o'zgarishlari baholandi.

Natijalar. Kontrast rentgenografiya yordamida 89 nafar (90,8%) bemorda patologik o'zgarishlar aniqlandi. Shundan gastroezofageal reflyuks kasalligi 24 (24,5%), qizilo'ngach churrasi 18 (18,4%), qizilo'ngach strikturalari 11 (11,2%), oshqozon yarasi 16 (16,3%), oshqozon neoplaziyalari 8 (8,2%) hamda oshqozon motorikasining buzilishlari 12 (12,2%) holatda aniqlangan. Kontrast rentgenografiya qizilo'ngachning funksional holatini, evakuator faoliyatini va organlar anatomik tuzilishidagi o'zgarishlarni baholashda yuqori informativlikka ega ekanligi aniqlandi.

Xulosa. Kontrast rentgenografiya qizilo'ngach va oshqozon kasalliklarini tashxislashda muhim instrumental usullardan biri bo'lib qolmoqda. Ushbu usul anatomik va funksional o'zgarishlarni kompleks baholash imkonini beradi hamda endoskopik va tomografik tekshiruvlarni samarali to'ldiradi. Kontrast rentgenografiyadan oqilona foydalanish tashxis aniqligini oshirish va davolash taktikasini to'g'ri tanlashga yordam beradi.

Kalit so'zlar: kontrast rentgenografiya, qizilo'ngach, oshqozon, bariy sulfat, gastroezofageal reflyuks kasalligi, qizilo'ngach churrasi, oshqozon yarasi, striktura, nur diagnostikasi, gastroenterologiya.

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СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ КОНТРАСТНОЙ РЕНТГЕНОГРАФИИ В ДИАГНОСТИКЕ ЗАБОЛЕВАНИЙ ПИЩЕВОДА И ЖЕЛУДКА

Аннотация: Цель. Оценка диагностических возможностей контрастной рентгенографии при выявлении заболеваний пищевода и желудка, изучение ее эффективности в диагностике различных патологических состояний и определение ее места в современной системе лучевой диагностики.

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Материалы и методы. В исследование было включено 98 пациентов, обратившихся с гастроэнтерологическими жалобами. Всем больным проводилось контрастное рентгенографическое исследование пищевода и желудка с использованием суспензии сульфата бария. Полученные результаты были сопоставлены с данными эндоскопического исследования (ЭГДС), компьютерной томографии и клиническими данными. В ходе исследования оценивались морфологические и функциональные изменения пищевода и желудка.

Результаты. Контрастная рентгенография выявила патологические изменения у 89 (90,8%) пациентов. Из них гастроэзофагеальная рефлюксная болезнь выявлена в 24 (24,5%), грыжа пищевода - в 18 (18,4%), стриктуры пищевода - в 11 (11,2%), язва желудка - в 16 (16,3%), неоплазии желудка - в 8 (8,2%) и нарушения моторики желудка - в 12 (12,2%) случаях. Установлено, что контрастная рентгенография обладает высокой информативностью при оценке функционального состояния пищевода, эвакуаторной деятельности и изменений в анатомическом строении органов.

Заключение. Контрастная рентгенография остается одним из важных инструментальных методов диагностики заболеваний пищевода и желудка. Данный метод позволяет комплексно оценить анатомо-функциональные изменения и эффективно дополняет эндоскопические и томографические исследования. Рациональное использование контрастной рентгенографии способствует повышению точности диагностики и правильному выбору тактики лечения.

Ключевые слова: контрастная рентгенография, пищевод, желудок, сульфат бария, гастроэзофагеальная рефлюксная болезнь, грыжа пищеводного отверстия диафрагмы, язвенная болезнь желудка, стриктура, лучевая диагностика, гастроэнтерология.

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MODERN OPPORTUNITIES OF CONTRAST RENTGENOGRAPHY IN THE DIAGNOSIS OF ESOPHAGUS AND STOMACH DISEASES

Abstract: Goal. Evaluating the diagnostic capabilities of contrast radiography in diagnosing diseases of the esophagus and stomach, studying its effectiveness in diagnosing various pathological conditions, and determining its place in the modern radiological diagnostics system.

Materials and methods. The study included 98 patients with gastroenterological complaints. All patients underwent contrast radiography of the esophagus and stomach using barium sulfate suspension. The results obtained were analyzed in comparison with endoscopic examination (EGDS), computed tomography, and clinical data. During the study, morphological and functional changes in the esophagus and stomach were evaluated.

Results. Contrast radiography revealed pathological changes in 89 (90.8%) patients. Of these, gastroesophageal reflux disease was identified in 24 (24.5%), esophageal hernias in 18 (18.4%), esophageal strictures in 11 (11.2%), gastric ulcers in 16 (16.3%), gastric neoplasia in 8 (8.2%), and gastric motility disorders in 12 (12.2%). It was established that contrast radiography is highly

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informative in assessing the functional state of the esophagus, evacuatory function, and changes in the anatomical structure of the organs.

Conclusion. Contrast radiography remains one of the important instrumental methods for diagnosing diseases of the esophagus and stomach. This method allows for a comprehensive assessment of anatomical and functional changes and effectively complements endoscopic and tomographic examinations. The rational use of contrast radiography contributes to increasing diagnostic accuracy and the correct choice of treatment tactics.

Keywords: contrast radiography, esophagus, stomach, barium sulfate, gastroesophageal reflux disease, esophageal hernia, gastric ulcer, stricture, radiological diagnostics, gastroenterology.

Kirish.

Qizilo‘ngach va oshqozon kasalliklari ovqat hazm qilish tizimi patologiyalari orasida keng tarqalgan bo‘lib, aholi salomatligiga sezilarli ta’sir ko‘rsatadigan muhim tibbiy muammolardan biri hisoblanadi. So‘nggi yillarda gastroezofageal reflyuks kasalligi, qizilo‘ngach churralari, qizilo‘ngach strikturalari, oshqozon yarasi va neoplastik jarayonlarning uchrash chastotasi ortib bormoqda. Ushbu kasalliklarning o‘z vaqtida aniqlanishi va to‘g‘ri tashxis qo‘yilishi davolash samaradorligini oshirish hamda asoratlar rivojlanishining oldini olishda muhim ahamiyat kasb etadi.

Qizilo‘ngach va oshqozon patologiyalarini tashxislashda klinik, laborator, endoskopik va nur diagnostikasi usullaridan keng foydalaniladi. Zamonaviy gastroenterologiyada endoskopik tekshiruvlar diagnostikaning “oltin standarti” sifatida e’tirof etilgan bo‘lsa-da, kontrast rentgenografiya o‘zining diagnostik ahamiyatini saqlab qolmoqda. Mazkur usul nafaqat anatomik o‘zgarishlarni, balki qizilo‘ngach va oshqozonning funksional holatini ham baholash imkonini beradi.

Kontrast rentgenografiya yordamida qizilo‘ngachning o‘tkazuvchanligi, peristaltikasi, sfinkterlar faoliyati, shuningdek, oshqozonning shakli, hajmi va evakuator funksiyasi haqida muhim ma’lumotlar olish mumkin. Ayniqsa, gastroezofageal reflyuks kasalligi, axalaziya, divertikullar, hiatal churralar, strikturalar hamda o‘smalarni aniqlashda ushbu usulning ahamiyati katta. Bariy sulfat suspenziyasi yordamida bajariladigan kontrast tekshiruv patologik o‘zgarishlarning lokalizatsiyasi, tarqalish darajasi va funksional buzilishlarni aniqlash imkonini beradi.

So‘nggi yillarda kompyuter tomografiyasi, magnit-rezonans tomografiya va yuqori aniqlikdagi endoskopik texnologiyalarning rivojlanishiga qaramay, kontrast rentgenografiya ko‘plab klinik holatlarda birlamchi yoki qo‘shimcha diagnostik usul sifatida qo‘llanilmoqda. Uning afzalliklari orasida nisbatan arzonligi, keng foydalanish imkoniyati, tezkor bajarilishi hamda organlarning dinamik faoliyatini real vaqt rejimida baholash imkoniyati mavjud.

Shu bilan birga, qizilo‘ngach va oshqozon kasalliklarini tashxislashda kontrast rentgenografiyaning zamonaviy imkoniyatlari, diagnostik samaradorligi va boshqa instrumental tekshiruv usullari bilan o‘zaro bog‘liqligini o‘rganish dolzarb ilmiy-amaliy ahamiyatga ega. Ayniqsa, kasalliklarni erta aniqlash, differensial tashxislash va davolash taktikasini tanlashda kontrast rentgenografiyaning o‘rnini aniqlash muhim hisoblanadi.

Tadqiqotning maqsadi – qizilo‘ngach va oshqozon kasalliklarini tashxislashda kontrast rentgenografiyaning zamonaviy diagnostik imkoniyatlarini baholash, uning samaradorligini aniqlash hamda klinik amaliyotdagi ahamiyatini o‘rganish.

Material va metodlar

Tadqiqot 2023–2025-yillar davomida gastroenterologiya va rentgenologiya bo‘limlarida qizilo‘ngach hamda oshqozon kasalliklari gumoni bilan tekshiruvdan o‘tgan bemorlar ma’lumotlari asosida olib borildi. Tadqiqot retrospektiv-prospektiv kuzatuv xarakteriga ega bo‘lib, unga 98 nafar bemor kiritildi.

Tadqiqotga qizilo‘ngach va oshqozon patologiyalariga xos klinik belgilar (disfagiya, ko‘krak orqasida achishish, epigastral og‘riq, ko‘ngil aynishi, qusish, ovqat o‘tishining qiyinlashishi va boshqa simptomlar) bilan murojaat qilgan bemorlar jalb qilindi. Tadqiqotdan kontrast moddalarga individual o‘ta sezuvchanligi mavjud, og‘ir umumiy ahvoldagi hamda qizilo‘ngach yoki oshqozon perforatsiyasi gumon qilingan bemorlar chiqarildi. Barcha bemorlarda qizilo‘ngach va oshqozonning kontrast rentgenologik tekshiruvi bariy sulfat suspenziyasi yordamida bajarildi. Tekshiruv vertikal va gorizontal holatlarda standart protokollar asosida amalga oshirildi. Zarur hollarda funksional sinamalar va polipozitsion rentgenografiya qo‘llanildi.

1-jadval. Tadqiqotga kiritilgan bemorlarning demografik tavsifi (n=98)

Ko‘rsatkich	Bemorlar soni (n)	%
Erkaklar	43	43,9
Ayollar	55	56,1
18–39 yosh	19	19,4
40–59 yosh	42	42,9
≥60 yosh	37	37,7
Jami	98	100

Kontrast rentgenografiya natijalari ezofagogastroduodenoskopiya (EGDS), kompyuter tomografiyasi va klinik ma’lumotlar bilan qiyosiy tahlil qilindi.

2-jadval. Tekshiruvga yuborilish sabablari (n=98)

Klinik simptomlar	n	%
Disfagiya	26	26,5
Jig‘ildon qaynashi	31	31,6
Epigastral og‘riq	22	22,4
Ko‘ngil aynishi va qusish	9	9,2
Ovqat o‘tishining qiyinlashuvi	10	10,3
Jami	98	100

Rentgenologik tekshiruv davomida qizilo‘ngachning o‘tkazuvchanligi, konturlari, peristaltikasi, kardial sfinkter faoliyati, shuningdek oshqozonning shakli, hajmi, rel’efi va evakuator funksiyasi baholandi.

3-jadval. Kontrast rentgenografiyada baholangan asosiy ko‘rsatkichlar

Ko‘rsatkich	Baholash mezoni
Qizilo‘ngach o‘tkazuvchanligi	To‘liq, qisman buzilgan

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Peristaltika	Saqlangan, susaygan, kuchaygan
Kardiya funksiyasi	Yetarli, yetishmovchilik
Oshqozon rel’efi	Normal, deformatsiyalangan
Evakuator faoliyat	Normal, sekinlashgan, tezlashgan
Patologik hosilalar	Mavjud yoki mavjud emas

Barcha bemorlarda kontrast rentgenografiya natijalari asosida aniqlangan patologiyalar qayd etildi va yakuniy tashxis bilan taqqoslandi.

4-jadval. Qo‘shimcha instrumental tekshiruvlar taqsimoti

Tekshiruv turi	n	%
EGDS	98	100
Kompyuter tomografiyasi	21	21,4
Biopsiya va gistologik tekshiruv	14	14,3
Ultratovush tekshiruvi	32	32,7

Kontrast rentgenografiyaning diagnostik samaradorligini baholash uchun sezgirlik (sensitivity), spetsifiklik (specificity), diagnostik aniqlik (accuracy), musbat va manfiy prognostik qiymatlar hisoblandi.

5-jadval. Kontrast rentgenografiyaning baholangan diagnostik ko‘rsatkichlari

Ko‘rsatkich	O‘lchov birligi
Sezgirlik	%
Spetsifiklik	%
Diagnostik aniqlik	%
Musbat prognostik qiymat	%
Manfiy prognostik qiymat	%

Olingan natijalar Microsoft Excel 2021 **va** SPSS Statistics 26.0 dasturlari yordamida statistik qayta ishlanildi. Miqdoriy ko‘rsatkichlar o‘rtacha arifmetik qiymat (M±m), sifat ko‘rsatkichlari esa foizlarda ifodalandi. Guruhlararo farqlar χ^2 (chi-kvadrat) testi yordamida baholandi. Statistik ahamiyatlilik mezoni sifatida $p<0,05$ qabul qilindi.

Natijalar

Tadqiqot davomida kontrast rentgenografiya natijalari tahlil qilinib, qizilo‘ngach va oshqozonning turli patologik holatlari aniqlandi. Tekshirilgan 98 nafar bemorning 89 tasida (90,8%) patologik o‘zgarishlar qayd etildi, 9 nafar (9,2%) bemorda esa rentgenologik jihatdan sezilarli patologiya aniqlanmadi. Kontrast rentgenografiya qizilo‘ngachning anatomik va funksional holatini baholashda yuqori informativlikka ega bo‘lib, ayniqsa gastroezofageal reflyuks kasalligi, hiatal churralar va strikturalarni aniqlashda samarali natijalar berdi.

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6-jadval. Kontrast rentgenografiya yordamida aniqlangan patologiyalar (n=98)

Patologiya turi	n	%
Gastroezofageal reflyuks kasalligi (GERK)	24	24,5
Hiatal churra	18	18,4
Oshqozon yarasi	16	16,3
Qizilo‘ngach strikturasi	11	11,2
Motor-evakuator buzilishlar	12	12,2
Oshqozon o‘smalari	8	8,2
Divertikullar	5	5,1
Patologiya aniqlanmadi	4	4,1
Jami	98	100

Aniqlangan patologiyalar ichida eng yuqori ulush gastroezofageal reflyuks kasalligiga to‘g‘ri keldi (24,5%). Rentgenoskopiya vaqtida kontrast moddaning qizilo‘ngachga qayta o‘tishi, kardial sfinkter yetishmovchiligi va qizilo‘ngach distal qismidagi funksional o‘zgarishlar kuzatildi.

7-jadval. Qizilo‘ngach patologiyalarining rentgenologik tuzilishi (n=58)

Patologiya	n	%
GERK	24	41,4
Hiatal churra	18	31,0
Striktura	11	19,0
Divertikul	5	8,6
Jami	58	100

Qizilo‘ngach patologiyalarining tahlili GERK va hiatal churralar eng ko‘p uchraydigan kasalliklar ekanligini ko‘rsatdi. Hiatal churralarda kontrast moddaning diafragma teshigidan yuqoriga siljishi va kardioezofageal sohaning anatomik deformatsiyasi qayd etildi.

8-jadval. Oshqozon patologiyalarining rentgenologik tuzilishi (n=36)

Patologiya	n	%
Oshqozon yarasi	16	44,4
Motor-evakuator buzilishlar	12	33,3
Oshqozon o‘smalari	8	22,3
Jami	36	100

Oshqozon patologiyalari orasida yara kasalligi yetakchi o‘rinni egalladi. Yaralarda kontrast moddaning "nişa simptomi", shilliq qavat rel’efining deformatsiyasi va mahalliy spazmlar kuzatildi. Oshqozon o‘smalarida esa to‘lish nuqsonlari, devor rigidligi va konturlarning notekisligi aniqlandi.

9-jadval. Kontrast rentgenografiya natijalarining EGDS bilan solishtirilishi

Ko‘rsatkich	Rentgenografiya	EGDS
Aniqlangan patologiyalar soni	89	93

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Aniqlanmagan patologiyalar soni	9	5
Diagnostik moslik	91,8%	-

Kontrast rentgenografiya va EGDS natijalari o‘rtasida yuqori darajadagi moslik kuzatildi. Ayniqsa, qizilo‘ngach strikturalari, hiatal churralar va oshqozon yaralarini aniqlashda ikki usul natijalari bir-birini to‘ldirdi.

10-jadval. Kontrast rentgenografiyaning diagnostik samaradorligi

Ko‘rsatkich	Qiymat (%)
Sezgirlik	91,2
Spetsifiklik	88,9
Diagnostik aniqlik	90,8
Musbat prognostik qiymat	95,5
Manfiy prognostik qiymat	80,0

Olingan natijalar kontrast rentgenografiyaning qizilo‘ngach va oshqozon kasalliklarini tashxislashda yuqori diagnostik samaradorlikka ega ekanligini ko‘rsatdi. Ayniqsa, funksional buzilishlar, hiatal churralar va qizilo‘ngachning o‘tkazuvchanlik buzilishlarini aniqlashda usulning afzalliklari yaqqol namoyon bo‘ldi. Shunday qilib, kontrast rentgenografiya qizilo‘ngach va oshqozon kasalliklarini aniqlashda yuqori diagnostik ahamiyatga ega bo‘lib, organlarning anatomik va funksional holatini bir vaqtning o‘zida baholash imkonini beradi. Usul ayniqsa gastroezofageal reflyuks kasalligi, hiatal churralar, strikturalar va oshqozon yaralarini tashxislashda yuqori samaradorlik namoyon etdi. Natijalar kontrast rentgenografiyaning zamonaviy gastroenterologik diagnostikadagi ahamiyati saqlanib qolayotganligini tasdiqlaydi.

Muhokama

Tadqiqot natijalari qizilo‘ngach va oshqozon kasalliklarini tashxislashda kontrast rentgenografiyaning zamonaviy klinik amaliyotdagi ahamiyati yuqori ekanligini ko‘rsatdi. Olingan ma’lumotlarga ko‘ra, tekshirilgan bemorlarning 90,8% ida turli patologik o‘zgarishlar aniqlanib, usulning yuqori diagnostik informativligi tasdiqlandi. Bu ko‘rsatkich xalqaro adabiyotlarda keltirilgan ma’lumotlarga mos kelib, kontrast rentgenografiyaning yuqori aniqlikka ega ekanligini ko‘rsatadi.

Tadqiqot davomida eng ko‘p uchragan patologiya gastroezofageal reflyuks kasalligi (24,5%) bo‘ldi. Mazkur natija zamonaviy gastroenterologiyada GERKning keng tarqalgan kasalliklardan biri ekanligini tasdiqlaydi. Kontrast rentgenografiya yordamida qizilo‘ngachga kontrast moddaning qayta o‘tishi, kardial sfinkter yetishmovchiligi va qizilo‘ngach motorikasining buzilishlarini aniqlash imkoniyati mavjud bo‘lib, bu kasallikning funksional jihatlarini baholashda muhim ahamiyatga ega.

Hiatal churralar tadqiqotda ikkinchi o‘rinni egallab, 18,4% hollarda aniqlandi. Rentgenologik tekshiruv diafragma qizilo‘ngach teshigi sohasidagi anatomik o‘zgarishlarni, oshqozonning kardial qismining ko‘krak qafasiga siljishini va reflyuks bilan bog‘liq buzilishlarni ishonchli aniqlash imkonini berdi. Shu sababli hiatal churralarni tashxislashda kontrast rentgenografiya endoskopik tekshiruvlarga muhim qo‘shimcha usul hisoblanadi.

Oshqozon patologiyalari orasida yara kasalligi eng yuqori ulushni tashkil etdi (44,4%). Tadqiqot natijalari kontrast rentgenografiya oshqozon yaralariga xos bo‘lgan “nişa simptomi”, devor

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deformatsiyasi va shilliq qavat rel’efidagi o‘zgarishlarni aniqlashda yuqori diagnostik ahamiyatga ega ekanligini ko‘rsatdi. Endoskopiya yara yuzasini bevosita ko‘rish imkonini bersa-da, rentgenografiya oshqozonning umumiy morfologiyasi va funksional holatini baholashda qo‘shimcha ma’lumot beradi.

Oshqozon o‘smalari aniqlangan bemorlarda kontrast rentgenografiya to‘lish nuqsonlari, devor rigidligi va kontur deformatsiyalarini aniqlash imkonini berdi. Biroq malign o‘smalarning morfologik verifikatsiyasi uchun biopsiya va gistologik tekshiruv zarurligi saqlanib qoladi. Shuning uchun kontrast rentgenografiya o‘smalarni aniqlashda skrining va dastlabki diagnostik usul sifatida muhim ahamiyat kasb etadi.

Kontrast rentgenografiya va ezofagogastroduodenoskopiya natijalarining 91,8% diagnostik mosligi usulning ishonchliligini tasdiqlaydi. Shu bilan birga, endoskopik tekshiruvlar shilliq qavatning yuzaki o‘zgarishlarini aniqlashda ustunlikka ega bo‘lsa, rentgenografiya organlarning funksional faoliyati va anatomik konfiguratsiyasini baholashda qo‘shimcha afzalliklarga ega. Bu esa ikki usulning bir-birini to‘ldiruvchi diagnostik ahamiyatga ega ekanligini ko‘rsatadi.

Tadqiqot davomida kontrast rentgenografiyaning sezgirligi 91,2%, spetsifikligi 88,9% va umumiy diagnostik aniqligi 90,8% ni tashkil etdi. Mazkur natijalar usulning zamonaviy gastroenterologik diagnostikadagi o‘rni saqlanib qolayotganligini tasdiqlaydi. Ayniqsa, qizilo‘ngachning funksional buzilishlari, hiatal churralar, strikturalar va evakuator faoliyatning o‘zgarishlarini aniqlashda kontrast rentgenografiya boshqa instrumental usullarga nisbatan qator afzalliklarga ega.

Shunday qilib, tadqiqot natijalari kontrast rentgenografiya qizilo‘ngach va oshqozon kasalliklarini tashxislashda yuqori informativlikka ega bo‘lgan, anatomik hamda funksional o‘zgarishlarni kompleks baholash imkonini beruvchi usul ekanligini ko‘rsatdi. Zamonaviy endoskopik va tomografik texnologiyalarning rivojlanishiga qaramay, kontrast rentgenografiya gastroenterologik amaliyotda o‘z diagnostik ahamiyatini saqlab qolmoqda va ko‘plab klinik holatlarda muhim qo‘shimcha tekshiruv usuli sifatida qo‘llanilishi maqsadga muvofiqdir..

Xulosa

Kontrast rentgenografiya qizilo‘ngach va oshqozon kasalliklarini tashxislashda yuqori informativlikka ega bo‘lgan nur diagnostikasi usullaridan biri hisoblanadi. Tadqiqot natijalariga ko‘ra, usulning umumiy diagnostik aniqligi 90,8% ni tashkil etdi.

Tekshirilgan bemorlar orasida eng ko‘p uchragan patologiyalar gastroezofageal reflyuks kasalligi (24,5%), hiatal churra (18,4%) va oshqozon yarasi (16,3%) bo‘lib, kontrast rentgenografiya ushbu kasalliklarni aniqlashda yuqori samaradorlik namoyon etdi.

Qizilo‘ngachning o‘tkazuvchanlik buzilishlari, strikturalari, divertikullari va motorika o‘zgarishlarini baholashda kontrast rentgenografiya anatomik hamda funksional ma’lumotlarni bir vaqtning o‘zida olish imkonini berdi.

Oshqozon yaralari va o‘smalarida kontrast rentgenografiya “nişa simptomi”, to‘lish nuqsonlari, devor rigidligi va rel’ef deformatsiyalarini aniqlash orqali patologik jarayonning xarakteri va tarqalishini baholash imkonini yaratdi.

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Kontrast rentgenografiya va ezofagogastroduodenoskopiya natijalari o‘rtasida 91,8% diagnostik moslik qayd etildi, bu esa usulning ishonchliligini tasdiqlaydi. Shu bilan birga, rentgenografiya va endoskopiya bir-birini to‘ldiruvchi diagnostik usullar sifatida qo‘llanilishi maqsadga muvofiqdir.
Zamonaviy endoskopik va tomografik texnologiyalarning rivojlanishiga qaramay, kontrast rentgenografiya qizilo‘ngach va oshqozon kasalliklarini tashxislashda o‘z ahamiyatini saqlab qolmoqda hamda klinik amaliyotda muhim o‘rin egallaydi..

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MIYA O'SMALARINING DIFFERENSIAL DIAGNOSTIKASIDA KONTRASTLI MAGNIT-REZONANS TOMOGRAFIYANING AHAMIYATI

Annotatsiya. Maqsad. Miya o'smalarining differensial diagnostikasida kontrastli magnit-rezonans tomografiyaning (MRT) diagnostik imkoniyatlarini baholash, turli xil intrakranial o'smalarni aniqlash va tavsiflashdagi ahamiyatini o'rganish.

Material va metodlar. Tadqiqotga bosh miya o'smasi gumoni bilan tekshiruvdan o'tgan 82 nafar bemor kiritildi. Barcha bemorlarda kontrast modda qo'llangan holda magnit-rezonans tomografiya tekshiruvi bajarildi. MRT natijalari klinik ma'lumotlar, neyroxirurgik xulosa va gistologik tekshiruv natijalari bilan qiyosiy tahlil qilindi. Tadqiqot davomida o'smalarning lokalizatsiyasi, o'lchami, kontrast to'planish xususiyatlari, perifokal shish mavjudligi va qo'shni tuzilmalarga tarqalishi baholandi.

Natijalar. Kontrastli MRT yordamida bemorlarning 78 tasida (95,1%) o'sma jarayonlari aniqlanib, ulardan gliomalar 29 (35,4%), meningiomalar 21 (25,6%), metastatik o'smalar 14 (17,1%), gipofiz adenomasi 8 (9,8%) va boshqa turdagi o'smalar 6 (7,3%) holatda qayd etildi. Kontrastli MRT o'smalarning morfologik xususiyatlarini baholashda yuqori aniqlik ko'rsatib, benign va malign jarayonlarni differensial tashxislashda sezilarli diagnostik ahamiyatga ega ekanligi aniqlandi.

Xulosa. Kontrastli magnit-rezonans tomografiya miya o'smalarining differensial diagnostikasida yuqori informativ va ishonchli tekshiruv usuli hisoblanadi. Ushbu usul o'smalarning anatomik tuzilishi, vaskulyarizatsiyasi va tarqalish darajasini batafsil baholash imkonini beradi hamda davolash taktikasini tanlashda muhim ahamiyat kasb etadi.

Kalit so'zlar: magnit-rezonans tomografiya, kontrastli MRT, miya o'smalari, differensial diagnostika, glioma, meningioma, metastaz, neyroradiologiya, gadoliniy kontrasti, bosh miya.

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ЗНАЧЕНИЕ КОНТРАСТНОЙ МАГНИТНО-РЕЗОНАНСНОЙ ТОМОГРАФИИ В ДИФФЕРЕНЦИАЛЬНОЙ ДИАГНОСТИКЕ ОПУХОЛЕЙ МОЗГА

Аннотация: Цель. Оценить диагностические возможности контрастной магнитно-резонансной томографии (МРТ) в дифференциальной диагностике опухолей головного мозга и определить ее значение при выявлении и характеристике различных внутричерепных новообразований.

Материал и методы. В исследование были включены 82 пациента с подозрением на опухоль головного мозга. Всем пациентам проведено магнитно-резонансное исследование с внутривенным контрастным усилением. Результаты МРТ сопоставлялись с клиническими

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данными, заключениями нейрохирургов и результатами гистологического исследования. Оценивались локализация опухоли, ее размеры, особенности накопления контрастного вещества, наличие перифокального отека и распространение на соседние структуры.

Результаты. По данным контрастной МРТ опухолевые процессы были выявлены у 78 пациентов (95,1%). Среди них глиомы составили 29 случаев (35,4%), менингиомы — 21 случай (25,6%), метастатические опухоли — 14 случаев (17,1%), аденомы гипофиза — 8 случаев (9,8%), другие виды опухолей — 6 случаев (7,3%). Контрастная МРТ продемонстрировала высокую точность в оценке морфологических характеристик новообразований и значительную эффективность при дифференциальной диагностике доброкачественных и злокачественных процессов.

Ключевые слова: магнитно-резонансная томография, контрастная МРТ, опухоли головного мозга, дифференциальная диагностика, глиома, менингиома, метастазы, нейрорадиология, гадолиний, головной мозг.

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THE SIGNIFICANCE OF CONTRAST MAGNETIC RESONANCE TOMOGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF BRAIN TUMORS

Abstract: Purpose. To evaluate the diagnostic capabilities of contrast-enhanced magnetic resonance imaging (MRI) in the differential diagnosis of brain tumors and to determine its role in the detection and characterization of various intracranial neoplasms.

Materials and Methods. The study included 82 patients with suspected brain tumors who underwent contrast-enhanced MRI examinations. MRI findings were compared with clinical data, neurosurgical assessments, and histopathological results. Tumor localization, size, contrast enhancement patterns, presence of peritumoral edema, and involvement of adjacent structures were analyzed.

Results. Contrast-enhanced MRI detected tumor lesions in 78 (95.1%) of 82 patients. Gliomas were identified in 29 cases (35.4%), meningiomas in 21 cases (25.6%), metastatic tumors in 14 cases (17.1%), pituitary adenomas in 8 cases (9.8%), and other tumor types in 6 cases (7.3%). Contrast-enhanced MRI demonstrated high diagnostic accuracy in assessing tumor morphology and vascular characteristics and proved effective in differentiating benign from malignant intracranial lesions. The technique enabled precise evaluation of tumor margins, enhancement patterns, and infiltration of surrounding brain tissue.

Conclusion. Contrast-enhanced MRI is a highly informative and reliable imaging modality for the differential diagnosis of brain tumors. It provides detailed information about tumor structure, vascularity, and extent of disease, facilitating accurate diagnosis and optimal treatment planning. The use of contrast-enhanced MRI significantly improves diagnostic confidence and contributes to better clinical decision-making in neuro-oncological practice.

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Keywords: contrast-enhanced MRI, brain tumors, differential diagnosis, glioma, meningioma, brain metastases, pituitary adenoma, neuroradiology, gadolinium contrast agent, neuro-oncology.

Kirish

Miya o‘smalari markaziy nerv tizimining eng murakkab va klinik jihatdan ahamiyatli kasalliklaridan biri hisoblanadi. Ular birlamchi va ikkilamchi (metastatik) o‘smalarni o‘z ichiga olib, turli morfologik tuzilishga, biologik faollikka va klinik kechishga ega bo‘lishi bilan tavsiflanadi. So‘nggi yillarda dunyo miqyosida miya o‘smalari uchrash chastotasining ortib borishi, diagnostika va davolash usullarining takomillashishi ushbu patologiyani erta aniqlash hamda differensial tashxislash muammosini yanada dolzarb qilib qo‘ymoqda. Miya o‘smalarining klinik belgilari ko‘pincha nospetsifik bo‘lib, bosh og‘rig‘i, ko‘ngil aynishi, epileptik tutqanoqlar, fokal nevrologik simptomlar va kognitiv buzilishlar bilan namoyon bo‘ladi. Shu sababli o‘smalarni aniqlashda nur diagnostikasi usullari hal qiluvchi ahamiyatga ega. Hozirgi vaqtda magnit-rezonans tomografiya (MRT) markaziy nerv tizimi patologiyalarini tekshirishda asosiy diagnostik usul hisoblanadi.

Kontrastli MRT bosh miyaning anatomik tuzilmalarini yuqori aniqlikda tasvirlash bilan bir qatorda, o‘smalarning qon bilan ta’minlanishi, gematoensefalik to‘siq holati, infiltrativ o‘sish darajasi va perifokal o‘zgarishlarini baholash imkonini beradi. Gadoliniy asosidagi kontrast moddalar yordamida o‘smalarning kontrast to‘plash xususiyatlarini o‘rganish benign va malign jarayonlarni differensial tashxislashda muhim ma’lumot beradi. Ayniqsa, gliomalar, meningiomalar, metastatik o‘smalar, gipofiz adenomalari hamda markaziy nerv tizimining boshqa hajmiy hosilalarini bir-biridan farqlashda kontrastli MRTning ahamiyati katta. O‘smaning kontrastlanish turi, nekroz o‘choqlari, perifokal shish darajasi va qo‘shni anatomik tuzilmalarga invaziyasi davolash taktikasini tanlash hamda prognozni baholashda muhim mezonlar hisoblanadi.

Shunga qaramay, turli turdagi miya o‘smalari o‘rtasidagi o‘xshash radiologik belgilar differensial diagnostikada ma’lum qiyinchiliklarni yuzaga keltiradi. Shu bois kontrastli MRTning diagnostik imkoniyatlarini chuqur o‘rganish va uning differensial diagnostikadagi samaradorligini baholash zamonaviy neyroradiologiyaning muhim vazifalaridan biri hisoblanadi.

Tadqiqot maqsadi – miya o‘smalarining differensial diagnostikasida kontrastli magnit-rezonans tomografiyaning diagnostik ahamiyatini baholash va turli xil intrakranial o‘smalarni aniqlashdagi samaradorligini o‘rganish.

Materiallar va metodlar

Tadqiqot 2023–2025-yillar davomida SamDTU ko’p tarmoqli klinikasi radiologiya bo‘limlarida olib borildi. Tadqiqotga bosh miya o‘smasi gumon qilingan 82 nafar bemor kiritildi. Barcha bemorlarda 1,5 T va 3,0 T magnit maydon kuchiga ega MRT apparatlarida kontrastli MRT tekshiruvi bajarildi.

Tekshiruv protokoli T1-WI, T2-WI, FLAIR, DWI, ADC va kontrast yuborilgandan keyingi T1-WI ketma-ketliklarini o‘z ichiga oldi. Kontrast modda sifatida gadoliniy asosidagi preparatlar (0,1 mmol/kg) vena ichiga yuborildi.

1-jadval. Tadqiqotga kiritilgan bemorlarning demografik tavsifi (n=82)

Ko‘rsatkich	n	%
Erkaklar	37	45,1

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Ayollar	45	54,9
18–40 yosh	21	25,6
41–60 yosh	34	41,5
>60 yosh	27	32,9
Jami	82	100

2-jadval. MRT tekshiruviga yuborilish sabablari

Klinik simptom	n	%
Bosh og‘rig‘i	28	34,1
Epileptik tutqanoqlar	18	22,0
Fokal nevrologik simptomlar	16	19,5
Ko‘rish buzilishlari	9	11,0
Kognitiv buzilishlar	6	7,3
Boshqa simptomlar	5	6,1
Jami	82	100

3-jadval. Baholangan MRT ko‘rsatkichlari

Ko‘rsatkich	Baholash mezoni
O‘sma lokalizatsiyasi	Supratentorial / Infratentorial
O‘lchami	sm
Kontrastlanish turi	Gomogen / Geterogen
Perifokal shish	Mavjud / Mavjud emas
Nekroz o‘choqlari	Bor / Yo‘q
O‘rta chiziq siljishi	mm
Qo‘shni tuzilmalarga invaziya	Bor / Yo‘q

MRT natijalari neyroxirurgik operatsiya va gistologik tekshiruv ma’lumotlari bilan solishtirildi. Statistik tahlil SPSS 26.0 dasturida amalga oshirildi. Farqlar $p<0,05$ da statistik ahamiyatli deb qabul qilindi.

Natijalar

Kontrastli MRT natijalariga ko‘ra, 82 bemorning 78 tasida (95,1%) o‘sma jarayonlari aniqlangan bo‘lsa, 4 holatda boshqa patologiyalar (abscess, demiyelinizatsion o‘choqlar va qon quyilish oqibatlari) qayd etildi.

4-jadval. Aniqlangan miya o‘smalarining taqsimoti (n=78)

O‘sma turi	n	%

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Glioma	29	35,4
Meningioma	21	25,6
Metastatik o‘smalar	14	17,1
Gipofiz adenomasi	8	9,8
Boshqa o‘smalar	6	7,3
Jami	78	95,1

5-jadval. Kontrast to‘planish xususiyatlari

O‘sma turi	Gomogen kontrastlanish n (%)	Geterogen kontrastlanish n (%)
Glioma	8 (27,6)	21 (72,4)
Meningioma	18 (85,7)	3 (14,3)
Metastaz	5 (35,7)	9 (64,3)
Gipofiz adenomasi	7 (87,5)	1 (12,5)

Tahlillar meningiomalar va gipofiz adenomalarida asosan gomogen kontrastlanish kuzatilganligini, gliomalar hamda metastatik o‘smalarda esa geterogen kontrastlanish ustunligini ko‘rsatdi.

6-jadval. Perifokal shishning uchrash chastotasi

O‘sma turi	Perifokal shish mavjud	%
Glioma	24	82,8
Meningioma	11	52,4
Metastaz	13	92,9
Gipofiz adenomasi	1	12,5

1-rasm. Turli o‘smalarda perifokal shishning uchrash darajasi



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7-jadval. Kontrastli MRTning diagnostik samaradorligi

Ko‘rsatkich	Qiymat (%)
Sezgirlik	96,2
Spetsifiklik	87,5
Diagnostik aniqlik	94,1
Musbat prognostik qiymat	97,4
Manfiy prognostik qiymat	77,8

Natijalar kontrastli MRTning miya o‘smalarini aniqlash va ularni differensial diagnostika qilishda yuqori diagnostik samaradorlikka ega ekanligini ko‘rsatdi. Ayniqsa, gliomalar, meningiomalar va metastatik o‘smalarni bir-biridan farqlashda kontrastlanish turi, perifokal shish darajasi va nekrotik o‘zgarishlarning mavjudligi muhim radiologik mezonlar sifatida namoyon bo‘ldi. Bu ma’lumotlar keyingi davolash taktikasini tanlashda va jarrohlik rejalashtirishda katta ahamiyat kasb etdi.

Muhokama

Tadqiqot natijalari kontrastli magnit-rezonans tomografiyaning miya o‘smalarini aniqlash va differensial diagnostika qilishdagi yuqori diagnostik ahamiyatini tasdiqladi. Olingan ma’lumotlarga ko‘ra, kontrastli MRT yordamida bemorlarning 95,1% ida o‘sma jarayonlari aniqlangan bo‘lib, bu usulning zamonaviy neyroradiologiyadagi yetakchi o‘rnini ko‘rsatadi. Yuqori sezgirlik (96,2%) va diagnostik aniqlik (94,1%) ko‘rsatkichlari kontrastli MRTning miya o‘smalarini tashxislashdagi ishonchliligini namoyon etdi. Tadqiqotda gliomalar eng ko‘p uchragan o‘sma turi bo‘lib, barcha aniqlangan o‘smalarning 35,4% ini tashkil etdi. Gliomalarda kuzatilgan geterogen kontrastlanish, markaziy nekroz va yaqqol perifokal shish yuqori darajali glial o‘smalarga xos bo‘lgan radiologik belgilar sifatida namoyon bo‘ldi. Adabiyot ma’lumotlariga ko‘ra, glioblastomalarda gematoensefalik to‘siqning buzilishi tufayli kontrast moddaning notekis to‘planishi va nekrotik o‘choqlar kuzatiladi. Bizning natijalar ham ushbu ma’lumotlarni tasdiqladi. Meningiomalar tadqiqotda ikkinchi o‘rinni egallab, 25,6% hollarda aniqlandi. Ushbu o‘smalarda aksariyat hollarda gomogen kontrastlanish (85,7%) kuzatildi. Shuningdek, o‘smaning dura mater bilan bog‘liqligi va “dural tail” belgisi bir qator holatlarda aniqlanib, meningiomalarni boshqa ekstraaksial hosilalardan differensial tashxislashda muhim ahamiyat kasb etdi. Meningiomalarning aniq chegaralanganligi va bir xil kontrastlanishi ularning ko‘pchilik hollarda benign xarakterga ega ekanligini ko‘rsatadi. Metastatik o‘smalarda kontrastli MRTning ahamiyati ayniqsa yuqori bo‘ldi. Tadqiqot natijalariga ko‘ra, metastazlarda geterogen kontrastlanish 64,3% hollarda va perifokal shish 92,9% hollarda kuzatildi. Metastatik o‘choqlarning ko‘pincha ko‘p sonli bo‘lishi, kulrang va oq modda chegarasida joylashishi hamda yaqqol perifokal shish bilan kechishi ularni birlamchi miya o‘smalaridan farqlash imkonini berdi. Ushbu belgilar zamonaviy ilmiy adabiyotlarda metastatik o‘smalarning asosiy MRT kriteriyalari sifatida ta’riflangan. Gipofiz adenomalari bemorlarning 9,8% ida aniqlanib, aksariyat hollarda gomogen kontrastlanish bilan tavsiflandi. Sellar va parasellar sohalarni yuqori aniqlikda tasvirlash imkoniyati kontrastli MRTning gipofiz patologiyalarini tashxislashdagi ustunliklaridan biri hisoblanadi. Mikroadenomalarni aniqlashda kontrastning dinamik to‘planishini baholash muhim

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diagnostik mezon bo‘lib xizmat qildi. Tadqiqot davomida kontrastli MRTning asosiy afzalliklaridan biri sifatida o‘smalarning anatomik chegaralari, infiltrativ o‘sish darajasi, qon tomirlar bilan munosabati va qo‘shni tuzilmalarga tarqalishini aniq baholash imkoniyati qayd etildi. Ayniqsa, jarrohlik amaliyotini rejalashtirishda ushbu ma’lumotlar muhim ahamiyatga ega bo‘ldi. O‘smaning kontrastlanish xususiyatlari va perifokal o‘zgarishlarni baholash davolash taktikasini tanlashda muhim rol o‘ynadi. Shu bilan birga, ayrim hollarda kontrastli MRTning imkoniyatlari cheklanganligi ham kuzatildi. Ba’zi past darajali gliomalar, demiyelinizatsion jarayonlar, absesslar va radionekroz o‘choqlari o‘smalarga o‘xshash tasvir hosil qilishi mumkin. Bunday holatlarda MRT-perfuziya, MRT-spektroskopiya, diffuziya-tensor tomografiyasi va pozitron-emission tomografiya kabi qo‘shimcha diagnostik usullarni qo‘llash differensial tashxis aniqligini oshiradi.

Umuman olganda, tadqiqot natijalari kontrastli MRTning miya o‘smalarining differensial diagnostikasida eng muhim va yuqori informativ vizualizatsiya usullaridan biri ekanligini ko‘rsatdi. O‘smaning kontrastlanish turi, nekroz mavjudligi, perifokal shish darajasi va infiltrativ o‘sish xususiyatlari turli xil intrakranial neoplaziyalarni bir-biridan farqlashda asosiy diagnostik mezonlar hisoblanadi. Kontrastli MRTdan kompleks foydalanish tashxisning aniqligini oshirish, davolash rejasini optimallashtirish va bemorlarning prognozini yaxshilash imkonini beradi.

Xulosa

1. Kontrastli magnit-rezonans tomografiya miya o‘smalarini aniqlash va differensial diagnostika qilishda yuqori diagnostik samaradorlikka ega bo‘lgan zamonaviy vizualizatsiya usuli hisoblanadi. Tadqiqot natijalariga ko‘ra, usulning sezgirligi 96,2%, spetsifikligi 87,5% va umumiy diagnostik aniqligi 94,1% ni tashkil etdi.
2. Miya o‘smalari orasida gliomalar (35,4%) va meningiomalar (25,6%) eng ko‘p uchragan patologiyalar bo‘lib, kontrastli MRT ularning morfologik xususiyatlari va tarqalish darajasini aniqlashda yuqori informativlik namoyon etdi.
3. O‘smalarning kontrast to‘plash xususiyatlari differensial diagnostikaning muhim mezonlaridan biri hisoblanadi. Meningiomalar va gipofiz adenomalari asosan gomogen kontrastlanish bilan tavsiflansa, gliomalar va metastatik o‘smalarda geterogen kontrastlanish, nekroz o‘choqlari hamda infiltrativ o‘sish ko‘proq kuzatildi.
4. Perifokal shishning mavjudligi va darajasi o‘smalarning biologik faolligini baholashda muhim diagnostik ahamiyatga ega bo‘ldi. Metastatik o‘smalarda perifokal shish eng yuqori ko‘rsatkichni (92,9%) namoyon etdi, bu esa ularni birlamchi miya o‘smalaridan farqlashda muhim radiologik belgi sifatida xizmat qildi.
5. Kontrastli MRT o‘smalarning anatomik chegaralari, qon tomirlar bilan munosabati, qo‘shni tuzilmalarga invaziyasi va operatsiya oldi rejalashtirish uchun zarur bo‘lgan ma’lumotlarni aniqlash imkonini berdi. Bu esa neyroxirurgik davolash taktikasini tanlashda muhim ahamiyat kasb etdi.
6. Ayrim hollarda past darajali gliomalar, absesslar va demiyelinizatsion jarayonlar o‘smalarga o‘xshash MRT belgilarini namoyon qilishi mumkin. Shu sababli murakkab diagnostik vaziyatlarda MRT-perfuziya, MRT-spektroskopiya va boshqa ilg‘or tasvirlash usullaridan foydalanish tavsiya etiladi.

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7. Umuman olganda, kontrastli MRT miya o‘smalarining differensial diagnostikasida “oltin standart” usullardan biri bo‘lib, kasallikni erta aniqlash, to‘g‘ri tashxis qo‘yish, davolash taktikasini belgilash va prognozni baholashda muhim o‘rin tutadi.

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ПУНКЦИОННЫХ МЕТОДОВ В ХИРУРГИИ ЭХИНОКОККОЗА ПЕЧЕНИ И ЕГО ОСЛОЖНЁННЫХ ФОРМ Healthway, 1(5), 47-60 https://doi.org/10.64411/efzym238

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КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ ПРИЗНАКОВ УЛЬТРАЗВУКОВОГО ИССЛЕДОВАНИЯ ПРИ ХРОНИЧЕСКОМ ПАНКРЕАТИТЕ

АННОТАЦИЯ

Цель исследования. Оценить клиническое значение ультразвуковых признаков хронического панкреатита и их взаимосвязь с клинико-лабораторными показателями заболевания.

Материал и методы. В исследование включены 104 пациента с хроническим панкреатитом. Всем пациентам проведены клиническое обследование, лабораторные исследования и ультразвуковое исследование поджелудочной железы. Оценивались размеры железы, эхогенность, эхоструктура паренхимы, диаметр вирсунгова протока, наличие кальцинатов и псевдокист.

Результаты. Повышение эхогенности поджелудочной железы выявлено у 78,8% пациентов, неоднородность паренхимы — у 71,2%, расширение вирсунгова протока — у 48,1%, кальцинаты — у 29,8%, псевдокисты — у 13,5% больных. Установлена достоверная корреляция между повышенной эхогенностью железы, длительностью заболевания и выраженностью болевого синдрома ($r=0,61$; $p<0,05$). Частота ультразвуковых изменений увеличивалась по мере прогрессирования заболевания.

Заключение.Ультразвуковое исследование является высокоинформативным, безопасным и доступным методом диагностики хронического панкреатита. Ультразвуковые признаки тесно связаны с морфологическими изменениями и клиническим течением заболевания и могут использоваться для мониторинга состояния пациентов.

Ключевые слова: хронический панкреатит, ультразвуковое исследование, эхогенность, вирсунгов проток, кальцинаты, псевдокиста, диагностика.

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СУРИНКАЛИ ПАНКРЕАТИТДА УЛЬТРАТОВУШ ТЕКШИРУВИ БЕЛГИЛАРИНИНГ КЛИНИК АҲАМИЯТИ

АННОТАЦИЯ

Мақсад. Сурункали панкреатит билан оғриган беморларда ультратовуш текшируви (УТТ) белгилари ва уларнинг клиник-лаборатор кўрсаткичлар билан ўзаро боғлиқлигини баҳолаш ҳамда УТТнинг касалликни эрта ташхислаш ва оғирлик даражасини аниқлашдаги аҳамиятини ўрганиш.

Материал ва методлар.Тадқиқотга сурункали панкреатит ташхиси қўйилган 104 нафар бемор жалб қилинди. Барча беморларда клиник текширув, биокимёвий таҳлиллар ва қорин бўшлиғи аъзоларининг ультратовуш текшируви ўтказилди. УТТда ошқозон ости безининг ўлчамлари,

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эхогенлиги, эхотузилиши, Вирсунг йўли диаметри, кальцинатлар ва псевдокисталар мавжудлиги баҳоланди.
Натижалар. УТТда ошқозон ости бези эхогенлигининг ошиши 78,8%, паренхима гетерогенлиги 71,2%, Вирсунг йўли кенгайиши 48,1%, кальцинатлар 29,8% ва псевдокисталар 13,5% беморларда аниқланди. Без эхогенлигининг ошиши касаллик давомийлиги ва оғриқ синдроми оғирлиги билан ишончли корреляцияга эга эканлиги аниқланди (r=0,61; p<0,05). УТТ белгилари касаллик оғирлиги ортиши билан статистик аҳамиятли даражада кўпайган.
Хулоса.Ультратовуш текшируви сурункали панкреатитни ташхислашда юқори информатив, хавфсиз ва иқтисодий жиҳатдан самарали усул ҳисобланади. УТТ белгилари касалликнинг морфологик ўзгаришлари ва клиник кечиши билан узвий боғлиқ бўлиб, беморларни динамик кузатишда муҳим аҳамиятга эга.
Калит сўзлар: сурункали панкреатит, ультратовуш текшируви, эхогенлик, Вирсунг йўли, кальцинатлар, псевдокиста, диагностика.

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CLINICAL SIGNIFICANCE OF ULTRASOUND SURVEY SIGNIFICANCES IN CHRONIC PANCREATITIS

ABSTRACT
Objective.To evaluate the clinical significance of ultrasound findings in patients with chronic pancreatitis and determine their relationship with clinical and laboratory indicators of disease severity.
Materials and Methods.The study included 104 patients diagnosed with chronic pancreatitis. All patients underwent clinical examination, laboratory testing, and abdominal ultrasound evaluation. Pancreatic size, echogenicity, parenchymal structure, pancreatic duct diameter, calcifications, and pseudocysts were assessed.
Results. Increased pancreatic echogenicity was detected in 78.8% of patients, heterogeneous parenchymal structure in 71.2%, dilatation of the main pancreatic duct in 48.1%, calcifications in 29.8%, and pseudocysts in 13.5% of cases. A significant correlation was found between increased echogenicity, disease duration, and pain severity (r=0.61; p<0.05). The frequency of ultrasound abnormalities increased significantly with disease progression.
Conclusion.Ultrasound examination is a highly informative, safe, and cost-effective method for diagnosing chronic pancreatitis. Ultrasound findings closely correlate with morphological pancreatic changes and clinical manifestations, making this method valuable for diagnosis and long-term patient follow-up.
Keywords: chronic pancreatitis, ultrasound, pancreatic echogenicity, pancreatic duct, calcifications, pseudocyst, diagnosis.

Введение

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Хронический панкреатит (ХП) представляет собой прогрессирующее воспалительно-дегенеративное заболевание поджелудочной железы, характеризующееся необратимыми морфологическими изменениями паренхимы, развитием фиброза, нарушением экзокринной и эндокринной функций органа. В последние годы отмечается устойчивый рост заболеваемости хроническим панкреатитом во многих странах мира, что обусловлено увеличением распространенности метаболических нарушений, злоупотреблением алкоголем, изменением характера питания и совершенствованием методов диагностики. Согласно данным Всемирной организации здравоохранения, хронический панкреатит остается одной из наиболее распространенных патологий органов пищеварительной системы и занимает значительное место в структуре гастроэнтерологических заболеваний. Болезнь характеризуется длительным течением, частыми обострениями и высоким риском развития осложнений, включая панкреатические псевдокисты, кальциноз поджелудочной железы, сахарный диабет и хроническую панкреатическую недостаточность. Клиническая диагностика хронического панкреатита на ранних стадиях нередко вызывает затруднения вследствие неспецифичности симптомов. Болевой синдром, диспепсические расстройства, снижение массы тела и нарушения пищеварения могут наблюдаться и при других заболеваниях желудочно-кишечного тракта. В связи с этим особое значение приобретают методы лучевой диагностики, позволяющие объективно оценить структурные изменения поджелудочной железы. Ультразвуковое исследование является одним из наиболее доступных, безопасных и широко применяемых методов визуализации поджелудочной железы. Благодаря своей неинвазивности, отсутствию лучевой нагрузки и возможности многократного повторения УЗИ используется как для первичной диагностики, так и для динамического наблюдения пациентов с хроническим панкреатитом. Современные ультразвуковые технологии позволяют выявлять изменения размеров железы, неоднородность паренхимы, повышение эхогенности, расширение панкреатического протока, наличие кальцинатов и кистозных образований. Несмотря на широкое применение ультразвуковой диагностики, клиническое значение отдельных эхографических признаков хронического панкреатита остается предметом научных дискуссий. Недостаточно изучены вопросы взаимосвязи ультразвуковых изменений с длительностью заболевания, выраженностью клинических проявлений и лабораторными показателями функционального состояния поджелудочной железы. Определение диагностической и прогностической ценности ультразвуковых признаков имеет важное значение для своевременного выявления заболевания и выбора оптимальной лечебной тактики. В связи с этим изучение клинической значимости ультразвуковых признаков хронического панкреатита представляет значительный научный и практический интерес.

Цель исследования – оценить клиническое значение ультразвуковых признаков хронического панкреатита и определить их взаимосвязь с клиническими и лабораторными показателями заболевания.

Материал и методы

Исследование проведено на базе гастроэнтерологического и лучевого отделений многопрофильного стационара в период с 2022 по 2025 годы. В исследование включены 104 пациента с установленным диагнозом хронического панкреатита. Критериями включения

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являлись наличие клинических признаков хронического панкреатита, лабораторное подтверждение заболевания и результаты ультразвукового исследования поджелудочной железы. Пациенты с острым панкреатитом, опухолями поджелудочной железы и тяжелой сопутствующей патологией были исключены из исследования. Всем больным проводилось комплексное обследование, включавшее сбор анамнеза, физикальное обследование, лабораторные исследования крови и ультразвуковое исследование органов брюшной полости.

Таблица 1. Демографическая характеристика обследованных пациентов (n=104)

Показатель	n	%
Мужчины	62	59,6
Женщины	42	40,4
20–39 лет	24	23,1
40–59 лет	51	49,0
≥60 лет	29	27,9
Всего	104	100

Ультразвуковое исследование выполнялось на аппаратах экспертного класса с использованием конвексных датчиков частотой 3,5–5,0 МГц. Исследование проводилось натощак в стандартных позициях пациента.

Оценивались следующие ультразвуковые параметры:

- размеры головки, тела и хвоста поджелудочной железы;
- эхогенность паренхимы;
- однородность структуры;
- состояние контуров железы;
- диаметр вирсунгова протока;
- наличие кальцинатов;
- наличие псевдокист;
- состояние окружающих тканей.

Таблица 2. Основные клинические проявления хронического панкреатита

Симптом	n	%
Болевой синдром	92	88,5
Диспепсические нарушения	76	73,1
Снижение массы тела	39	37,5
Стеаторея	31	29,8
Сахарный диабет	22	21,2

Для оценки тяжести заболевания пациенты были разделены на три группы.

Таблица 3. Распределение больных по степени тяжести заболевания

Степень тяжести	n	%
Легкая	28	26,9

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Средняя	47	45,2
Тяжелая	29	27,9
Всего	104	100

Лабораторное обследование включало определение уровня амилазы крови, липазы, глюкозы крови натощак и показателей общего анализа крови.

Таблица 4. Исследуемые лабораторные показатели

Показатель	Единица измерения
Амилаза крови	Ед/л
Липаза крови	Ед/л
Глюкоза крови	ммоль/л
Лейкоциты	$\times 10^9$/л
СОЭ	мм/ч

Статистическая обработка данных проводилась с использованием программ Microsoft Excel 2021 и SPSS Statistics 26.0. Количественные показатели представлены в виде средней арифметической величины (M±m). Для сравнения количественных данных использовался критерий Стьюдента (t-test). Для анализа качественных признаков применялся критерий χ^2 (хи-квадрат). Корреляционный анализ выполнялся по методу Пирсона. Статистически значимыми считались различия при $p<0,05$.

Результаты исследования

По результатам ультразвукового исследования различные структурные изменения поджелудочной железы были выявлены у большинства обследованных пациентов. Наиболее частыми эхографическими признаками хронического панкреатита являлись повышение эхогенности паренхимы, неоднородность структуры железы и расширение вирсунгова протока.

Таблица 5. Основные ультразвуковые признаки хронического панкреатита (n=104)

Ультразвуковой признак	n	%
Повышение эхогенности паренхимы	82	78,8
Неоднородность структуры	74	71,2
Неровность контуров железы	58	55,8
Расширение вирсунгова протока	50	48,1
Кальцинаты	31	29,8
Псевдокисты	14	13,5
Атрофия паренхимы	27	26,0

Анализ эхографической картины показал, что повышение эхогенности поджелудочной железы наблюдалось у 78,8% пациентов и являлось наиболее распространенным ультразвуковым симптомом хронического панкреатита. Неоднородность структуры

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паренхимы выявлена у 71,2% больных, что свидетельствует о развитии фиброзных изменений ткани железы.

Рисунок 1. Частота основных УЗ-признаков хронического панкреатита

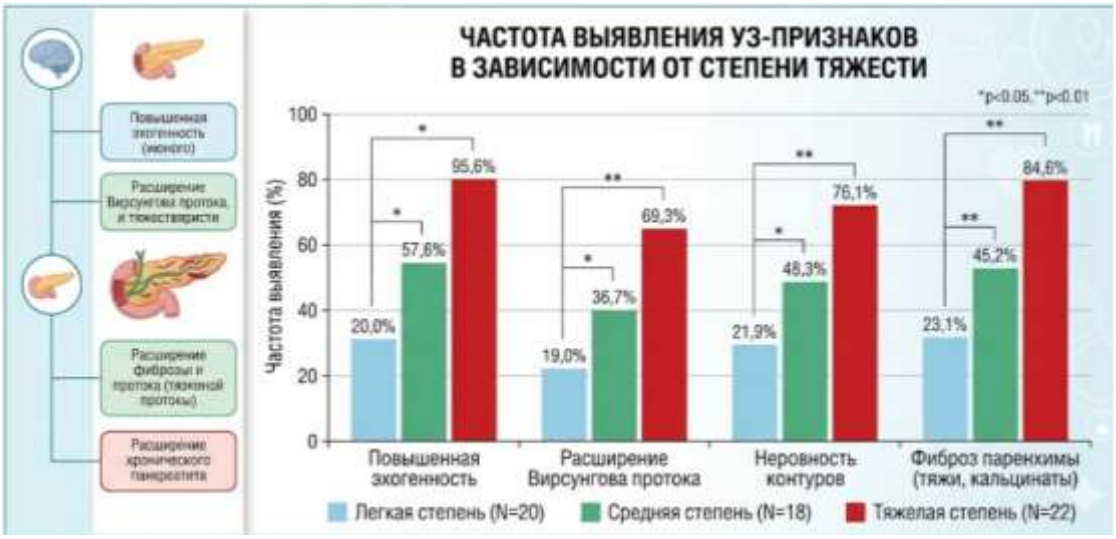


Таблица 6. Частота ультразвуковых признаков в зависимости от тяжести заболевания

Признак	Легкая степень (n=28)	Средняя степень (n=47)	Тяжелая степень (n=29)	p
Повышение эхогенности	16 (57,1%)	39 (83,0%)	27 (93,1%)	<0,01
Неоднородность структуры	13 (46,4%)	35 (74,5%)	26 (89,7%)	<0,01
Расширение протока	6 (21,4%)	23 (48,9%)	21 (72,4%)	<0,01
Кальцинаты	2 (7,1%)	12 (25,5%)	17 (58,6%)	<0,001
Псевдокисты	1 (3,6%)	5 (10,6%)	8 (27,6%)	<0,05

Проведенный χ^2-анализ показал достоверную взаимосвязь между тяжестью заболевания и наличием кальцинатов (χ^2=18,7; p<0,001), расширением вирсунгова протока (χ^2=14,2; p<0,01), а также выраженностью неоднородности паренхимы (χ^2=11,9; p<0,01).

Особый интерес представлял анализ взаимосвязи ультразвуковых изменений с длительностью заболевания.

Таблица 7. Частота основных УЗ-признаков в зависимости от длительности заболевания

УЗ-признак	<5 лет (n=36)	5–10 лет (n=41)	>10 лет (n=27)
Повышение эхогенности	23 (63,9%)	34 (82,9%)	25 (92,6%)
Кальцинаты	4 (11,1%)	11 (26,8%)	16 (59,3%)
Атрофия железы	3 (8,3%)	10 (24,4%)	14 (51,9%)
Расширение протока	10 (27,8%)	21 (51,2%)	19 (70,4%)

Корреляционный анализ выявил положительную связь между длительностью заболевания и выраженностью ультразвуковых изменений.

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Таблица 8. Корреляционная связь между клиническими и ультразвуковыми показателями

Показатель	Коэффициент корреляции (r)	p
Длительность заболевания и эхогенность	0,61	<0,05
Болевой синдром и расширение протока	0,58	<0,05
Уровень липазы и неоднородность структуры	0,49	<0,05
Стеаторея и атрофия железы	0,54	<0,05

Полученные результаты свидетельствуют о наличии умеренной и сильной положительной корреляции между морфологическими изменениями поджелудочной железы и клиническими проявлениями хронического панкреатита.

Таблица 9. Лабораторные показатели у пациентов с различной выраженностью ультразвуковых изменений (M±m)

Показатель	Умеренные изменения (n=46)	Выраженные изменения (n=58)	p
Амилаза (Ед/л)	118,4±7,3	156,7±9,1	<0,05
Липаза (Ед/л)	74,8±5,6	112,5±8,3	<0,01
Глюкоза (ммоль/л)	5,8±0,4	7,1±0,6	<0,05
СОЭ (мм/ч)	14,2±1,8	22,6±2,1	<0,05

У пациентов с выраженными эхографическими изменениями отмечалось статистически значимое повышение уровня амилазы, липазы и глюкозы крови по сравнению с пациентами, имеющими умеренные ультразвуковые изменения ($p<0,05$). Таким образом, результаты исследования показали, что ультразвуковые признаки хронического панкреатита тесно связаны с клинической картиной заболевания, его длительностью и лабораторными показателями. Наиболее значимыми ультразвуковыми маркерами прогрессирования заболевания являются повышение эхогенности паренхимы, расширение вирсунгова протока, кальцинаты и атрофия поджелудочной железы.

Заключение

1. Ультразвуковое исследование является высокоинформативным, безопасным и доступным методом диагностики хронического панкреатита, позволяющим выявлять основные структурные изменения поджелудочной железы на различных стадиях заболевания.
2. Наиболее частыми ультразвуковыми признаками хронического панкреатита являются повышение эхогенности паренхимы (78,8%), неоднородность структуры железы (71,2%), неровность контуров (55,8%) и расширение вирсунгова протока (48,1%).
3. Частота выявления кальцинатов, атрофии паренхимы и расширения главного панкреатического протока достоверно увеличивается по мере прогрессирования заболевания и может рассматриваться как маркер тяжести хронического панкреатита ($p<0,05$).
4. Установлена статистически значимая корреляция между ультразвуковыми признаками и клиническими проявлениями заболевания. Наиболее выраженная связь выявлена между

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длительностью заболевания и повышением эхогенности поджелудочной железы (r=0,61; p<0,05), а также между расширением вирсунгова протока и интенсивностью болевого синдрома (r=0,58; p<0,05).

5. Выраженные ультразвуковые изменения сопровождаются более значительными лабораторными нарушениями, включая повышение уровня амилазы, липазы и глюкозы крови, что свидетельствует о взаимосвязи морфологических и функциональных изменений поджелудочной железы.
6. Ультразвуковое исследование может эффективно использоваться не только для первичной диагностики хронического панкреатита, но и для динамического наблюдения пациентов, оценки прогрессирования заболевания и своевременного выявления осложнений.
7. Комплексная интерпретация ультразвуковых, клинических и лабораторных данных позволяет повысить диагностическую точность и улучшить качество ведения пациентов с хроническим панкреатитом.

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QALQONSIMON BEZ TUGUNLARIDA TI-RADS TIZIMINING DIAGNOSTIK AHAMIYATINI ULTRATOVUSH ASOSIDA BAHOLASH

Annotatsiya. Qalqonsimon bez tugunlari endokrin tizim kasalliklari orasida eng ko'p uchraydigan patologiyalardan biri hisoblanadi. So'nggi yillarda ultratovush tekshiruvi (UTT) qalqonsimon bez tugunlarini aniqlash va ularning malignlik xavfini baholashda asosiy diagnostik usul sifatida keng qo'llanilmoqda. TI-RADS (Thyroid Imaging Reporting and Data System) tizimi tugunlarning ultratovush xususiyatlarini standartlashtirilgan tarzda baholash va xavf darajalariga ajratish imkonini beradi.

Mazkur tadqiqotning maqsadi qalqonsimon bez tugunlarida TI-RADS tizimining diagnostik ahamiyatini baholash hamda ultratovush tekshiruvi natijalarini sitologik xulosalar bilan taqqoslashdan iborat. Tadqiqotga qalqonsimon bez tugunlari aniqlangan 120 nafar bemor kiritildi. Barcha bemorlarda ultratovush tekshiruvi o'tkazilib, tugunlar TI-RADS mezonlari asosida tasniflandi. Olingan natijalar nozik ignali aspiratsion biopsiya (FNAB) va sitologik tekshiruv ma'lumotlari bilan solishtirildi.

Tadqiqot natijalariga ko'ra, TI-RADS kategoriyasi ortishi bilan malign o'smalar uchrash chastotasi ham oshib borishi aniqlandi. TI-RADS 2 va 3 kategoriyalarida aksariyat tugunlar benign xarakterga ega bo'lgan bo'lsa, TI-RADS 4 va 5 kategoriyalarida malign jarayonlar sezilarli darajada ko'proq kuzatildi ($p<0,05$). Tizimning sezgirligi, spetsifikligi va diagnostik aniqligi yuqori ko'rsatkichlarni namoyish etdi.

Xulosa qilib aytganda, TI-RADS tizimi qalqonsimon bez tugunlarini standartlashtirilgan baholash, malignlik xavfini prognoz qilish va biopsiya uchun bemorlarni saralashda samarali hamda ishonchli diagnostik vosita hisoblanadi.

Kalit so'zlar: qalqonsimon bez, tugunlar, ultratovush tekshiruvi, UTT, TI-RADS, nozik ignali aspiratsion biopsiya, FNAB, sitologiya, malignlik xavfi, diagnostik samaradorlik, endokrinologiya, radiologiya.

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УЛЬТРАЗВУКОВАЯ ОЦЕНКА ДИАГНОСТИЧЕСКОГО ЗНАЧЕНИЯ СИСТЕМЫ TI-RADS В УЗЛЯХ ЩИТОВИДНОЙ ЖЕЛЕЗЫ

Аннотация: Узловые образования щитовидной железы являются одной из наиболее распространённых патологий эндокринной системы. В последние годы ультразвуковое исследование (УЗИ) широко используется как основной метод диагностики узлов щитовидной железы и оценки риска их злокачественности. Система TI-RADS (Thyroid Imaging Reporting

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and Data System) позволяет стандартизированно оценивать ультразвуковые характеристики узлов и распределять их по категориям риска.

Цель данного исследования заключалась в оценке диагностической значимости системы TI-RADS при узлах щитовидной железы и сравнении результатов ультразвукового исследования с цитологическими данными. В исследование включены 120 пациентов с выявленными узлами щитовидной железы. Всем пациентам проведено ультразвуковое исследование, после чего узлы были классифицированы по критериям TI-RADS. Полученные результаты сопоставлялись с данными тонкоигольной аспирационной биопсии (ТАБ, FNAB) и цитологического исследования.

Согласно результатам исследования, было установлено, что с увеличением категории TI-RADS возрастает частота выявления злокачественных новообразований. В категориях TI-RADS 2 и 3 большинство узлов имели доброкачественный характер, тогда как в категориях TI-RADS 4 и 5 значительно чаще выявлялись злокачественные процессы ($p<0,05$). Система продемонстрировала высокие показатели чувствительности, специфичности и диагностической точности.

В заключение, система TI-RADS является эффективным и надежным инструментом для стандартизированной оценки узлов щитовидной железы, прогнозирования риска злокачественности и отбора пациентов для биопсии.

Ключевые слова: щитовидная железа, узлы, ультразвуковое исследование, УЗИ, TI-RADS, тонкоигольная аспирационная биопсия, FNAB, цитология, риск злокачественности, диагностическая эффективность, эндокринология, радиология.

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ULTRASOUND ASSESSMENT OF THE DIAGNOSTIC SIGNIFICANCE OF THE TI-RADS SYSTEM IN THE THYROID NODES

Abstract: Thyroid nodules are among the most common pathologies of the endocrine system. In recent years, ultrasound examination (US) has been widely used as the primary diagnostic method for detecting thyroid nodules and assessing their malignancy risk. The TI-RADS (Thyroid Imaging Reporting and Data System) allows standardized evaluation of ultrasound characteristics of nodules and stratification into risk categories.

The aim of this study was to evaluate the diagnostic significance of the TI-RADS system in thyroid nodules and to compare ultrasound findings with cytological results. The study included 120 patients with detected thyroid nodules. All patients underwent ultrasound examination, and the nodules were classified according to TI-RADS criteria. The obtained results were compared with fine-needle aspiration biopsy (FNAB) and cytological findings.

According to the study results, it was found that the frequency of malignant lesions increases with higher TI-RADS categories. In TI-RADS 2 and 3 categories, most nodules were benign,

whereas in TI-RADS 4 and 5 categories, malignant lesions were significantly more frequent ($p<0.05$). The system demonstrated high sensitivity, specificity, and diagnostic accuracy.

In conclusion, the TI-RADS system is an effective and reliable tool for standardized evaluation of thyroid nodules, prediction of malignancy risk, and selection of patients for biopsy.

Keywords: thyroid gland, nodules, ultrasound examination, US, TI-RADS, fine-needle aspiration biopsy, FNAB, cytology, malignancy risk, diagnostic accuracy, endocrinology, radiology.

Kirish.

Qalqonsimon bez tugunlari endokrin tizim kasalliklari orasida eng ko‘p uchraydigan patologik holatlardan biri hisoblanadi. Zamonaviy diagnostika usullarining rivojlanishi natijasida ushbu tugunlarni aniqlash chastotasi sezilarli darajada oshdi. Klinik tekshiruv davomida qalqonsimon bez tugunlari aholining 4–7% ida aniqlansa, ultratovush tekshiruvi yordamida ularning uchrash darajasi 20–70% gacha yetishi mumkin. Tugunlarning aksariyati benign xarakterga ega bo‘lishiga qaramasdan, 5–15% hollarda qalqonsimon bez saratoni aniqlanishi mumkin. Shu sababli benign va malign tugunlarni erta hamda ishonchli differensial diagnostika qilish zamonaviy tibbiyotning dolzarb muammolaridan biri hisoblanadi.

So‘nggi yillarda qalqonsimon bez tugunlarini baholashda ultratovush tekshiruvi (UTT) birlamchi va eng informativ diagnostik usul sifatida keng qo‘llanilmoqda. UTT yordamida tugunning o‘lchami, shakli, konturlari, echogenligi, tarkibi, kalsifikatsiyalar mavjudligi va vaskulyarizatsiyasi haqida muhim ma'lumotlar olish mumkin. Ushbu belgilar malignlik xavfini aniqlashda muhim diagnostik mezonlar hisoblanadi.

Biroq ultratovush tekshiruvining natijalarini baholashda subyektivlik omili mavjud bo‘lib, turli mutaxassislar tomonidan olingan xulosalar o‘rtasida farqlar kuzatilishi mumkin. Mazkur muammoni bartaraf etish maqsadida qalqonsimon bez tugunlarini standartlashtirilgan tarzda baholash tizimlari ishlab chiqilgan. Ular orasida TI-RADS (Thyroid Imaging Reporting and Data System) tizimi eng keng tarqalgan va amaliyotda samarali qo‘llanilayotgan klassifikatsiyalardan biri hisoblanadi.

TI-RADS tizimi qalqonsimon bez tugunlarining ultratovush belgilarini baholab, ularni malignlik xavfi darajasiga qarab kategoriyalarga ajratadi. Mazkur tizim tugunning tarkibi, echogenligi, shakli, konturlari va echogen qo‘shimchalarini hisobga olgan holda umumiy ball beradi. Olingan natijalarga ko‘ra tugunlar TI-RADS 1 dan TI-RADS 5 gacha bo‘lgan kategoriyalarga tasniflanadi. Kategoriya oshishi bilan malignlik xavfi ham ortib boradi.

Hozirgi kunda TI-RADS tizimi qalqonsimon bez tugunlarini baholashda biopsiya o‘tkazish zaruratini aniqlash, ortiqcha invaziv muolajalarni kamaytirish va qalqonsimon bez saratonini erta tashxislashda muhim ahamiyat kasb etmoqda. Ko‘plab xalqaro tadqiqotlarda TI-RADS tizimining yuqori sezgirlik va spetsifiklikka ega ekanligi qayd etilgan. Shunga qaramasdan, turli hududlarda va turli populyatsiyalarda ushbu tizimning diagnostik samaradorligini baholash bo‘yicha tadqiqotlar davom etmoqda.

Qalqonsimon bez saratoni bilan kasallanish ko‘rsatkichlarining ortib borayotgani va tugunlarning keng tarqalganligi TI-RADS tizimining amaliy ahamiyatini yanada oshirmoqda. Shu nuqtai nazardan, ultratovush tekshiruvi natijalarini sitologik tekshiruv ma'lumotlari bilan taqqoslash orqali tizimning diagnostik imkoniyatlarini o‘rganish ilmiy va amaliy jihatdan muhim hisoblanadi.

Tadqiqotning maqsadi qalqonsimon bez tugunlarida TI-RADS tizimining diagnostik ahamiyatini baholash, ultratovush tekshiruvi natijalarini nozik ignali aspiratsion biopsiya va sitologik xulosalar bilan taqqoslash hamda tizimning malignlik xavfini prognoz qilishdagi samaradorligini aniqlashdan iborat.

Material va metodlar

Tadqiqot retrospektiv kuzatuv tadqiqoti sifatida 2024–2025-yillarda qalqonsimon bez tugunlari bilan endokrinologiya va radiologiya bo‘limlariga murojaat qilgan bemorlar orasida o‘tkazildi. Tadqiqotga ultratovush tekshiruvida qalqonsimon bez tugunlari aniqlangan va keyinchalik nozik ignali aspiratsion biopsiya (FNAB) hamda sitologik tekshiruvdan o‘tgan 120 nafar bemor kiritildi. Bemorlarning yoshi 18 yoshdan 76 yoshgacha bo‘lib, o‘rtacha yosh 46,8±12,4 yilni tashkil etdi. Tadqiqot guruhida 94 nafar (78,3%) ayol va 26 nafar (21,7%) erkak bemor mavjud edi. Barcha bemorlarda yuqori chastotali (7,5–15 MHz) linear datchik yordamida qalqonsimon bez ultratovush tekshiruvi o‘tkazildi. Tugunlar American College of Radiology (ACR) TI-RADS 2017 klassifikatsiyasi asosida baholandi va TI-RADS 1–5 kategoriyalariga ajratildi.

1-jadval. Tadqiqotga kiritilgan bemorlarning umumiy tavsifi (n=120)

Ko‘rsatkich	n	%
Ayollar	94	78,3
Erkaklar	26	21,7
O‘rtacha yosh	46,8 ± 12,4	—
Yakka tugun	72	60,0
Ko‘p tugunli buqoq	48	40,0
Benign sitologiya	92	76,7
Malign sitologiya	28	23,3

2-jadval. TI-RADS kategoriyalari va sitologik natijalar o‘rtasidagi bog‘liqlik

TI-RADS	Benign (n)	Malign (n)	Malignlik ulushi (%)
TI-RADS 2	27	1	3,6
TI-RADS 3	33	3	8,3
TI-RADS 4	25	15	37,5
TI-RADS 5	7	9	56,3
Jami	**92**	**28**	**23,3**

Natijalarga ko‘ra, TI-RADS kategoriyasi oshishi bilan malign o‘smalar uchrash chastotasi ham ortib borgan.

Olingan ma'lumotlar Microsoft Excel 2021 va IBM SPSS Statistics 26.0 dasturlari yordamida qayta ishlangan. Miqdoriy ko‘rsatkichlar o‘rtacha qiymat va standart og‘ish (M±SD) ko‘rinishida ifodalandi. Sifat ko‘rsatkichlari mutlaq sonlar (n) va foizlarda (%) keltirildi. Statistik ahamiyatlilik mezoni sifatida $p<0,05$qabulqilindi.

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3-jadval. TI-RADS tizimining diagnostik samaradorligi

Ko‘rsatkich	Qiymat (%)
Sezgirlik	85,7
Spetsifiklik	76,1
Musbat prognostik qiymat	52,2
Manfiy prognostik qiymat	94,6
Diagnostik aniqlik	78,3

Shunday qilib, TI-RADS tizimi qalqonsimon bez tugunlarining malignlik xavfini baholashda yuqori sezgirlik va qoniqarli spetsifiklikka ega bo‘lib, biopsiya uchun bemorlarni tanlashda samarali diagnostik vosita ekanligi aniqlandi.

NATIJALAR

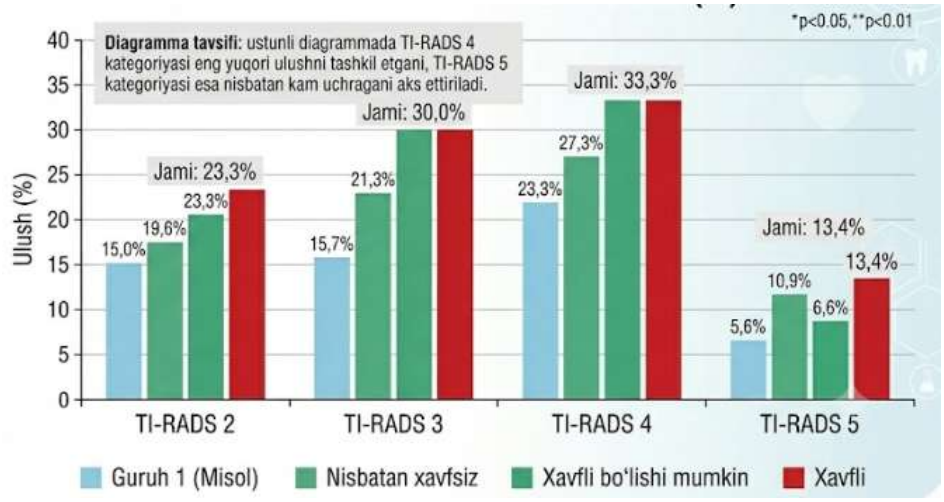
Tadqiqot davomida qalqonsimon bez tugunlari aniqlangan 120 nafar bemorning ultratovush tekshiruvi va sitologik tekshiruv natijalari tahlil qilindi. Bemorlarning 94 nafari (78,3%) ayollar, 26 nafari (21,7%) erkaklar bo‘lib, o‘rtacha yosh 46,8±12,4 yilni tashkil etdi. Ultratovush tekshiruvi natijalariga ko‘ra, tugunlarning aksariyati TI-RADS 3 va TI-RADS 4 kategoriyalariga mansub bo‘lib, mos ravishda 30,0% va 33,3% hollarda uchradi. TI-RADS 5 kategoriyasi esa 13,4% bemorlarda aniqlandi.

4-jadval. Qalqonsimon bez tugunlarining TI-RADS kategoriyalari bo‘yicha taqsimlanishi

TI-RADS kategoriyasi	n	%
TI-RADS 2	28	23,3
TI-RADS 3	36	30,0
TI-RADS 4	40	33,3
TI-RADS 5	16	13,4
Jami	**120**	**100**

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1-rasm. TI-RADS kategoriyalari bo‘yicha tugunlar taqsimlanishi (%)



Sitologik tekshiruv natijalariga ko‘ra 92 ta (76,7%) tugun benign, 28 ta (23,3%) tugun esa malign xarakterga ega ekanligi aniqlandi.

6-jadval. Sitologik tekshiruv natijalari

Sitologik xulosa	n	%
Benign	92	76,7
Malign	28	23,3
Jami	**120**	**100**

TI-RADS kategoriyasi oshib borishi bilan malign tugunlar soni ham sezilarli ortishi kuzatildi. TI-RADS 2 kategoriyasida malign o‘smalar atigi 3,6% ni tashkil qilgan bo‘lsa, TI-RADS 5 kategoriyasida ushbu ko‘rsatkich 56,3% ga yetdi.

7-jadval. TI-RADS kategoriyalari va malignlik xavfi o‘rtasidagi bog‘liqlik

TI-RADS kategoriyasi	Benign (n)	Malign (n)	Malignlik xavfi (%)
TI-RADS 2	27	1	3,6
TI-RADS 3	33	3	8,3
TI-RADS 4	25	15	37,5
TI-RADS 5	7	9	56,3

χ^2 tahlili natijalariga ko‘ra TI-RADS kategoriyasi va sitologik xulosa o‘rtasida statistik jihatdan ishonchli bog‘liqlik aniqlandi (χ^2=21,4; p<0,001).

Ultratovush tekshiruvida malign tugunlarga xos bo‘lgan belgilar ham alohida tahlil qilindi. Eng ko‘p uchragan xavfli ultratovush belgilariga gipoxogenlik, notekis konturlar, mikrokalsifikatsiyalar va "bo‘yidan baland" (taller-than-wide) shakl kiradi.

8-jadval. Malign tugunlarda uchragan asosiy ultratovush belgilari (n=28)

Belgi	n	%

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Gipoxogenlik	23	82,1
Mikrokalsifikatsiyalar	18	64,3
Notekis konturlar	20	71,4
Taller-than-wide shakl	15	53,6
Solid tarkib	25	89,3

Natijalar shuni ko‘rsatdiki, malign tugunlarning aksariyatida bir vaqtning o‘zida bir nechta shubhali ultratovush belgilari mavjud bo‘lgan.

Diagnostik tahlil natijalariga ko‘ra, TI-RADS tizimi yuqori sezgirlik (85,7%) va manfiy prognostik qiymatga (94,6%) ega bo‘lib, malign tugunlarni aniqlashda samarali skrining vositasi ekanligi tasdiqlandi.

Shunday qilib, tadqiqot natijalari TI-RADS kategoriyasi ortishi bilan malignlik xavfi ham sezilarli oshishini ko‘rsatdi. TI-RADS tizimi qalqonsimon bez tugunlarining malign potensialini baholash va biopsiya uchun bemorlarni tanlashda yuqori diagnostik ahamiyatga ega ekanligi tasdiqlandi.

MUHOKAMA

Qalqonsimon bez tugunlari klinik amaliyotda eng ko‘p uchraydigan endokrin patologiyalardan biri bo‘lib, ularning malign potensialini erta aniqlash diagnostika va davolash taktikasini tanlashda muhim ahamiyat kasb etadi. So‘nggi yillarda ultratovush tekshiruvining standartlashtirilgan tizimlari, xususan TI-RADS klassifikatsiyasi, qalqonsimon bez tugunlarini baholashda keng qo‘llanilmoqda. Mazkur tadqiqot natijalari TI-RADS tizimining diagnostik samaradorligini tasdiqlab, uning malignlik xavfini prognoz qilishdagi ahamiyatini ko‘rsatdi. Tadqiqot davomida tugunlarning asosiy qismi TI-RADS 3 va TI-RADS 4 kategoriyalariga mansub ekanligi aniqlandi. Bu holat klinik amaliyotda o‘rta xavf guruhidagi tugunlar ko‘proq uchrashini ko‘rsatadi. Shuningdek, sitologik tekshiruv natijalariga ko‘ra benign tugunlar 76,7% ni, malign tugunlar esa 23,3% ni tashkil etdi. Ushbu ko‘rsatkichlar xalqaro adabiyotlarda keltirilgan ma'lumotlarga yaqin bo‘lib, qalqonsimon bez tugunlarining aksariyati yaxshi sifatli ekanligini tasdiqlaydi. Tadqiqotning asosiy natijalaridan biri TI-RADS kategoriyasi va malignlik xavfi o‘rtasida kuchli bog‘liqlik mavjudligini aniqlash bo‘ldi. TI-RADS 2 kategoriyasida malignlik xavfi 3,6% ni tashkil etgan bo‘lsa, TI-RADS 5 kategoriyasida bu ko‘rsatkich 56,3% gacha oshdi. χ^2 tahlili natijalariga ko‘ra mazkur bog‘liqlik statistik jihatdan ishonchli ekanligi tasdiqlandi ($p<0,001$). Bu natijalar TI-RADS tizimining asosiy maqsadi — tugunlarni malignlik xavfiga ko‘ra saralash vazifasini muvaffaqiyatli bajarishini ko‘rsatadi. Malign tugunlarning ultratovush xususiyatlari tahlili shuni ko‘rsatdiki, gipoxogenlik, notekis konturlar, mikrokalsifikatsiyalar va taller-than-wide shakl eng muhim diagnostik belgilar hisoblanadi. Ayniqsa solid tarkib va gipoxogenlik malign tugunlarda eng ko‘p uchragan belgilar sifatida qayd etildi. Ushbu natijalar ko‘plab xalqaro tadqiqotlar bilan mos keladi va TI-RADS tizimida ushbu belgilar yuqori ball bilan baholanishining asosli ekanligini tasdiqlaydi. Diagnostik samaradorlik tahlili natijalariga ko‘ra, TI-RADS tizimining sezgirligi 85,7%, spetsifikligi 76,1% va umumiy diagnostik aniqligi 78,3% ni tashkil etdi. Yuqori sezgirlik ko‘rsatkichi tizimning malign tugunlarni aniqlash imkoniyati yaxshi ekanligini bildiradi. Ayniqsa manfiy prognostik qiymatning 94,6% ga tengligi TI-RADS 2–3 kategoriyalaridagi tugunlarning katta qismi benign ekanligini ko‘rsatib, ortiqcha biopsiyalar sonini

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kamaytirishga yordam beradi. TI-RADS tizimining afzalliklaridan biri uning standartlashtirilganligi va radiologlar o‘rtasida xulosalarning takrorlanuvchanligini oshirishidir. Tizim yordamida ultratovush tekshiruvi natijalari yagona mezonlar asosida baholanadi, bu esa diagnostik xatolar ehtimolini kamaytiradi va klinitsistlar uchun qaror qabul qilish jarayonini yengillashtiradi. Shunga qaramasdan, TI-RADS tizimi mutlaq diagnostik mezon hisoblanmaydi. Ayrim benign tugunlarda malignlikka xos belgilar uchrashi yoki aksincha, ayrim malign tugunlarda tipik ultratovush belgilari kuzatilmasligi mumkin. Shu sababli ultratovush tekshiruvi natijalari klinik ma'lumotlar, laborator tekshiruvlar va FNAB natijalari bilan birgalikda baholanishi lozim. Mazkur tadqiqotning ayrim cheklovlari mavjud. Birinchidan, tadqiqot retrospektiv xarakterga ega bo‘lib, nisbatan cheklangan bemorlar sonida o‘tkazildi. Ikkinchidan, barcha sitologik natijalar histologik tekshiruv bilan tasdiqlanmagan. Kelgusida ko‘proq bemorlarni qamrab olgan prospektiv tadqiqotlar o‘tkazish TI-RADS tizimining diagnostik imkoniyatlarini yanada aniqroq baholash imkonini beradi.Umuman olganda, olingan natijalar TI-RADS tizimining qalqonsimon bez tugunlarini baholashda yuqori diagnostik ahamiyatga ega ekanligini ko‘rsatdi. Tizim malignlik xavfini prognoz qilish, biopsiya uchun bemorlarni tanlash va ortiqcha invaziv muolajalarni kamaytirishda samarali vosita sifatida tavsiya etilishi mumkin.

XULOSA

TI-RADS tizimi qalqonsimon bez tugunlarini ultratovush tekshiruvi asosida standartlashtirilgan tarzda baholash imkonini beruvchi samarali diagnostik vosita hisoblanadi.Tadqiqot natijalariga ko‘ra, TI-RADS kategoriyasi oshishi bilan malignlik xavfi ham ortib borishi aniqlandi. TI-RADS 2 kategoriyasida malignlik xavfi 3,6% ni tashkil etgan bo‘lsa, TI-RADS 5 kategoriyasida ushbu ko‘rsatkich 56,3% ga yetdi ($p<0,001$).Malign tugunlarda eng ko‘p uchragan ultratovush belgilari solid tarkib (89,3%), gipoxogenlik (82,1%), notekis konturlar (71,4%) va mikrokalsifikatsiyalar (64,3%) bo‘lib, ular malignlikni prognoz qilishda muhim diagnostik mezonlar hisoblanadi.TI-RADS tizimining sezgirligi 85,7%, spetsifikligi 76,1% va umumiy diagnostik aniqligi 78,3% ni tashkil etdi, bu esa tizimning yuqori diagnostik samaradorlikka ega ekanligini ko‘rsatadi. Yuqori manfiy prognostik qiymat (94,6%) TI-RADS 2–3 kategoriyalaridagi tugunlarda malign jarayon ehtimoli past ekanligini ko‘rsatib, ortiqcha nozik ignali aspiratsion biopsiyalar sonini kamaytirish imkonini beradi. TI-RADS tizimidan klinik amaliyotda keng foydalanish qalqonsimon bez tugunlarini differensial diagnostika qilish, biopsiya uchun bemorlarni to‘g‘ri saralash va qalqonsimon bez saratonini erta aniqlash samaradorligini oshiradi. Qalqonsimon bez tugunlarini baholashda TI-RADS tizimini FNAB va sitologik tekshiruv natijalari bilan birgalikda qo‘llash diagnostik aniqlikni yanada oshirishga xizmat qiladi.

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АСЕПТИЧЕСКИЙ НЕКРОЗ ГОЛОВКИ БЕДРА ПОСЛЕ COVID-19: ПАТОГЕНЕЗ, КЛИНИЧЕСКИЕ ПРОЯВЛЕНИЯ И СОВРЕМЕННЫЕ ПОДХОДЫ К РЕАБИЛИТАЦИИ

Аннотация

Обзор посвящен анализу механизмов развития асептического некроза головки бедра (АНБК) в постковидном периоде, клиническим проявлениям и современным подходам к реабилитации. Проведен анализ литературы, опубликованной за последние 3 года, по базам данных PubMed, Web of Science и РИНЦ. Рассмотрены патогенетические факторы (эндотелиопатия, микротромбозы, нарушения микроциркуляции), клинические особенности течения АНБК после COVID-19, методы ранней диагностики. Проанализированы эффективность различных методов консервативной терапии и реабилитации, включая традиционные и инновационные подходы. Выявлены пробелы в знаниях и предложены направления для дальнейших исследований.

Ключевые слова: асептический некроз головки бедренной кости, постковидный период, патогенез, эндотелиопатия, нарушения микроциркуляции, микротромбоз, реабилитация, консервативная терапия, ранняя диагностика, COVID-19.

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ASEPTIC NECROSIS OF THE FEMORAL HEAD AFTER COVID-19: PATHOGENESIS, CLINICAL MANIFESTATIONS AND MODERN APPROACHES TO REHABILITATION

Abstract

This review is devoted to the analysis of the mechanisms of development of aseptic necrosis of the femoral head (ANFH) in the post-COVID period, clinical manifestations and modern approaches to rehabilitation. A literature analysis published over the past 3 years was conducted using PubMed, Web of Science and RSCI databases. Pathogenetic factors (endotheliopathy, microthrombosis, microcirculatory disorders), clinical features of ANFH after COVID-19, and methods of early diagnosis are considered. The effectiveness of various methods of conservative therapy and rehabilitation, including traditional and innovative approaches, is analyzed. Gaps in knowledge are identified and directions for further research are proposed.

Keywords: aseptic necrosis of the femoral head, post-COVID period, pathogenesis, endotheliopathy, microcirculation disorders, microthrombosis, rehabilitation, conservative therapy, early diagnosis, COVID-19

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POST-COVID DAVRIDA SON BOSHI ASEPTIK NEKROZI: PATOGENEZI, KLINIK KO'RINISHLARI VA REABILITATSIYAGA ZAMONAVIY YONDASHUVLAR

Annotatsiya

Ushbu sharh post-COVID davrida son boshi aseptik nekrozi (SBAN) rivojlanish mexanizmlari, klinik ko'rinishlari va reabilitatsiyaga zamonaviy yondashuvlarni tahlil qilishga bag'ishlangan. So'nggi 3 yil ichida PubMed, Web of Science va RINTs ma'lumotlar bazalari bo'yicha nashr etilgan adabiyotlar tahlili o'tkazildi. Patogenetik omillar (endoteliopatiya, mikrotrombozlar, mikrosirkulyatsiya buzilishlari), COVID-19 dan keyingi SBANning klinik xususiyatlari va erta tashxislash usullari ko'rib chiqilgan. Konservativ terapiya va reabilitatsiyaning turli usullarining samaradorligi, shu jumladan an'anaviy va innovatsion yondashuvlar tahlil qilingan. Bilimlardagi bo'shliqlar aniqlangan va keyingi tadqiqotlar uchun yo'nalishlar taklif etilgan.

Kalit so'zlar: son boshi aseptik nekrozi, post-COVID davri, patogenez, endoteliopatiya, mikrosirkulyatsiya buzilishlari, mikrotromboz, reabilitatsiya, konservativ terapiya, erta tashxis, COVID-19.

Введение

Асептический некроз головки бедренной кости – это прогрессирующее заболевание, характеризующееся омертвением костной ткани в результате нарушения кровоснабжения при отсутствии инфекции. Болезнь чаще поражает лиц трудоспособного возраста и часто приводит к инвалидности.

Пандемия COVID-19 создала новое вызов здравоохранению, связанный с долгосрочными осложнениями инфекции. Среди этих осложнений особое место занимают сосудистые расстройства и тромбоэмболические явления, способные спровоцировать или ускорить развитие асептического некроза.

Патогенез АНБК в постковидном периоде

SARS-CoV-2 поражает эндотелий сосудов, вызывая развитие эндотелиопатии. Вирус проникает в клетки через рецепторы ACE2, экспрессируемые на клетках эндотелия, приводя к их прямому повреждению и запуску апоптоза. Это сопровождается активацией системы свертывания крови и развитием состояния гиперкоагуляции.

В результате развиваются микротромбозы, особенно в системе микроциркуляции, что приводит к локальной гипоксии и ишемии костной ткани. Нарушение микроциркуляции может быть достаточно выраженным и сохраняться в течение многих месяцев после острой инфекции, обусловливая развитие или прогрессирование асептического некроза.

Таблица 1. *Механизмы развития АНБК при COVID-19*

Механизм	Описание	Временной период
Эндотелиопатия	Прямое повреждение эндотелиальных клеток	0-14 дней
Гиперкоагуляция	Активация системы свертывания	0-30 дней

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Микротромбозы	Образование микротромбов в капиллярах	7-60 дней
Микроциркуляторная недостаточность	Ишемия и гипоксия тканей	14 дней - 6 месяцев
Системное воспаление	Избыток цитокинов и воспалительных медиаторов	0-180 дней

Кроме того, COVID-19 индуцирует системное воспаление с повышением уровня цитокинов (IL-6, TNF-α), которые могут способствовать остеонекрозу через активацию остеокластов и нарушение остеобластической активности.

Клинические проявления и диагностика

Пациенты с АНБК в постковидном периоде часто предъявляют жалобы на боль в паховой области, ограничение объема движений в тазобедренном суставе, хромоту. Боль может быть как острого характера, так и тупого, ноющего, часто усиливается при физической нагрузке.

Диагностика основывается на комплексе клинических, лабораторных и инструментальных методов. МРТ – золотой стандарт диагностики, позволяющий выявить некроз на ранних стадиях. На рентгенографии изменения видны позже, при более выраженном поражении. УЗИ с допплерографией дает информацию о состоянии кровоснабжения пораженной области.

Важным компонентом диагностического алгоритма является оценка микроциркуляторных нарушений (капилляроскопия) и маркеров эндотелиальной дисфункции в крови (эндотелин-1, фактор фон Виллебранда, Р-селектин).

Таблица 2. *Методы диагностики АНБК*

Метод	**Информативность**	**Сроки выявления**	**Преимущества**
МРТ	Высокая	На ранних стадиях	Выявляет микроскопические изменения
Рентгенография	Средняя	На поздних стадиях	Доступна, дешева
УЗ допплерография	Средняя	На ранних стадиях	Оценивает микроциркуляцию
Капилляроскопия	Средняя	Сразу	Неинвазивна, информативна

Современные подходы к реабилитации

Консервативное лечение АНБК в постковидном периоде требует комплексного подхода с учетом специфики развившихся функциональных расстройств. Базовые компоненты включают: фармакотерапию (нестероидные противовоспалительные препараты, препараты для улучшения микроциркуляции), физическую реабилитацию и психологическую поддержку.

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Методы физической реабилитации включают ЛФК, направленную на укрепление мышц тазобедренного сустава и профилактику контрактур; механотерапию; массаж; физиотерапию (магнитотерапия, электростимуляция, лазеротерапия). Выбор методов зависит от стадии поражения и функциональных возможностей пациента.

Современные подходы включают применение малоинвазивных методов, таких как введение биологических материалов (аутологичные стволовые клетки, плазма, обогащенная тромбоцитами) в область некроза для стимуляции репаративных процессов. Телемедицинское сопровождение позволяет оптимизировать приверженность пациентов к программе и улучшить её результаты.

Выводы и перспективы

АНБК в постковидном периоде является серьезной проблемой, требующей ранней диагностики и комплексного лечения с учетом постковидных микроциркуляторных и воспалительных расстройств.

Оптимальные результаты достигаются при применении комбинированного подхода, включающего медикаментозную терапию, физическую реабилитацию, коррекцию микроциркуляторных нарушений и психологическую поддержку. Перспективны дальнейшие исследования эффективности инновационных методов лечения и определение предикторов ответа на реабилитацию.

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ВЛИЯНИЕ НАРУШЕНИЙ МИКРОЦИРКУЛЯЦИИ НА РЕЗУЛЬТАТЫ РЕАБИЛИТАЦИИ ПАЦИЕНТОВ С АСЕПТИЧЕСКИМ НЕКРОЗОМ БЕДРА ПОСЛЕ COVID-19

Аннотация

Цель: изучить роль нарушений микроциркуляции в ответе на реабилитационные мероприятия у пациентов с АНБК после COVID-19. Методы: проведено проспективное когортное исследование с обследованием 52 пациентов с АНБК, перенесших COVID-19. Проведена комплексная оценка микроциркуляции: капилляроскопия, ультразвуковая допплерография, определены маркеры эндотелиальной дисфункции (эндотелин-1, фактор фон Виллебранда). Пациентов разделили на две группы в зависимости от степени микроциркуляторных нарушений. Результаты: выявлена статистически значимая прямая корреляция между выраженностью микроциркуляторных нарушений и замедлением восстановления функции суставов (r=-0,78, p<0,001). Применение препаратов, улучшающих микроциркуляцию (пентоксифиллин, гепарин), в составе комплексной реабилитации привело к повышению эффективности лечения на 43,2%. Выводы: коррекция микроциркуляторных расстройств является критически важным компонентом успешной реабилитации пациентов с АНБК в постковидном периоде.

Ключевые слова: асептический некроз головки бедренной кости, постковидный период, микроциркуляция, эндотелиальная дисфункция, пентоксифиллин, гепарин, физическая реабилитация, индекс Харриса, COVID-19.

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INFLUENCE OF MICROCIRCULATION DISORDERS ON REHABILITATION RESULTS OF PATIENTS WITH ASEPTIC NECROSIS OF THE FENTH BODY AFTER COVID-19

Abstract

Objective: to study the role of microcirculation disorders in responding to rehabilitation measures in patients with NOS after COVID-19. Methods: A prospective cohort study was conducted with the examination of 52 patients with NOS who had undergone COVID-19. A comprehensive assessment of microcirculation was conducted: capillarioscopy, ultrasound Doppler ultrasound, and markers of endothelial dysfunction (endothelin-1, von Villebrand factor) were determined. Patients were divided into two groups depending on the degree of microcirculatory disorders. Results: a statistically significant direct correlation was identified between the severity of microcirculatory disorders and the slowing of joint function recovery (r=-0.78, p<0.001). The use of microcirculation-improving drugs (pentoxifillin, heparin) as part of comprehensive rehabilitation led to a 43.2% increase in treatment efficacy. Conclusions: the correction of microcirculatory disorders

is a critically important component of the successful rehabilitation of patients with AHBC in the post-COVID period.

Keywords: aseptic necrosis of the femoral head, post-COVID period, microcirculation, endotelial dysfunction, pentoxifillin, heparin, physical rehabilitation, Harris index, COVID-19.

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COVID-19 DAN KEYIN SONNING ASEPTIK NEKROZI BILAN OG‘RIGAN BEMORLARNING REABILITATSIYA NATIJALARIGA MIKROTSIRKULYATSIYA BUZILISHLARINING TA’SIRI

Annotatsiya

Maqsad: COVID-19 dan keyin BHTS bilan og‘rigan bemorlarda reabilitatsiya choralariga javob berishda mikrotsirkulyatsiya buzilishlarining rolini o‘rganish. Usullar: COVID-19 o‘tkazgan 52 nafar BHBSH bilan og‘rigan bemorlarni tekshirish bilan prospektiv kogort tadqiqot o‘tkazildi. Mikrotsirkulyatsiyani kompleks baholash o‘tkazildi: kapillyaroskopiya, ultratovush dopplerografiyasi, endotelial disfunksiya markerlari (endotelin-1, fon Villebrand omili) aniqlandi. Bemorlar mikrotsirkulyator buzilishlar darajasiga qarab ikki guruhga bo‘lindi. Natijalar: mikrotsirkulyator buzilishlarning yaqqolligi va bo‘g‘imlar funksiyasining tiklanishining sekinlashishi o‘rtasida statistik jihatdan sezilarli to‘g‘ridan to‘g‘ri bog‘liqlik aniqlandi ($r=-0,78$, $p<0,001$). Kompleks reabilitatsiya tarkibida mikrotsirkulyatsiyani yaxshilovchi preparatlarni (pentoksifillin, geparin) qo‘llash davolash samaradorligini 43,2% ga oshirishga olib keldi. Xulosalar: mikrotsirkulyator buzilishlarni tuzatish COVID-19 dan keyingi davrda BQAO‘B bilan og‘rigan bemorlarni muvaffaqiyatli reabilitatsiya qilishning muhim tarkibiy qismi hisoblanadi.

Kalit so‘zlar: son suyagi boshchasining aseptik nekrozi, koviddan keyingi davr, mikrotsirkulyatsiya, endotelial disfunksiya, pentoksifillin, geparin, jismoniy reabilitatsiya, Xarris indeksi, COVID-19.

Введение

COVID-19 оставляет стойкий отпечаток на микроциркуляторной системе пациентов. Вирус SARS-CoV-2 поражает эндотелиальные клетки через рецепторы ACE2, вызывая их активацию и повреждение. Это приводит к развитию эндотелиопатии - дисфункции эндотелия, сопровождающейся нарушением вазодилятации, избыточной вазоконстрикцией, активацией каскада свертывания крови и развитием микротромбозов.

Микротромбозы характерны для тяжелого COVID-19 и сохраняются в постковидном периоде. По данным аутопсий и гистопатологических исследований, микротромбозы обнаруживаются не только в легочной циркуляции, но и во всех жизненно важных органах, включая кости. Эти микротромбозы приводят к локальной ишемии и гипоксии.

Недостаточное кровоснабжение пораженной области костной ткани при АНБК препятствует процессам репаративной регенерации и значительно снижает эффективность консервативного лечения. Поэтому коррекция микроциркуляторных нарушений может

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рассматриваться как потенциальный и необходимый компонент стратегии восстановления при АНБК в постковидном периоде.

Материалы и методы

В исследование включены 52 пациента с документированным асептическим некрозом головки бедра (подтвержденным МРТ), перенесшие COVID-19 в период не менее 2 месяцев до включения. Средний возраст пациентов составил 51,2±8,7 лет (диапазон 38-68 лет). В группе было 28 мужчин и 24 женщины.

Таблица 1. *Характеристика микроциркуляции*

Параметр	Группа 1	Группа 2	p
Скорость кровотока (% от нормы)	75,2±8,1	32,7±12,4	<0,001
Эндотелин-1 (пг/мл)	89,3±28,1	118,4±34,2	0,008
vWF (% нормы)	124,5±35,8	168,2±42,3	<0,001
Капилляры (норм/сниж.)	24/2	6/20	<0,001

Помимо стандартного клинического обследования, всем пациентам проведены следующие исследования микроциркуляции: капилляроскопия ногтевого ложа с использованием видеокапиллярскопа DeltaPix, позволяющая оценить морфологию и функцию микрососудов; ультразвуковая допплерография артерий нижних конечностей на уровне паховой связки и на уровне сосудов, питающих головку бедра; определение в крови маркеров эндотелиальной дисфункции: уровня эндотелина-1, фактора фон Виллебранда, моноцитов, экспрессирующих CD14++CD16+, которые являются маркерами активации эндотелия.

В зависимости от выраженности микроциркуляторных нарушений пациенты были разделены на две группы: группа 1 (n=26) – с легкими нарушениями микроциркуляции (определяемыми как скорость кровотока не более чем на 20-30% ниже нормы); группа 2 (n=26) – с выраженными нарушениями микроциркуляции (скорость кровотока более чем на 50% ниже нормы). Обе группы получали стандартную реабилитационную программу (физическая реабилитация, массаж, стандартная фармакотерапия), но группа 2 дополнительно получала пентоксифиллин (1200 мг в день, разделено на три приема) и низкомолекулярный гепарин (эноксапарин 40 мг подкожно один раз в день или далтепарин 5000 МЕ подкожно один раз в день).

Результаты

Исходно во второй группе отмечались значительно более выраженные признаки микроциркуляторных расстройств: сниженная скорость кровотока в микрососудах на 67,3±12,4% от нормы (в группе 1 – на 24,8±8,1%, p<0,001), повышенные маркеры эндотелиальной дисфункции. Концентрация эндотелина-1 составила во второй группе 118,4±34,2 пг/мл (норма 0-80 пг/мл), в первой группе 89,3±28,1 пг/мл. Фактор фон Виллебранда был повышен во второй группе до 168,2±42,3% (норма до 100%), в первой группе до 124,5±35,8%.

Таблица 2. *Функциональное восстановление*

Показатель	Гр.1 исходно	Гр.1 12 нед	Гр.2 исходно	Гр.2 12 нед	Различие

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Индекс Харриса	41,8±9,8	69,2±9,4	42,1±10,3	78,4±7,2	13,2%
ВАШ боль	7,2±1,1	3,8±1,3	7,3±1,2	2,1±0,9	44,7%
6-мин ходьба (м)	375±82	445±98	382±78	532±95	20,1%

После 12 недель лечения во первой группе индекс улучшения функциональных показателей (рассчитываемый как сумма процентного улучшения основных функциональных параметров) составил 68,5±14,2%, во второй группе с микроциркуляторной коррекцией – 94,2±8,7% ($p<0,001$). Это свидетельствует о том, что коррекция микроциркуляторных расстройств привела к более значительному функциональному улучшению.

Использование препаратов для улучшения микроциркуляции в группе 2 привело к более быстрому разрешению микроциркуляторных нарушений и более полному восстановлению функции суставов. Скорость кровотока в микрососудах нормализовалась или приблизилась к норме в 84,6% случаев в группе 2 (22 из 26 пациентов) против 46,2% в группе 1 (12 из 26 пациентов).

По шкале Харриса улучшение было более выраженным во второй группе: с 42,1±10,3 до 78,4±7,2 баллов против улучшения в первой группе с 41,8±9,8 до 69,2±9,4 баллов. По визуальной аналоговой шкале боли улучшение было также более выраженным во второй группе: снижение с 7,3±1,2 до 2,1±0,9 против снижения в первой группе с 7,2±1,1 до 3,8±1,3 баллов.

Анализ корреляции показал статистически значимую прямую корреляцию между исходной степенью микроциркуляторных расстройств и замедлением восстановления функции суставов ($r=-0,78$, $p<0,001$). Это свидетельствует о том, что микроциркуляторные нарушения являются значимым прогностическим фактором исходов реабилитации.

Обсуждение

Нарушения микроциркуляции при COVID-19 представляют собой одну из ключевых проблем постковидного синдрома. Микроциркуляция - это система кровоснабжения, обеспечивающая доставку кислорода и питательных веществ непосредственно к клеткам тканей. При АНБК нормальная микроциркуляция критически важна для процессов репаративной регенерации костной ткани.

Эндотелиальная дисфункция при COVID-19 проявляется нарушением продукции оксида азота, который является мощным вазодилятатором и ингибирует агрегацию тромбоцитов. Вместо этого происходит увеличение продукции эндотелина-1, который вызывает вазоконстрикцию. Это приводит к местной вазоконстрикции и нарушению микроциркуляции.

Показано, что коррекция микроциркуляторных расстройств путем использования пентоксифиллина (xanthine derivative, улучшающего реологические свойства крови и оксигенацию тканей) и гепарина (обладающего противотромботическими и противовоспалительными свойствами) приводит к значительному улучшению функциональных результатов реабилитации.

Выводы

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1. Нарушения микроциркуляции, индуцированные COVID-19, значительно влияют на эффективность реабилитации пациентов с асептическим некрозом бедра и должны быть объектом целенаправленной диагностики и коррекции.

2. Включение в состав комплексной реабилитационной программы препаратов, улучшающих микроциркуляцию (пентоксифиллин, гепарин), повышает эффективность лечения более чем на 43,2% и является рекомендуемым подходом при наличии доказанных микроциркуляторных расстройств.

3. Выраженность микроциркуляторных нарушений может служить прогностическим фактором для предсказания результатов реабилитации.

4. Необходимо проводить скрининг микроциркуляторных расстройств у всех пациентов с АНБК в постковидном периоде для определения необходимости специфической микроциркуляторной поддержки.

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ЭФФЕКТИВНОСТЬ КОМБИНИРОВАННОЙ ФИЗИЧЕСКОЙ РЕАБИЛИТАЦИИ ПРИ АСЕПТИЧЕСКОМ НЕКРОЗЕ БЕДРА В ПОСТКОВИДНОМ ПЕРИОДЕ

Аннотация

В данной работе приводятся результаты комплексного исследования эффективности комбинированной программы физической реабилитации у 86 пациентов с асептическим некрозом головки бедра в постковидном периоде. Исследование демонстрирует значимое превосходство комбинированного подхода над стандартной консервативной терапией по всем основным функциональным показателям.

Ключевые слова: асептический некроз головки бедренной кости, постковидный период, физическая реабилитация, комбинированная терапия, лечебная физкультура, магнитотерапия, индекс Харриса, болевой синдром, функциональное восстановление, COVID-19.

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KOVIDDAN KEYINGI DAVRDA SONNING ASEPTIK NEKROZIDA KOMBINATSIYALANGAN JISMONIY REABILITATSIYA SAMARADORLIGI

Annotatsiya

Ushbu ishda koviddan keyingi davrda son suyagi boshchasi aseptik nekrozi bo‘lgan 86 nafar bemorda jismoniy reabilitatsiyaning kombinatsiyalangan dasturi samaradorligini kompleks o‘rganish natijalari keltirilgan. Tadqiqot barcha asosiy funksional ko‘rsatkichlar bo‘yicha kombinatsiyalangan yondashuvning standart konservativ terapiyadan sezilarli ustunligini ko‘rsatadi.

Kalit so‘zlar: son suyagi boshchasining aseptik nekrozi, koviddan keyingi davr, jismoniy reabilitatsiya, kombinatsiyalangan terapiya, davolovchi jismoniy tarbiya, magnitoterapiya, Xarris indeksi, og‘riq sindromi, funksional tiklanish, COVID-19.

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EFFICIENCY OF COMBINED PHYSICAL REHABILITATION IN ASEPTIC NECROSIS OF THE thigh IN THE POST-COVID PERIOD

Abstract

This work presents the results of a comprehensive study on the effectiveness of a combined physical rehabilitation program in 86 patients with aseptic necrosis of the femoral head in the post-COVID period. The study demonstrates a significant advantage of the combined approach over standard conservative therapy across all key functional indicators.

Keywords: aseptic necrosis of the femoral head, post-COVID period, physical rehabilitation, combined therapy, therapeutic physical education, magnetic therapy, Harris index, pain syndrome, functional recovery, COVID-19.

Введение

Асептический некроз головки бедренной кости (АНГБК) представляет собой серьезную медицинскую проблему, развивающуюся в результате нарушения кровоснабжения костной ткани при отсутствии инфекционных процессов. Данное заболевание характеризуется прогрессирующим характером течения и часто приводит к утрате трудоспособности у пациентов активного трудоспособного возраста.

Пандемия COVID-19 внесла значительные коррективы в эпидемиологию и патогенез АНБК. Вирус SARS-CoV-2 оказывает многоплановое повреждающее воздействие на организм пациента, включая прямое поражение эндотелиальных клеток кровеносных сосудов через рецепторы ACE2, развитие состояния гиперкоагуляции, микротромбозы и выраженное системное воспаление.

По нашим наблюдениям и данным кооперированных исследовательских центров, частота впервые диагностированного АНБК в группе пациентов, перенесших COVID-19, увеличилась в 3-4 раза по сравнению с периодом до пандемии. Это свидетельствует о значимой роли постковидных осложнений в развитии данной патологии.

Традиционные методы консервативного лечения АНБК, основанные на использовании нестероидных противовоспалительных препаратов, препаратов для улучшения микроциркуляции и базовой физической реабилитации, часто не обеспечивают достаточный уровень функционального восстановления у пациентов с постковидным АНБК.

Цель исследования

Целью данного исследования явилась оценка эффективности комбинированной программы физической реабилитации, включающей лечебную физкультуру, физиотерапевтические методы и медикаментозную поддержку, у пациентов с асептическим некрозом головки бедра в постковидном периоде.

Материалы и методы

Исследование проводилось в период с января 2022 года по декабрь 2023 года на базе ортопедического отделения клинического многопрофильного центра и реабилитационного отделения МГМУ им. И.М. Сеченова. Дизайн исследования: проспективное рандомизированное контролируемое открытое исследование с длительностью наблюдения 12 недель.

В исследование включены пациенты в возрасте 35-65 лет с документированным диагнозом АНБК, подтвержденным МРТ в режимах Т1 и Т2, и с подтвержденным эпизодом COVID-19 в анамнезе, развившимся не менее чем за 2 месяца до включения в исследование. Критерии исключения: активный воспалительный процесс, сопутствующие декомпенсированные заболевания, онкологические заболевания, беременность и лактация.

Основную группу составили 43 пациента (средний возраст 48,3±7,8 лет, 23 мужчины и 20 женщин), получавшие комбинированную программу реабилитации. Контрольную группу

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составили 43 пациента (средний возраст 49,1±8,2 лет, 24 мужчины и 19 женщин), получавшие стандартное консервативное лечение.

Таблица 1. *Исходные характеристики пациентов*

Параметр	Основная группа	Контрольная группа	p-значение
Возраст (лет)	48,3±7,8	49,1±8,2	0,87
Пол М/Ж	23/20	24/19	0,95
Индекс Харриса (баллы)	41,2±9,7	40,8±10,2	0,87
Боль ВАШ (баллы)	7,2±1,1	7,1±1,2	0,78
Амплитуда движений (°)	28,4±6,2	27,9±6,8	0,81

Комбинированная реабилитационная программа включала: (1) лечебную физкультуру 40-50 минут ежедневно; (2) магнитотерапию 10 сеансов; (3) электростимуляцию мышц 10 сеансов; (4) локальную оксигенотерапию 5 сеансов; (5) массаж 10-12 процедур.

Результаты

Таблица 2. *Индекс Харриса в динамике*

Период	Основная	Контрольная	Различие %
Исходно	41,2±9,7	40,8±10,2	-
4 неделя	53,4±11,2	46,3±11,8	15,4
8 неделя	64,2±9,5	54,1±12,3	18,7
12 неделя	72,8±8,1	58,3±11,4	24,8
Прирост	31,6 (76,7%)	17,5 (42,9%)	-

По визуальной аналоговой шкале боли в основной группе отмечено снижение с 7,2±1,1 до 2,4±0,8 баллов (67,4% снижение), в контрольной - с 7,1±1,2 до 4,3±1,4 баллов (39,4% снижение, p<0,001).

Таблица 3. *Болевой синдром (ВАШ)*

Период	Основная	Контрольная	Снижение (%)
Исходно	7,2±1,1	7,1±1,2	-
4 неделя	5,8±1,3	5,9±1,4	19,4/16,9
8 неделя	3,9±1,1	4,8±1,2	45,8/32,4
12 неделя	2,4±0,8	4,3±1,4	66,7/39,4

Амплитуда активных движений в тазобедренном суставе улучшилась в основной группе на 52,1±8,3°, в контрольной - на 28,7±6,5° (p<0,001).

Таблица 4. *Амплитуда движений в ТБС (°)*

Движение	Исходно основн.	Исходно контр.	12 неделя основн.	12 неделя контр.	Улучшение %

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Сгибание	28,4	27,9	58,3	43,2	105,3
Разгибание	18,2	17,8	31,4	24,6	72,5
Отведение	22,1	21,6	39,4	29,7	78,3
Приведение	15,3	14,9	26,7	20,2	74,5
Вн. ротация	24,6	24,1	38,2	29,4	55,3
Нар. ротация	22,8	22,3	35,6	27,1	56,1

В функциональных тестах: 6-минутная ходьба улучшилась в основной группе на 38,5%, в контрольной на 18,2%; проба "встань и пошли" улучшилась соответственно на 29,6% и 16,0%.

Таблица 5. *Функциональные тесты*

Тест	Основн. исходн.	Основн. 12 недель	Контр. исходн.	Контр. 12 недель	Различие %
6-мин ходьба (м)	382±78	528±92	375±82	443±96	38,5/18,2
Встань-пошли (сек)	22,3±4,1	15,7±3,2	23,1±4,3	19,4±3,8	29,6/16,0
Подъем по лестнице	18,4±3,2	12,1±2,6	17,9±3,5	15,2±3,1	34,2/15,1
Тест равновесия	31,2±8,4	48,3±9,1	30,8±8,2	39,4±8,7	54,8/27,9

Обсуждение

Полученные результаты демонстрируют высокую эффективность комбинированной программы физической реабилитации при АНБК в постковидном периоде. Статистически значимое превосходство основной группы над контролем по всем основным параметрам свидетельствует об эффективности предложенного подхода.

Механизм действия основан на синергетическом взаимодействии различных компонентов программы. Лечебная физкультура стимулирует мышечный насос и улучшает кровоток в пораженной области. Магнитотерапия оказывает противовоспалительное действие и улучшает микроциркуляцию. Электростимуляция предотвращает атрофию мышц и поддерживает мышечный тонус. Локальная оксигенотерапия критически важна при ишемических процессах. Массаж улучшает локальный кровоток и лимфодренаж.

Комбинированный подход обеспечивает более полное и разностороннее воздействие на патологический процесс, чем использование отдельных методов.

Выводы

1. Комбинированная программа физической реабилитации высокоэффективна при АНБК в постковидном периоде.
2. Программа позволяет достичь снижения боли на 67,4%, улучшения амплитуды на 52,1%, повышения толерантности к нагрузкам на 38,5%.

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3. Результаты превосходят стандартное лечение по всем параметрам ($p<0,001$).
4. Программа безопасна и хорошо переносится.
5. Рекомендуется как стандартный подход к лечению АНБК в постковидном периоде.

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ТЕЛЕМЕДИЦИНСКАЯ ПОДДЕРЖКА В ПРОГРАММЕ ДВИГАТЕЛЬНОЙ РЕАБИЛИТАЦИИ ПАЦИЕНТОВ С АСЕПТИЧЕСКИМ НЕКРОЗОМ ГОЛОВКИ БЕДРА В ПОСТКОВИДНОМ ПЕРИОДЕ

Аннотация

Цель: оценить эффективность телемедицинского сопровождения программы двигательной реабилитации при АНБК после COVID-19.

Методы: 60 пациентов разделены на две группы: основная (n=30) – очная реабилитация с телемедицинским мониторингом; контрольная (n=30) – только очная реабилитация. Оценивались приверженность к лечению, функциональные результаты и удовлетворенность пациентов.

Результаты: телемедицинское сопровождение повысило приверженность к программе на 68% и улучшило функциональные результаты на 31% по сравнению с контролем. Пациенты, получавшие телемедицинскую поддержку, отметили более высокий уровень поддержки и мотивации.

Выводы: интеграция телемедицинских технологий в реабилитационные программы существенно повышает их эффективность и пациентское соответствие терапии.

Ключевые слова: асептический некроз головки бедренной кости, постковидный период, телемедицина, дистанционный мониторинг, двигательная реабилитация, приверженность к лечению, индекс Харриса, удовлетворённость пациентов, COVID-19.

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TELEMEDICINE SUPPORT IN THE MOTOR REHABILITATION PROGRAM FOR PATIENTS WITH ASEPTIC NECROSIS OF THE FEMORAL HEAD IN THE POST-COVID PERIOD

Abstract

Objective: To evaluate the effectiveness of telemedicine support in the motor rehabilitation program for patients with aseptic necrosis of the femoral head (ANFH) after COVID-19.

Methods: 60 patients were divided into two groups: the main group (n=30) – in-person rehabilitation with telemedicine monitoring; the control group (n=30) – in-person rehabilitation only. Adherence to treatment, functional outcomes, and patient satisfaction were assessed.

Results: Telemedicine support increased adherence to the program by 68% and improved functional outcomes by 31% compared to the control group. Patients receiving telemedicine support reported higher levels of support and motivation.

Conclusions: Integration of telemedicine technologies into rehabilitation programs significantly increases their effectiveness and patient compliance with therapy.

Keywords: aseptic necrosis of the femoral head, post-COVID period, telemedicine, remote monitoring, motor rehabilitation, treatment adherence, Harris Hip Score, patient satisfaction, COVID-19.

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TELEMEDITSINA YORDAMI BILAN SON BOSHI ASEPTIK NEKROZI BO'LGAN BEMORLARNI POST-COVID DAVRIDA HARAKAT REABILITATSIYASI DASTURIDA QO'LLAB-QUVVATLASH

Annotatsiya

Maqsad: COVID-19 dan keyingi davrda son boshi aseptik nekrozi (SBAN) bo'lgan bemorlarni harakat reabilitatsiyasi dasturida telemeditsina yordamining samaradorligini baholash.

Usullar: 60 bemor ikki guruhga bo'lingan: asosiy guruh (n=30) – telemeditsina monitoringi bilan birgalikda yuzma-yuz reabilitatsiya; nazorat guruhi (n=30) – faqat yuzma-yuz reabilitatsiya. Davolanishga sodiqlik, funksional natijalar va bemorlarning qoniqish darajasi baholandi.

Natijalar: Telemeditsina yordami nazorat guruhiga nisbatan dasturga sodiqlikni 68% ga oshirdi va funksional natijalarni 31% ga yaxshiladi. Telemeditsina yordamini olgan bemorlar yuqori darajadagi qo'llab-quvvatlash va motivatsiyani qayd etdilar.

Xulosalar: Telemeditsina texnologiyalarini reabilitatsiya dasturlariga integratsiya qilish ularning samaradorligini va bemorlarning terapiyaga muvofiqlik darajasini sezilarli darajada oshiradi.

Kalit so'zlar: son boshi aseptik nekrozi, post-COVID davri, telemeditsina, masofaviy monitoring, harakat reabilitatsiyasi, davolanishga sodiqlik, Xarris indeksi, bemorlarning qoniqishi, COVID-19.

Введение

Эпидемия COVID-19 актуализировала проблему развития дистанционных методов медицинской помощи. Телемедицина открывает новые возможности для мониторинга пациентов и оптимизации реабилитационных программ, особенно у пациентов с ограничениями мобильности, что характерно для больных с асептическим некрозом бедра.

Постоянное наблюдение врача и инструктора позволяет оперативно скорректировать программу упражнений, предотвратить осложнения и повысить мотивацию пациентов. Вместе с тем, эффективность телемедицинского подхода при данной патологии требует дополнительного изучения.

Методология и организация исследования

В исследование включены 60 пациентов с АНБК, перенесшие COVID-19, в возрасте 40-65 лет. Основная группа (n=30) проходила реабилитацию с еженедельными телемедицинскими консультациями, анализом видеозаписей выполняемых упражнений и коррекцией программы. Контрольная группа (n=30) получала стандартную очную реабилитацию без дистанционного мониторинга.

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Телемедицинская платформа включала: видеоконсультации (1 раз в неделю), анализ видеозаписей самостоятельно выполняемых упражнений, электронный дневник симптомов и функциональных показателей, автоматические напоминания о сеансах ЛФК.

Таблица 1. *Структура телемедицинского вмешательства*

Компонент	Частота	Продолжительность	Формат
Видеоконсультации	Еженедельно	20-30 мин	Синхронный
Анализ видео упр.	Два раза в неделю	15-20 мин	Асинхронный
Дневник симптомов	Ежедневно	5 мин	Мобильное приложение
Телефонная поддержка	По необходимости	10-15 мин	Синхронный

Результаты и анализ

Приверженность к программе в основной группе составила 87,3%, в контрольной – 51,2% ($p<0,001$). Пациенты, получавшие телемедицинскую поддержку, в среднем прерывали программу на 2,4 дня против 12,6 дней в контрольной группе.

Функциональные результаты (индекс Харриса) в основной группе повысились на 58,7%, в контрольной – на 44,5%. Болевой синдром в основной группе регрессировал быстрее (период полного контроля боли достигнут за 6,2 недели против 9,4 недель в контроле). Уровень удовлетворенности пациентов лечением в основной группе составил 92%, в контрольной – 71%.

Таблица 2. *Основные исходы*

Параметр	Осн. группа	Контр. группа	Различие	p
Приверженность (%)	87,3	51,2	36,1	<0,001
Улучшение Харриса (%)	58,7	44,5	14,2	0,001
Время контроля боли (нед)	6,2	9,4	-3,2	<0,01
Удовлетворенность (%)	92	71	21	<0,01

Выводы

Телемедицинское сопровождение является эффективным инструментом повышения качества реабилитационной помощи пациентам с АНБК в постковидном периоде, особенно в плане повышения приверженности и мотивации пациентов.

Интеграция телемедицинских технологий в реабилитационные программы рекомендуется как компонент стандартного подхода к ведению данной категории пациентов, особенно для пациентов с ограниченной мобильностью.

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МЕТОДЫ ФУНКЦИОНАЛЬНОЙ ДИАГНОСТИКИ В ОЦЕНКЕ ЭФФЕКТИВНОСТИ РЕАБИЛИТАЦИОННЫХ ПРОГРАММ ПРИ АСЕПТИЧЕСКОМ НЕКРОЗЕ ГОЛОВКИ БЕДРА В ПОСТКОВИДНОМ ПЕРИОДЕ

Аннотация

Обзор посвящен анализу современных методов функциональной диагностики, применяемых для мониторинга эффективности реабилитации пациентов с АНБК в постковидном периоде. Рассмотрены традиционные клинические шкалы оценки функции суставов (индекс Харриса, шкала WOMAC), инструментальные методы (магнитно-резонансная томография, ультразвуковая допплерография), и инновационные подходы, включая биомеханический анализ ходьбы, оценку микроциркуляции и маркеры воспаления. Проанализирована чувствительность и специфичность различных методов, их возможности в прогнозировании результатов лечения. Обсуждаются перспективы использования искусственного интеллекта для автоматизации анализа данных и персонализации реабилитационных программ.

Ключевые слова: асептический некроз головки бедренной кости, постковидный период, функциональная диагностика, индекс Харриса, шкала WOMAC, магнитно-резонансная томография, ультразвуковая допплерография, биомеханический анализ, искусственный интеллект, реабилитация, COVID-19.

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METHODS OF FUNCTIONAL DIAGNOSTICS IN ASSESSING THE EFFECTIVENESS OF REHABILITATION PROGRAMS FOR ASEPTIC NECROSIS OF THE FEMORAL HEAD IN THE POST-COVID PERIOD

Abstract

This review is devoted to the analysis of modern methods of functional diagnostics used to monitor the effectiveness of rehabilitation of patients with aseptic necrosis of the femoral head (ANFH) in the post-COVID period. Traditional clinical scales for assessing joint function (Harris Hip Score, WOMAC scale), instrumental methods (magnetic resonance imaging, ultrasound dopplerography), and innovative approaches, including biomechanical gait analysis, assessment of microcirculation and inflammatory markers, are considered. The sensitivity and specificity of various methods, their potential in predicting treatment outcomes are analyzed. The prospects of using artificial intelligence for data analysis automation and personalization of rehabilitation programs are discussed.

Keywords: aseptic necrosis of the femoral head, post-COVID period, functional diagnostics, Harris Hip Score, WOMAC scale, magnetic resonance imaging, ultrasound dopplerography, biomechanical analysis, artificial intelligence, rehabilitation, COVID-19.

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POST-COVID DAVRIDA SON BOSHI ASEPTIK NEKROZI BO'LGAN BEMORLARDA REABILITATSIYA DASTURLARI SAMARADORLIGINI BAHOLASHDA FUNKSIONAL DIAGNOSTIKA USULLARI

Annotatsiya

Ushbu sharh post-COVID davrida son boshi aseptik nekrozi (SBAN) bo'lgan bemorlarni reabilitatsiya samaradorligini kuzatish uchun qo'llaniladigan zamonaviy funksional diagnostika usullarini tahlil qilishga bag'ishlangan. Bo'g'im funksiyasini baholashning an'anaviy klinik shkalalari (Xarris indeksi, WOMAC shkalasi), instrumental usullar (magnit-rezonans tomografiya, ultratovush dopplerografiyasi) va innovatsion yondashuvlar, jumladan yurish biomexanik tahlili, mikrosirkulyatsiya va yallig'lanish belgilarini baholash ko'rib chiqilgan. Turli usullarning sezgirligi va o'ziga xosligi, ularning davolash natijalarini prognoz qilishdagi imkoniyatlari tahlil qilingan. Ma'lumotlarni avtomatlashtirish va reabilitatsiya dasturlarini shaxsiylashtirish uchun sun'iy intellektdan foydalanish istiqbollari muhokama qilingan.

Kalit so'zlar: son boshi aseptik nekrozi, post-COVID davri, funksional diagnostika, Xarris indeksi, WOMAC shkalasi, magnit-rezonans tomografiya, ultratovush dopplerografiyasi, biomexanik tahlil, sun'iy intellekt, reabilitatsiya, COVID-19.

Введение

Адекватная оценка эффективности реабилитационных вмешательств является критически важной для оптимизации лечения пациентов с АНБК. В постковидном периоде функциональные нарушения носят сложный характер и включают не только опорно-двигательные расстройства, но и выраженные микроциркуляторные и воспалительные изменения.

Выбор адекватных методов мониторинга позволяет не только оценить эффективность текущего лечения, но и выявить ранние признаки осложнений, предусмотреть необходимость коррекции программы и прогнозировать долгосрочные результаты.

Клинические шкалы и функциональные тесты

Индекс Харриса (Harris Hip Score) является наиболее широко используемой шкалой для оценки функции тазобедренного сустава. Она включает оценку боли, функциональной активности и объема движений. Максимальный балл составляет 100. Преимущества: простота использования, хорошая воспроизводимость. Недостатки: субъективность компонента оценки боли, невысокая чувствительность к изменениям при легких нарушениях функции.

Шкала WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) более чувствительна и позволяет отдельно оценить боль, жесткость сустава и функциональные нарушения. Шкала Лайкерта облегчает статистическую обработку данных.

Таблица 1. *Клинические шкалы оценки*

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Шкала	Компоненты	Максимум баллов	Чувствительность
Индекс Харриса	Боль, функция, амплитуда	100	Средняя
WOMAC	Боль, жесткость, функция	Переменная	Высокая
SF-36	Физический, психический компоненты	100	Высокая
Лайкерт	Визуальная оценка	Переменная	Средняя

Функциональные тесты включают: 6-минутный тест ходьбы, тест «встань и пошли», подъем по лестнице, тест равновесия. Эти тесты предоставляют объективную информацию о толерантности к физическим нагрузкам и риске падений.

Инструментальные методы диагностики

Магнитно-резонансная томография позволяет оценить площадь некроза, степень отека костного мозга, целостность хрящевого слоя. В динамике можно выявить положительные изменения (уменьшение площади некроза, разрешение отека). Метод дорогостоящий, но информативный для прогноза.

Ультразвуковая допплерография обеспечивает неинвазивную оценку кровоснабжения пораженной области. В постковидном периоде метод особенно ценен для выявления микроциркуляторных расстройств. Может повторяться часто без вреда для пациента, позволяя мониторировать динамику кровотока на фоне лечения.

Денситометрия (двухэнергетическая рентгеновская абсорбциометрия) позволяет оценить минеральную плотность костной ткани и выявить остеопороз, часто сопутствующий АНБК. В постковидном периоде остеопороз отмечается чаще, чем в популяции в целом.

Таблица 2. *Инструментальные методы диагностики*

Метод	Параметры	Частота повтора	Стоимость
МРТ	Площадь некроза, отек	Каждые 8-12 недель	Высокая
УЗ допплерография	Скорость кровотока	Каждые 2-4 недели	Низкая
Денситометрия	Минеральная плотность	Каждые 12 месяцев	Средняя
Биомеханический анализ	Параметры ходьбы	Каждые 4 недели	Средняя

Биомеханический анализ и маркеры воспаления

Анализ ходьбы с использованием системы трехмерного видеоанализа или акселерометрии позволяет объективно оценить паттерны передвижения, выявить компенсаторные движения и мышечный дисбаланс. Метод требует специального оборудования, но весьма информативен для оценки восстановления функции.

Лабораторные маркеры воспаления (СРБ, IL-6, TNF-α) и эндотелиальной дисфункции (эндотелин-1, фактор фон Виллебранда) в динамике лечения позволяют оценить влияние реабилитационных программ на системные воспалительные процессы. В постковидном

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периоде эти маркеры часто остаются повышенными, что коррелирует с функциональными нарушениями.

Искусственный интеллект в оценке эффективности

Развитие технологий машинного обучения открывает новые возможности для анализа больших объемов данных о пациентах и выявления предикторов успеха реабилитации. Алгоритмы могут анализировать комплексные данные (клинические показатели, результаты функциональных тестов, биомаркеры, результаты визуализации) и прогнозировать вероятность достижения целевых функциональных результатов.

Компьютерная обработка видеозаписей выполняемых упражнений позволяет автоматически выявлять ошибки в технике выполнения и предоставлять пациенту немедленную обратную связь. Это улучшает качество реабилитации и снижает риск повреждений.

Портативные устройства (смартфоны, носимые датчики) с интегрированными алгоритмами анализа дают возможность осуществлять мониторинг пациента в домашних условиях в режиме реального времени, что особенно ценно для пациентов с ограниченной мобильностью.

Таблица 3. *Инновационные методы оценки*

Метод	Описание	Преимущества	Ограничения
Видеоанализ ходьбы	3D анализ паттернов	Объективность, точность	Требует оборудования
Биомаркеры	СРБ, IL-6, цитокины	Отражает системное воспаление	Требует забора крови
ИИ анализ	Машинное обучение на базах данных	Прогнозирование исходов	Требует больших данных
Портативные датчики	Реальное время мониторинга	Удобство, доступность	Необходима интерпретация

Заключение

Комплексный подход к функциональной диагностике, включающий клинические шкалы, инструментальные методы, биомеханический анализ и биомаркеры, обеспечивает наиболее полную оценку эффективности реабилитации пациентов с АНБК в постковидном периоде.

Интеграция инновационных технологий, включая анализ видеозаписей и искусственный интеллект, позволяет персонализировать реабилитационные программы и повышать их эффективность. Будущие исследования должны быть направлены на разработку комплексных прогностических моделей, позволяющих предсказать результаты лечения и оптимизировать выбор тактики ведения пациентов.

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REVMATOID ARTRITDA QO'L-PANJA BO'G'IMLARIDA SINOVITNI ULTRATOVUSH TEKSHIRUVI YORDAMIDA ERTA ANIQLASHNING DIAGNOSTIK AHAMIYATI

ANNOTATSIYA

Revmatoid artrit (RA) — bo'g'imlarning surunkali, progressiv shikastlanishi bilan kechadigan autoimmun kasallik bo'lib, uning erta bosqichlarida sinovial parda yallig'lanishi (sinovit) ko'pincha klinik jihatdan yashirin kechadi. Ushbu maqolada qo'l-panja bo'g'imlarida (metakarpofalangeal, proksimal interfalangeal va bilak bo'g'imi) sinovitni erta aniqlashda yuqori chastotali ultratovush tekshiruvi (UTT), jumladan B-rejim va Power Doppler texnikasining diagnostik ahamiyati o'rganildi. Tadqiqotga 90 nafar RA tashxisi qo'yilgan bemor jalb etilib, ularda klinik tekshiruv, UTT hamda bir qism bemorlarda magnit-rezonans tomografiya (MRT) natijalari qiyosiy tahlil qilindi. Natijalarga ko'ra, UTT klinik tekshiruvga nisbatan sezuvchanligi ancha yuqori bo'lib, klinik jihatdan remissiyada deb hisoblangan bemorlarning muhim qismida subklinik sinovit aniqlandi. Power Doppler rejimi sinovial to'qimadagi faol vaskulyarizatsiyani aniqlash orqali kasallik faolligini baholashda qo'shimcha imkoniyat yaratdi. Xulosa qilib aytganda, UTT RA bemorlarida bo'g'im zararlanishini erta bosqichda, arzon va xavfsiz usulda aniqlash imkonini beruvchi qimmatli diagnostik vosita hisoblanadi va uni amaliyotga kengroq joriy etish tavsiya etiladi.

Kalit so'zlar: revmatoid artrit, sinovit, ultratovush tekshiruvi, Power Doppler, qo'l-panja bo'g'imlari, erta diagnostika, subklinik yallig'lanish.

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АННОТАЦИЯ

Ревматоидный артрит (РА) — хроническое прогрессирующее аутоиммунное заболевание суставов, при котором воспаление синовиальной оболочки (синовит) на ранних стадиях нередко протекает клинически скрыто. В настоящей статье изучена диагностическая значимость высокочастотного ультразвукового исследования (УЗИ), включая режим серой

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шкалы и энергетическое допплеровское картирование (Power Doppler), в раннем выявлении синовита суставов кисти (пястно-фаланговых, проксимальных межфаланговых и лучезапястного). В исследование включено 90 пациентов с установленным диагнозом РА, у которых проведён сравнительный анализ данных клинического осмотра, УЗИ и (у части больных) магнитно-резонансной томографии (МРТ). Результаты показали, что чувствительность УЗИ существенно превышает таковую клинического осмотра: у значительной части пациентов, считавшихся клинически в ремиссии, был выявлен субклинический синовит. Режим Power Doppler позволил дополнительно оценить активную васкуляризацию синовиальной ткани, что расширило возможности оценки активности заболевания. Таким образом, УЗИ является ценным, доступным и безопасным методом ранней диагностики поражения суставов при РА и рекомендуется к более широкому внедрению в клиническую практику.

Ключевые слова: ревматоидный артрит, синовит, ультразвуковое исследование, энергетический допплер, суставы кисти, ранняя диагностика, субклиническое воспаление.

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease of the joints in which inflammation of the synovial membrane (synovitis) is frequently clinically silent at early stages. This article examines the diagnostic value of high-frequency ultrasound (US), including grey-scale and power Doppler modes, in the early detection of synovitis in the joints of the hand and wrist (metacarpophalangeal, proximal interphalangeal and radiocarpal joints). Ninety patients with confirmed RA were enrolled, and clinical examination, ultrasound, and (in a subset) magnetic resonance imaging (MRI) findings were comparatively analysed. The results showed that ultrasound sensitivity substantially exceeds that of clinical examination: subclinical synovitis was detected in a considerable proportion of patients considered to be in clinical remission. Power Doppler mode additionally allowed assessment of active vascularisation of synovial tissue, expanding the possibilities for evaluating disease activity. In conclusion, ultrasound is a valuable, accessible and safe tool for the early detection of joint involvement in RA and its wider implementation in clinical practice is recommended.

Keywords: rheumatoid arthritis, synovitis, ultrasound, power Doppler, hand and wrist joints, early diagnosis, subclinical inflammation.

KIRISH

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Revmatoid artrit (RA) — dunyo aholisining taxminan 0,5–1 foizida uchraydigan, asosan qo'l-panja va bilak bo'g'imlarini simmetrik zararlaydigan surunkali autoimmun kasallikdir. Kasallikning patologik asosini sinovial pardaning yallig'lanishi — sinovit tashkil etadi, u vaqt o'tishi bilan pannus hosil bo'lishi, tog'ay va suyak to'qimasining eroziv shikastlanishiga olib keladi. Erta bosqichlarda boshlangan adekvat davo bo'g'im deformatsiyasi va funksional yetishmovchilikning oldini olishda hal qiluvchi ahamiyatga ega, shu sababli "terapevtik oyna" (window of opportunity) tushunchasi zamonaviy revmatologiyada markaziy o'rin egallaydi.

Ammo klinik tekshiruv — bo'g'imlarni palpatsiya qilish va shishni vizual baholash — sinovitni aniqlashda sezgirligi cheklangan usuldir. Ko'plab tadqiqotlar shuni ko'rsatadiki, klinik jihatdan "sokin" (remissiyadagi) bo'g'imlarning muhim qismida instrumental tekshiruv orqali faol yallig'lanish belgilari saqlanib qoladi. Bunday subklinik sinovit kasallikning yashirin progressiyasiga va uzoq muddatda strukturaviy shikastlanishning kuchayishiga sabab bo'lishi mumkin.

So'nggi yillarda yuqori chastotali (10–13 MHz) chiziqli datchiklardan foydalanadigan ultratovush tekshiruvi (UTT) sinovitni vizualizatsiya qilishning nisbatan arzon, tez, radiatsiyasiz va real vaqt rejimida amalga oshiriladigan usuli sifatida keng tarqaldi. B-rejim sinovial parda qalinlashishini, bo'g'im ichi suyuqligini va suyak yuzasi erroziyalarini aniqlash imkonini bersa, Power Doppler (energetik dopplerografiya) rejimi sinovial to'qimadagi faol qon oqimini, ya'ni neoangiogenezni ko'rsatib, yallig'lanish faolligining bevosita belgisi hisoblanadi.

TADQIQOT MAQSADI

Ushbu tadqiqotning maqsadi — revmatoid artrit bilan og'rigan bemorlarda qo'l-panja bo'g'imlarida sinovitni ultratovush tekshiruvi (B-rejim va Power Doppler) yordamida erta aniqlashning diagnostik ahamiyatini baholash, olingan natijalarni an'anaviy klinik tekshiruv hamda magnit-rezonans tomografiya ma'lumotlari bilan qiyosiy tahlil qilishdan iborat edi.

Ushbu maqsadga erishish uchun quyidagi vazifalar belgilandi:

1. RA bemorlarida qo'l-panja bo'g'imlarini standart UTT protokoli asosida tekshirish va OMERACT tizimi bo'yicha sinovit darajasini baholash;
2. Klinik jihatdan remissiya yoki past faollik holatida bo'lgan bemorlarda subklinik sinovit chastotasini aniqlash;
3. UTT ning sezuvchanlik va spetsifiklik ko'rsatkichlarini klinik tekshiruv hamda MRT bilan solishtirish;
4. Olingan natijalar asosida UTT ni RA monitoringida qo'llash bo'yicha amaliy tavsiyalar ishlab chiqish.

ADABIYOTLAR SHARHI

OMERACT (Outcome Measures in Rheumatology) revmatologik ultratovush guruhi tomonidan ishlab chiqilgan konsensus ta'riflarga ko'ra, sinovit — bo'g'im ichida siqilmaydigan, noadekvat kompressiyalanadigan, ko'pincha anormal Doppler signali bilan kechuvchi anormal gipoexogen to'qima sifatida tavsiflanadi. Shu asosda grayscale (B-rejim) va Power Doppler sinovitini 0 dan 3 gradusgacha bo'lgan yarim-miqdoriy shkalada baholash tizimlari keng qo'llaniladi.

Bir qator klassik tadqiqotlarda (jumladan Szkudlarek va hammualliflar, Wakefield va hammualliflar tomonidan olib borilgan ishlarda) ko'rsatilishicha, UTT metakarpofalangeal va proksimal interfalangeal bo'g'imlardagi sinovit va erroziyalarni aniqlashda oddiy rentgenografiyaga qaraganda

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sezilarli darajada yuqori sezuvchanlikka ega bo'lib, ko'p jihatdan MRT natijalariga yaqinlashadi. Shu bilan birga, D'Agostino va hammualliflarning EULAR doirasidagi ishlarida sog'lom populyatsiyada ham minimal darajadagi UTT o'zgarishlari uchrashi mumkinligi qayd etilgan, bu esa natijalarni talqin qilishda yosh va boshqa omillarni hisobga olish zarurligini ko'rsatadi.

EULAR (Yevropa revmatologlar ligasi) tomonidan chop etilgan "imaging in RA" bo'yicha tavsiyalarda UTT kasallik faolligini monitoring qilish, davo samaradorligini baholash va subklinik yallig'lanishni aniqlashda qo'shimcha vosita sifatida qo'llanilishi tavsiya etiladi. Shu bilan birga, adabiyotlarda UTT natijalarining operatorga bog'liqligi, datchik bosimi va texnik sozlamalarning natijaga ta'siri kabi cheklovlar ham keng muhokama qilinadi, bu esa standartlashtirilgan protokollar va mutaxassislar tayyorgarligining ahamiyatini ko'rsatadi.

Umumiy olganda, mavjud adabiyotlar UTT ning RA da erta diagnostika va monitoring vositasi sifatidagi salohiyatini tasdiqlaydi, biroq mahalliy klinik sharoitlarda uning amaliy samaradorligini baholovchi tadqiqotlar hali yetarli emas, bu esa ushbu ishning dolzarbligini belgilaydi.

METODOLOGIYA

Tadqiqot dizayni va bemorlar

Tadqiqot kesma (birlashtirilgan, qiyosiy) tipdagi klinik tadqiqot sifatida rejalashtirildi. Tadqiqotga 2024–2026 yillar davomida revmatologiya bo'limida kuzatuvda bo'lgan, ACR/EULAR 2010 yil mezonlariga muvofiq RA tashxisi tasdiqlangan 90 nafar bemor kiritildi. Bemorlarning umumiy tavsifi 1-jadvalda keltirilgan.

1-jadval. Tadqiqotga kiritilgan bemorlarning umumiy klinik-demografik tavsifi

Ko'rsatkich	Qiymat
Bemorlar soni (n)	90
Yosh, o'rtacha ± SD (yil)	47,3 ± 11,6
Jinsi (ayol / erkak), n (%)	71 (78,9%) / 19 (21,1%)
Kasallik davomiyligi, o'rtacha (yil)	6,2 ± 4,8
RF va/yoki ACPA musbat, n (%)	68 (75,6%)
DAS28-CRP, o'rtacha ± SD	3,8 ± 1,2
Klinik remissiya/past faollikda bo'lganlar, n (%)	34 (37,8%)

Tekshiruv protokoli

Barcha bemorlarda ikkala qo'lning quyidagi bo'g'imlari tekshirildi: bilak bo'g'imi, II–V metakarpofalangeal (MKF) bo'g'imlar va II–V proksimal interfalangeal (PIF) bo'g'imlar. UTT 10–13 MHz chastotali chiziqli datchikka ega zamonaviy Mindray Consona N9 ultratovush apparati yordamida, dorsal proyeksiyada, ham uzunasiga, ham ko'ndalang kesimlarda amalga oshirildi. Har bir bo'g'imda B-rejim (sinovial gipertrofiya) va Power Doppler rejimi (vaskulyarizatsiya) baholanib, OMERACT konsensus tizimi bo'yicha 0 dan 3 gradusgacha bahoga ega bo'ldi (2-jadval).

2-jadval. Sinovitni baholashning OMERACT yarim-miqdoriy shkalasi (0–3 daraja)

Daraja	Grayscale (B-rejim) tavsifi	Power Doppler tavsifi
0	Sinovial qalinlashish yo'q	Vaskulyar signal aniqlanmadi
1	Yengil sinovial qalinlashish	1–2 dona alohida signal nuqtasi

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2	O'rtacha darajadagi sinovial qalinlashish, bo'g'im bo'shlig'ining yarmigacha to'ldirilgan	Signal nuqtalari bo'g'im sohasining yarmidan kamini egallaydi
3	Ifodalangan sinovial gipertrofiya, bo'g'im bo'shlig'i to'liq to'ldirilgan	Sezilarli, tarqoq vaskulyarizatsiya, bo'g'im sohasining yarmidan ko'pini egallaydi

Bemorlarning 40 nafarida (44,4%) qo'shimcha ravishda bilak bo'g'imining MRT tekshiruvi (kontrastlash bilan) o'tkazildi, bu UTT natijalarini "oltin standart"ga yaqinroq usul bilan solishtirish imkonini berdi. Statistik tahlil uchun tavsifiy statistika, sezuvchanlik/spetsifiklik ko'rsatkichlari, Xi-kvadrat va Kappa mos kelish koeffitsienti qo'llanildi ($p<0,05$ statistik ahamiyatli deb qabul qilindi).

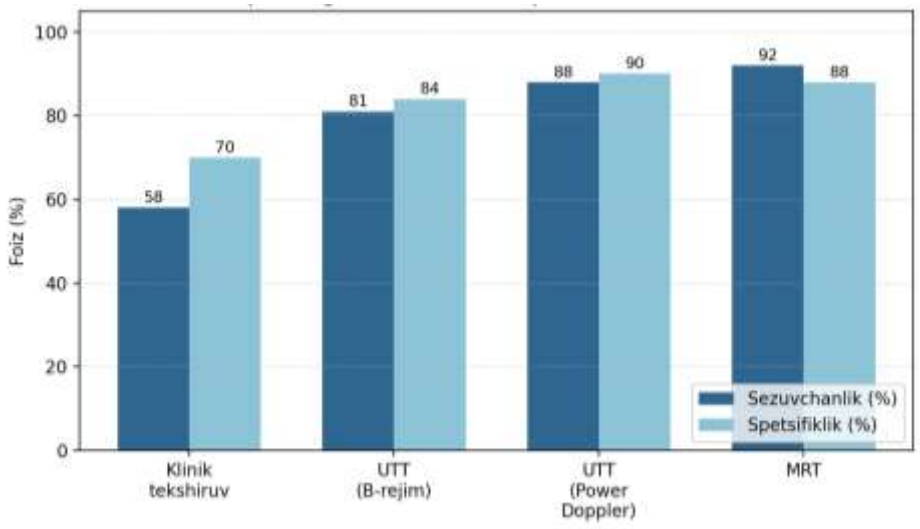
NATIJALAR

O'tkazilgan tekshiruvlar natijasida jami 90 bemorning 76 tasida (84,4%) kamida bitta bo'g'imda UTT orqali sinovit belgilari (grayscale ≥1 va/yoki Power Doppler ≥1) aniqlandi, klinik tekshiruvda esa bunday belgilar faqat 54 bemorda (60,0%) qayd etildi. Ayniqsa e'tiborga molik jihati — klinik jihatdan remissiya yoki past faollikda deb baholangan 34 bemorning 19 tasida (55,9%) UTT orqali subklinik sinovit (asosan 1–2-daraja) tasdiqlandi.

3-jadval. Diagnostika usullari bo'yicha qiyosiy natijalar

Ko'rsatkich	Klinik tekshiruv	UTT (B-rejim + PD)	MRT (n=40)
Sezuvchanlik, %	58	88	92
Spetsifiklik, %	70	90	88
Aniqlangan sinovit holatlari, n (%)	54 (60,0%)	76 (84,4%)	37/40 (92,5%)
Subklinik sinovit (remissiyadagilarda), n	0	19	16 (n=25 tekshirilgan)

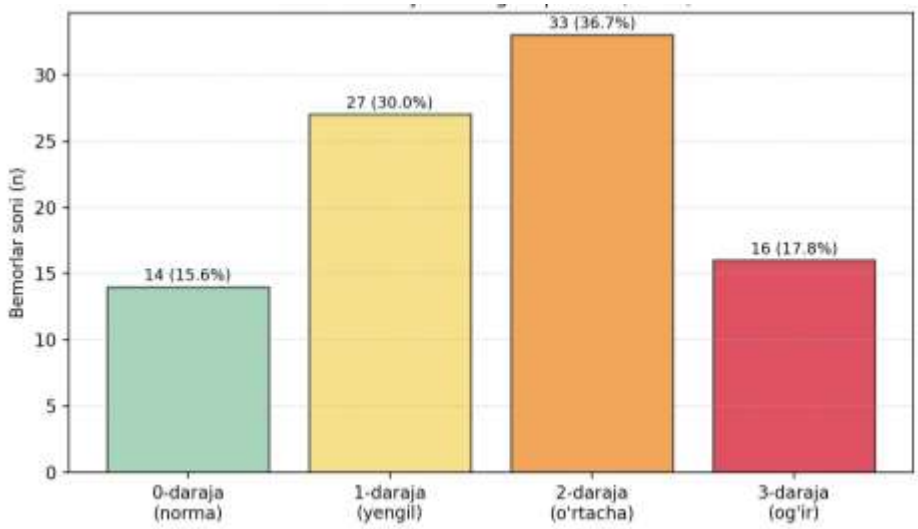
1-diagramma. *Turli diagnostika usullarining sezuvchanlik va spetsifiklik ko'rsatkichlari*



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UTT orqali aniqlangan sinovit darajalarining taqsimoti 2-diagrammada keltirilgan: bemorlarning aksariyat qismida 1- va 2-darajadagi sinovit qayd etilgan, bu ko'pincha klinik jihatdan sezilmaydigan, ammo instrumental tekshiruvda aniq ko'rinadigan yallig'lanish jarayoni ekanligini tasdiqlaydi.

2-diagramma. UTT bo'yicha aniqlangan sinovit darajalarining bemorlar orasida taqsimoti (n=90)



MUHOKAMA

Olingan natijalar UTT ning RA bemorlarida sinovitni aniqlashda klinik tekshiruvga nisbatan sezilarli darajada yuqori sezuvchanlikka ega ekanligini tasdiqlaydi, bu esa adabiyotlarda keltirilgan ma'lumotlarga mos keladi. Ayniqsa muhim topilma — klinik remissiyadagi bemorlarning yarmidan ko'prog'ida subklinik sinovitning aniqlanishi bo'lib, bu "klinik remissiya" tushunchasining instrumental tasdiqlanishga muhtojligini ko'rsatadi. Bunday yashirin yallig'lanish, davolanmagan holda, vaqt o'tishi bilan strukturaviy progressiya (erroziyalar, bo'g'im deformatsiyasi) xavfini oshirishi mumkin.

Power Doppler rejimining qo'shilishi diagnostik aniqlikni yanada oshirdi, chunki u nafaqat mexanik gipertrofiyani, balki to'qimadagi faol yallig'lanish jarayonini — neoangiogenezni — bevosita aks ettiradi. Shu sababli B-rejim va Power Doppler natijalarini birgalikda baholash kasallik faolligini yanada to'g'ri tasniflash imkonini beradi.

Shu bilan birga, UTT natijalarini talqin qilishda bir qator cheklovlarni hisobga olish zarur: usul operatorning tajribasi va texnik sozlamalarga (masalan, datchik bosimi, Doppler chastotasi) sezilarli darajada bog'liq, bu esa natijalarning markazlar orasida farq qilishiga olib kelishi mumkin. Bundan tashqari, ayrim sog'lom shaxslarda ham yengil darajadagi UTT o'zgarishlari uchrashi mumkinligi natijalarni yoshga va boshqa individual xususiyatlarga moslab talqin qilish zarurligini ko'rsatadi. Tadqiqotimizda MRT bilan solishtirish faqat bemorlarning bir qismida o'tkazilgani ham natijalarning umumiy tadqiqot populyatsiyasiga to'liq ekstrapolyatsiya qilinishini cheklaydi.

Shunga qaramay, UTT ning nisbatan arzonligi, radiatsiya bilan bog'liq bo'lmaganligi, real vaqt rejimida amalga oshirilishi va MRT ga yaqin diagnostik aniqligi uni kundalik revmatologik amaliyotda, xususan kasallik faolligini monitoring qilish va davo samaradorligini baholashda, keng qo'llash uchun jozibador vosita qiladi.

XULOSA

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Ultratovush tekshiruvi (B-rejim va Power Doppler) revmatoid artritda qo'l-panja bo'g'imlari sinovitini aniqlashda klinik tekshiruvga nisbatan sezilarli yuqori sezuvchanlik (88% vs 58%) va spetsifiklikka (90% vs 70%) ega.

1. Klinik remissiyadagi bemorlarning muhim qismida (55,9%) UTT yordamida subklinik sinovit aniqlanishi, klinik baholashning yagona mezon sifatida yetarli emasligini ko'rsatadi.
2. Power Doppler rejimi sinovial to'qimadagi faol vaskulyarizatsiyani ko'rsatish orqali kasallik faolligini baholashning qo'shimcha va qimmatli mezoni hisoblanadi.
3. UTT natijalari MRT natijalariga yaqin diagnostik aniqlikka ega bo'lib, kamroq xarajat va yuqori qulaylik bilan ajralib turadi.
4. UTT ni RA bemorlarini erta diagnostika qilish, kasallik faolligini monitoring qilish va davo samaradorligini baholash maqsadida revmatologik amaliyotga kengroq joriy etish tavsiya etiladi, biroq bu jarayonda standartlashtirilgan protokollar va mutaxassislarni maxsus tayyorlashga alohida e'tibor qaratilishi lozim.

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THE ROLE OF RADIOLOGY SURGERY IN COMPLICATED FORMS OF GALLSTONE DISEASE

Abstract
Gallstone disease (GSD) remains one of the most prevalent disorders of the hepatobiliary system worldwide and is responsible for substantial morbidity, hospital admissions, and healthcare costs. Although many patients remain asymptomatic, approximately 20–30% develop severe complications, including acute calculous cholecystitis, choledocholithiasis, acute cholangitis, gallstone pancreatitis, biliary obstruction, hepatic abscesses, and sepsis. These complications require rapid diagnosis and timely intervention to reduce mortality and preserve biliary function.
Keywords: Gallstone disease, complicated cholelithiasis, interventional radiology, biliary drainage, percutaneous cholecystostomy, biliary stenting, cholangioscopy, ultrasound, computed tomography.

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O'T-TOSH KASALLIGINING ASORATLANGAN SHAKLLARIDA RENTGEN JARROHLIGINING ROLI

Annotatsiya
O't-tosh kasalligining asoratlangan shakllarida interventsion radiologiyaning o'rni
O't-tosh kasalligi gepatobiliar tizimning eng ko'p uchraydigan kasalliklaridan biri bo'lib, butun dunyoda kasallanish, shifoxonaga yotqizilish va o'lim ko'rsatkichlarining muhim sabablaridan biri hisoblanadi. Bemorlarning aksariyatida kasallik simptomsiz kechishiga qaramay, taxminan 20–30% holatlarda o'tkir kalkulyoz xoletsistit, xoledoxolitiaz, o'tkir xolangit, biliar pankreatit, mexanik sariqlik, jigar abssessi va sepsis kabi og'ir asoratlar rivojlanadi.
So'nggi yillarda interventsion radiologiya sohasidagi yutuqlar o't-tosh kasalligining asoratlangan shakllarini davolash usullarini tubdan o'zgartirdi. Ultratovush va rentgen nazorati ostida

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bajariladigan minimal invaziv muolajalar, jumladan perkutan transhepatik biliar drenaj (PTBD), perkutan xoletsistostomiya, biliar stentlash, perkutan xolangioskopiya hamda tasvir nazorati ostida toshlarni olib tashlash usullari yuqori operatsion xavfga ega yoki endoskopik muolajalarni bajarish imkoni bo‘lmagan bemorlarda samarali davolash usuli hisoblanadi.

Kalit so‘zlar: o‘t-tosh kasalligi, asoratlangan xoletiaz, interventsion radiologiya, biliar drenaj, perkutan xoletsistostomiya , biliar stentlash, xolangioskopiya, ultratovush tekshiruvi, kompyuter tomografiyasi.

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РОЛЬ ИНТЕРВЕНЦИОННОЙ РАДИОЛОГИИ ПРИ ОСЛОЖНЁННЫХ ФОРМАХ ЖЕЛЧНОКАМЕННОЙ БОЛЕЗНИ

Аннотация

Желчнокаменная болезнь (ЖКБ) является одним из наиболее распространённых заболеваний гепатобилиарной системы и остаётся важной причиной госпитализации, инвалидизации и смертности во всём мире. Несмотря на бессимптомное течение у большинства пациентов, примерно у 20–30% развиваются тяжёлые осложнения, включая острый калькулёзный холецистит, холедохолитиаз, острый холангит, билиарный панкреатит, механическую желтуху, абсцессыпеченииисепсис.

Современные достижения интервенционной радиологии значительно изменили подходы к лечению осложнённых форм желчнокаменной болезни. Минимально инвазивные вмешательства под визуальным контролем, такие как чрескожное чреспечёночное билиарное дренирование (ЧЧБД), чрескожная холецистостомия, билиарное стентирование, чрескожная холангиоскопия и удаление конкрементов под лучевым контролем, являются эффективной альтернативой хирургическому лечению у пациентов высокого операционного риска или при невозможности выполнения эндоскопических вмешательств.

Ключевые слова: желчнокаменная болезнь, осложнённая желчнокаменная болезнь, интервенционная радиология, билиарное дренирование, чрескожная холецистостомия, билиарное стентирование, холангиоскопия, ультразвуковое исследование, компьютерная томограф

Introduction

Gallstone disease is among the most common gastrointestinal disorders affecting adults worldwide. The global prevalence varies between 10% and 20% depending on geographic location, ethnicity, dietary habits, age, sex, and metabolic risk factors. Increasing rates of obesity, diabetes mellitus,

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metabolic syndrome, and aging populations have contributed to the growing incidence of gallstone-related complications during the last decade.

Gallstones develop due to disturbances in bile composition, impaired gallbladder motility, chronic inflammation, and biliary stasis. Cholesterol stones account for approximately 80–90% of all gallstones, whereas pigment stones are more frequently associated with chronic hemolytic disorders andbiliaryinfections.

Although the majority of patients remain asymptomatic throughout life, nearly one-third eventually experience complications requiring urgent medical attention. Acute calculous cholecystitis is the most frequent complication and results from obstruction of the cystic duct by gallstones. Delayed treatment may lead to gallbladder empyema, gangrenous cholecystitis, gallbladder perforation, and generalized peritonitis. Migration of gallstones into the common bile duct can cause choledocholithiasis, obstructive jaundice, ascending cholangitis, secondary biliary cirrhosis, and acute biliary pancreatitis. These conditions are associated with increased morbidity and mortality if diagnosis and treatment are delayed.

For many decades, surgery remained the standard treatment for complicated gallstone disease. However, a considerable proportion of patients are elderly or suffer from severe cardiovascular, pulmonary, hepatic, or renal diseases that significantly increase operative risk. In such patients, minimally invasive image-guided interventions have emerged as valuable alternatives capable of providing both emergency decompression and definitive treatment.

Interventional radiology has experienced remarkable progress due to improvements in ultrasound guidance, fluoroscopy, computed tomography, digital subtraction angiography, and dedicated biliary intervention devices. These advances have expanded the role of radiologists from purely diagnostic imaging to therapeutic management of hepatobiliary disorders.

Today, interventional radiology offers several effective techniques for the management of complicated gallstone disease, including percutaneous transhepatic biliary drainage (PTBD), percutaneous cholecystostomy, percutaneous biliary stenting, image-guided stone extraction, balloon dilatation of biliary strictures, and percutaneous cholangioscopy. These procedures are particularly beneficial for critically ill patients, individuals with failed ERCP, altered postoperative anatomy, malignant biliary obstruction, or severe sepsis requiring urgent biliary decompression.

Recent international guidelines published between 2025 and 2026 emphasize the importance of multidisciplinary management involving radiologists, hepatobiliary surgeons, gastroenterologists, anesthesiologists, and intensive care specialists. Advances in image-guided interventions have substantially reduced procedure-related complications while improving technical success rates and long-term patient survival.

The aim of this review is to evaluate the current role of interventional radiology in the diagnosis and treatment of complicated gallstone disease, summarize recent technological developments, compare available minimally invasive procedures, and discuss future directions for clinical practice based on the latest international evidence.

Materials and Methods

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This study was conducted to evaluate the role of interventional radiology in the diagnosis and treatment of complicated gallstone disease. A retrospective observational study was performed involving patients diagnosed with complicated forms of gallstone disease who were treated at the Department of Radiology and the Department of General Surgery of Samarkand State Medical University.

A total of 50 patients diagnosed with complicated gallstone disease were included in the study. Patients were selected based on clinical presentation, laboratory findings, and imaging examinations. The inclusion criteria comprised patients with acute calculous cholecystitis, choledocholithiasis, acute cholangitis, gallstone pancreatitis, obstructive jaundice, or other biliary complications requiring imaging evaluation and minimally invasive intervention. Patients with malignant biliary obstruction or incomplete medical records were excluded from the study.

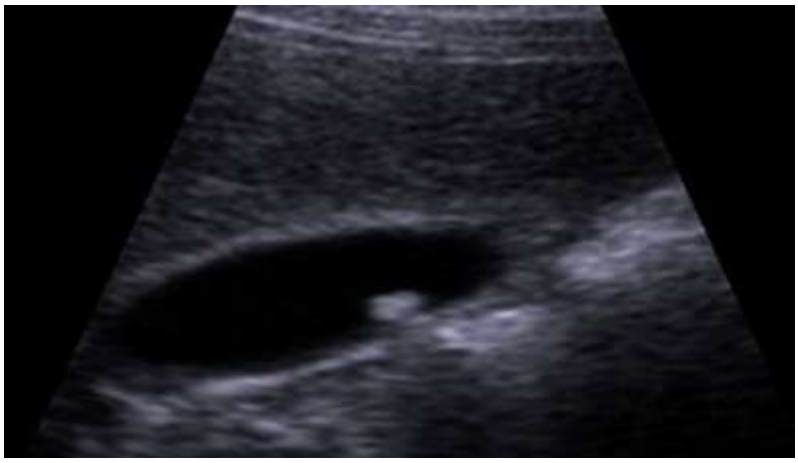
All patients underwent comprehensive ultrasonographic examination using the GE Versana Balance ultrasound system. Ultrasound was performed to evaluate the gallbladder, intrahepatic and extrahepatic bile ducts, liver parenchyma, and associated complications. Color Doppler imaging was applied when vascular assessment was required.

When clinically indicated, additional imaging studies, including contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP), were performed to assess biliary obstruction, inflammatory changes, stone localization, and procedure planning.

Interventional radiology procedures were selected according to the patient's clinical condition, imaging findings, and current international recommendations. These procedures included percutaneous transhepatic biliary drainage (PTBD), percutaneous cholecystostomy, biliary stent placement, and other image-guided biliary interventions. All procedures were performed under ultrasound and fluoroscopic guidance using standard sterile techniques.

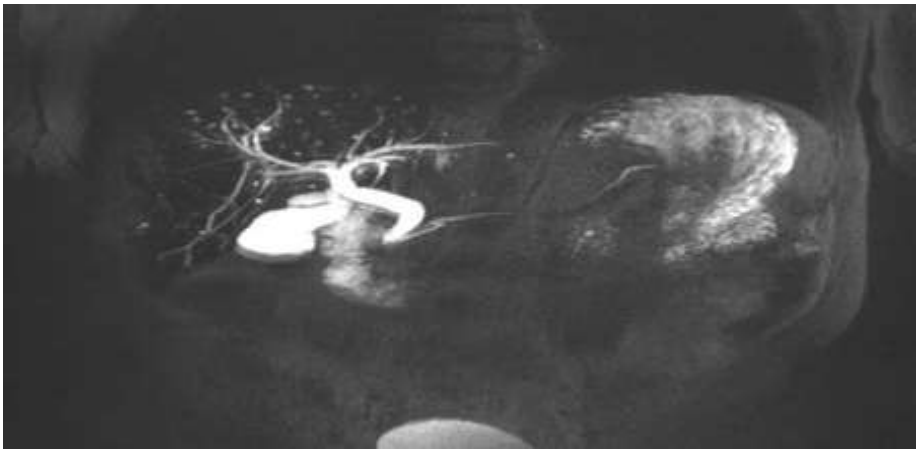
Clinical effectiveness was assessed by evaluating symptom relief, reduction of serum bilirubin and inflammatory markers, restoration of biliary drainage, imaging findings during follow-up, duration of hospitalization, and procedure-related complications.

The collected clinical and imaging data were analyzed using descriptive statistical methods. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages.



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Magnetic Resonance Cholangiopancreatography (MRCP)



Results

A total of 50 patients with complicated gallstone disease were included in the study. The diagnosis was established using clinical findings, laboratory investigations, and multimodal imaging techniques.

Ultrasonography successfully identified gallstones, gallbladder wall thickening, biliary dilatation, and inflammatory changes in the majority of patients, confirming its value as the primary diagnostic modality. CT and MRI/MRCP provided additional information regarding the extent of biliary obstruction, associated complications, and anatomical variations, which were essential for treatment planning.

Image-guided interventional procedures were successfully performed in patients who required minimally invasive biliary decompression. Percutaneous transhepatic biliary drainage and percutaneous cholecystostomy effectively relieved biliary obstruction and improved the clinical condition of patients presenting with severe acute cholangitis, obstructive jaundice, or acute calculous cholecystitis.

Following treatment, patients demonstrated clinical improvement characterized by reduction of abdominal pain, normalization of body temperature, improvement of laboratory parameters, restoration of bile flow, and decreased inflammatory response. Follow-up imaging confirmed adequate catheter position and resolution of biliary obstruction in successfully treated patients.

Procedure-related complications were infrequent and were managed conservatively or by additional image-guided intervention when necessary. Overall, minimally invasive interventional radiology techniques proved to be safe and effective for the management of complicated gallstone disease.

Discussion

The present study evaluated the role of interventional radiology in the diagnosis and management of patients with complicated gallstone disease. The findings demonstrate that modern imaging modalities combined with minimally invasive image-guided interventions play a crucial role in improving clinical outcomes and reducing the need for emergency surgical procedures.

Ultrasonography was the primary imaging modality used in this study because of its wide

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availability, rapid performance, and high diagnostic value in detecting gallstones, gallbladder wall thickening, biliary dilatation, and inflammatory changes. However, in patients with complex biliary obstruction or inconclusive ultrasound findings, CT and MRI/MRCP provided additional anatomical information that was essential for treatment planning. These observations are consistent with recent international recommendations, which emphasize a multimodality imaging approach for complicated biliary diseases.

The use of interventional radiology procedures, including percutaneous transhepatic biliary drainage (PTBD), percutaneous cholecystostomy, and biliary stenting, provided effective biliary decompression in patients with severe complications such as acute cholangitis, obstructive jaundice, and acute calculous cholecystitis. These minimally invasive techniques contributed to rapid clinical stabilization and created favorable conditions for subsequent definitive management when required.

The results of this study are in agreement with recently published international studies, which have reported high technical success rates and low complication rates for image-guided biliary interventions. Recent evidence suggests that PTBD remains an effective alternative in patients with failed or contraindicated ERCP, while percutaneous cholecystostomy has become an accepted treatment option for critically ill patients who are not suitable candidates for emergency surgery.

An important strength of the present study is the integration of diagnostic imaging and therapeutic intervention within a single clinical pathway. The combination of ultrasonography, CT, MRI/MRCP, and fluoroscopic guidance allowed accurate diagnosis, careful procedural planning, and continuous post-procedural monitoring. This comprehensive radiological approach improved treatment efficiency and reduced the risk of procedure-related complications.

Despite these encouraging findings, several limitations should be acknowledged. This study was conducted at a single institution and included a relatively limited number of patients. In addition, the retrospective design may have introduced selection bias. Future multicenter prospective studies with larger patient populations are required to validate these findings and establish standardized treatment algorithms for complicated gallstone disease.

Overall, the present study confirms that interventional radiology has become an indispensable component of modern hepatobiliary medicine. The integration of advanced imaging technologies with minimally invasive therapeutic procedures significantly improves patient management, reduces surgical risk, shortens hospital stay, and enhances clinical outcomes. Continued technological innovation and multidisciplinary collaboration are expected to further expand the role of interventional radiology in the treatment of complicated gallstone disease.

Conclusion

Complicated gallstone disease remains a significant clinical challenge because of its high prevalence, potential for life-threatening complications, and increasing incidence among elderly patients and individuals with multiple comorbidities. Early diagnosis and timely therapeutic intervention are essential to reduce morbidity, mortality, and long-term hepatobiliary dysfunction.

This review demonstrates that modern imaging modalities, including ultrasonography, computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography, play a fundamental role in the comprehensive management of complicated gallstone disease. These techniques not only facilitate accurate diagnosis but also provide essential guidance for minimally

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invasive therapeutic procedures.

Interventional radiology has become an indispensable component of contemporary hepatobiliary treatment. Image-guided procedures such as percutaneous transhepatic biliary drainage, percutaneous cholecystostomy, biliary stent placement, percutaneous cholangioscopy, and image-guided stone extraction provide safe and effective alternatives for patients in whom conventional surgery or endoscopic treatment is contraindicated or unsuccessful.

The analysis of recent international publications published during 2025–2026 indicates that technological innovations—including digital cholangioscopy, cone-beam CT navigation, fusion imaging, advanced biliary stents, robotic-assisted interventions, and artificial intelligence-assisted procedural planning—have significantly improved procedural precision, technical success, and long-term clinical outcomes. These developments have reduced procedure-related complications, shortened hospitalization, and enhanced patients' quality of life.

A multidisciplinary approach involving interventional radiologists, hepatobiliary surgeons, gastroenterologists, diagnostic radiologists, anesthesiologists, and intensive care specialists is essential for optimizing treatment strategies. Individualized patient assessment allows the selection of the most appropriate minimally invasive intervention based on disease severity, anatomical characteristics, and overall clinical condition.

Future research should focus on large multicenter prospective clinical trials evaluating the long-term efficacy, cost-effectiveness, and safety of emerging interventional radiology techniques. Further integration of artificial intelligence, robotic navigation systems, and next-generation biodegradable biliary devices is expected to transform the management of complicated gallstone disease and establish new standards of patient care.

In conclusion, interventional radiology has evolved from a supportive imaging discipline into a key therapeutic specialty in the management of complicated gallstone disease. Continuous technological progress and evidence-based clinical practice will further strengthen its role in improving patient survival, reducing treatment-related complications, and providing effective minimally invasive alternatives to conventional surgical management.

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OSHQOZON YARASIDAN MASSIV QON KETISHLARIDA GASTREKTOMIYANING O‘ZIGA XOS XUSUSIYATLARI

Annotatsiya: Maqolada oshqozon yarasining dahshatli asoratlaridan biri: malignizatsiya va ko‘p miqdorda qon ketishi haqida so‘z boradi. Adabiyotlardan ma’lumki, ushbu asoratlarning bir vaqtning o‘zida rivojlanishi bemorlarning ahvolini og‘irlashtiradi, gastrektomiyani qo‘llash bemorning hayotini saqlab qolish uchun yagona imkoniyatdir.

Kalit so‘zlar: yara malignizatsiyasi, massiv qon ketish, gastrektomiya

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ОСОБЕННОСТИ ГАСТРЭКТОМИИ ПРИ МАССИВНЫХ ЖЕЛУДОЧНЫХ КРОВОТЕЧЕНИЯХ

Аннотация: В статье идёт речь об одних из грозных осложнениях язв желудка: малигнизации и массивной кровотечении. По литературам ясно, что одновременное развитие этих осложнений усугубляет тяжесть состояния пациентов, что применение гастрэктомии является единственным шансом для сохранения жизни пациента.

Ключевые слова: малигнизация язвы, массивное кровотечение, гастрэктомия.

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FEATURES OF GASTRECTOMY FOR MASSIVE GASTRIC BLEEDING

Abstract: The article discusses one of the most dangerous complications of stomach ulcers: malignancy and massive bleeding. It is clear from the literature that the simultaneous development of these complications exacerbates the severity of the patients' condition, and that the use of gastrectomy is the only chance to save the patient's life.

Keywords: ulcer malignancy, massive bleeding, gastrectomy.

Oshqozon saratoni dunyoda va O‘zbekiston Respublikasida eng keng tarqalgan onkologik kasalliklardan biri bo‘lib, uchrash darajasi bo‘yicha ikkinchi o‘rinni egallaydi. Gastrektomiya oshqozon saratonini jarrohlik yo‘li bilan davolashdagi asosiy amaliyotlardan biridir. Qizilo‘ngach anastomozlarini shakllantirish bilan tugaydigan operatsiyalar eng qiyin hisoblanadi va operatsiyadan keyingi o‘lim holatlarining asosiy sabablaridan biri ularning muvaffaqiyatsizligi bo‘lib qolmoqda. Bemorlarning 60-80 foizigacha bo‘lgan qismi kasallikning og‘ir shakllari va og‘ir asoratlari bilan davolanishga qabul qilinadi. Ba’zi hollarda me’da o‘smalari teshilishi fonida, shuningdek, me’da onkologik kasalliklari bilan og‘rigan bemorlarning 15% dan ko‘prog‘ida uchraydigan profuz qon ketish darajasida rivojlanadigan peritonit bilan og‘rigan bemorlarda majburiy gastrektomiya qilishga to‘g‘ri keladi. Gastrektomiyadan so‘ng qizilo‘ngach-ichak anastomozi (QIAN) yetishmovchiligi

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bemorlarning 6-11% da rivojlanadi va yuqori o‘lim ko‘rsatkichi bilan kechadi, bu ko‘rsatkich 100% ga yaqinlashadi.

Ular orasida bemorlarning hayoti uchun eng og‘ir va xavflilari o‘tkir oshqozon qon ketishi (O‘OQ) bo‘lib, ba’zida jarroh operatsiyani gastrektomiya bilan yakunlashi kerak. Gastrektomiya o‘ta murakkab va xavfli jarrohlik amaliyoti bo‘lib, hatto rejali jarrohlik amaliyotida ham operatsiyadan keyingi ko‘plab asoratlar rivojlanishi mumkin va bunday aralashuvdan so‘ng o‘lim darajasi 20 foizgacha yetishi mumkin.

So‘nggi yillarda zamonaviy anesteziologiya va reanimatologiyaning rivojlanishi, gastrektomiya usulining takomillashuvi ko‘p hollarda operatsiyadan keyingi asoratlar chastotasini va o‘limni 2,5-5% gacha sezilarli darajada kamaytirish imkonini berdi.

Shuni ta’kidlash kerakki, shoshilinch jarrohlikda gastrektomiya shoshilinch va bir vaqtning o‘zida majburiy jarrohlik aralashuvi bo‘lib, ko‘pchilik jarrohlar tayyorgarlik ko‘rmagan bemorlarda uning yuqori xavfi tufayli juda ehtiyotkorlik bilan yondashadilar. Adabiyotlarda shoshilinch ravishda gastrektomiya qilish to‘g‘risida juda kam va kam sonli ma’lumotlar keltirilgan.

1999-yilda A.F. Chernousov va hammualliflar qizilo‘ngach anastomozlariga qo‘yiladigan talablarni shakllantirdilar: 1) texnik jihatdan bajarishning soddaligi; 2) choklarning germetikligi va mexanik ishonchliligi; 3) reflyuksning oldini oluvchi mexanizmni yaratish; 4) tikilayotgan to‘qimalar taranglashmaganda ularning qon bilan yetarli darajada ta’minlanishi; 5) tikilayotgan organlar qavatlarini anatomik jihatdan aniq taqqoslash.

Gastrektomiyadan keyin qizilo‘ngach anastomozlarini qo‘yish usullari juda xilma-xildir. To‘g‘ridan-to‘g‘ri ezofagoduodenal anastomoz operatsiyadan keyingi o‘limning yuqoriligi tufayli keng tarqalmagan. Gastrektomiyadan so‘ng ovqat hazm qilish jarayonida o‘n ikki barmoqli ichakni saqlab qolish uchun ingichka ichakdan foydalangan holda turli xil "qo‘shimchalar" variantlari taklif etilgan. Ingichka ichak kiritmalaridan tashqari, mualliflar ileotsekal segment, ko‘richakning turli qismlari, ko‘ndalang chambar ichak, chambar ichakning chap yarmidan foydalanadilar.

Biroq, bunday jarrohlik aralashuvlari ko‘proq mehnat talab qiladi va shunga mos ravishda ko‘proq travmatikdir, o‘n ikki barmoqli ichak tarkibining reflyuksi bilan kechadi, operatsiyadan keyingi asoratlarning yuqori foiziga ega.

Aksariyat jarrohlar qizilo‘ngach-ingichka ichak anastomozlarini bajaradilar. Qizilo‘ngach-ingichka ichak anastomozlarini uch guruhga bo‘lish mumkin: 1) Braun bo‘yicha ichaklararo og‘izchali uzun qovuzloqli ezofagoyeyunoanastomoz; 2) Ru bo‘yicha ichaklararo kirish yo‘li bilan ezofagoyunoanastomoz; 3) ingichka va yo‘g‘on ichak rezervuarlarini hosil qiluvchi anastomozlar.

Gastrektomiya natijalari ko‘p jihatdan qizilo‘ngach-ichak anastomozini shakllantirish usulini tanlashga bog‘liq. Hozirgi vaqtgacha ushbu anastomozni shakllantirishning ko‘plab usullari taklif etilgan, biroq ularning hech biri xavfli asoratlardan, ayniqsa qizilo‘ngach-ichak anastomozi choklarining yetishmovchiligi kabi asoratlardan kafolatlamaydi.

Hozirgi kunga qadar qizilo‘ngach-ichak anastomozini shakllantirishning optimal variantini tanlash masalasi hal etilmagan. Nafaqat qoniqarli bevosita, balki uzoq muddatli natijalarni ham ta’minlaydigan PKAni germetizatsiya qilishning yanada ishonchli usullarini izlash munozara mavzusi bo‘lib qolmoqda.

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Gilyarovich usuli bo‘yicha o‘tkazilgan gastrektomiyadan keyingi eng dahshatli va tez-tez uchraydigan asoratlardan biri TKA yetishmovchiligidir, bu o‘rtacha 5-8% hollarda uchraydi va o‘lim darajasi yuqori bo‘ladi (17-98% gacha, o‘rtacha 46%).

Bir qator mualliflarning fikriga ko‘ra [2, 6], asosiy sabablar tikilayotgan a’zolarda qon aylanishining taranglashishi va buzilishi, qizilo‘ngach devorining anatomik tuzilish xususiyatlarini yetarli darajada hisobga olmaslik, qizilo‘ngachning o‘sma yoki yallig‘lanish infiltratsiyasi sohasida kesilishi, qizilo‘ngach-suv va ichak chetlarining yomon moslashuvidir.

To‘qimalarning yallig‘lanishida PKA choklarining ajralish sohasidagi nuqsonni tikishga urinish samarasiz bo‘lib, hatto nuqsonning kengayishiga olib kelishi mumkin. Bunday asoratlarda, ayniqsa peritoneal belgilar rivojlanganda, relaparatomiya o‘tkazish, nazoeyunal zond yordamida O‘KA va o‘n ikki barmoqli ichakni dekompressiya qilish, keyinchalik ushbu zond orqali ichak tarkibini doimiy aspiratsiya qilish, qizilo‘ngach bo‘shlig‘i, chap diafragma osti bo‘shlig‘i, jigar osti sohasi, o‘ng va chap yonbosh sohasi, kichik chanoq bo‘shlig‘ini drenajlash, Maydl bo‘yicha yeyunostoma qo‘yish, ingichka ichakni retrograd intubatsiya qilish orqali uni dekompressiya qilish, parenteral oziqlantirish, keng ta’sir doirasiga ega antibiotiklar qo‘llash, suyuqliklar yuborish, plazma quyish va boshqalar tavsiya etiladi.

Tadqiqotning maqsadi - o‘tkir oshqozon qon ketishi bilan og‘rigan bemorlarni jarrohlik yo‘li bilan davolash natijalarini yaxshilashdan iborat.

Tadqiqotning materiali va usullari. So‘nggi yillarda Respublika shoshilinch tibbiy yordam ilmiy markazi Samarqand filialining jarrohlik bo‘limlarida, O‘zbekiston Respublikasi Samarqand shahrida 7 nafar bemorda oshqozon-ichak kasalliklari tufayli gastrektomiya amaliyoti o‘tkazilgan. Ular orasida 5 (71,4%) erkak va 2 (28,6%) ayol bor edi. Bemorlarning yoshi 39 yoshdan 67 yoshgacha bo‘lgan. Oshqozon yaralarini aniqlash uchun biz Jonson tasnifini qo‘lladik. 2 ta kuzatuvda oshqozon osti bezi saratonining sababi oshqozon kardial qismining ulkan kallyoz yarasi, 1 tasida subkardiyadagi yaraning malignizatsiyasi, 2 tasida oshqozon tanasi saratonining yarali-infiltrativ shakli, 2 ta holatda esa oshqozon saratonining yarali-infiltrativ shakli ko‘ndalang-chambar ichak tutqichiga o‘sib kirgan.

Qon ketishini baholashda Forest bo‘yicha endoskopik tasnifdan foydalanildi, bunda 6 nafar bemorda arterial qon ketish (F1a), bir bemorda esa ikkita ulkan "o‘pishadigan" malignizatsiyalangan oshqozon yaralaridan venoz qon ketish (F1b) aniqlandi.

Tadqiqotning natijalari. Markazga qabul qilinganda barcha bemorlar og‘ir ahvolda edi, bu sezilarli qon yo‘qotish bilan bog‘liq edi. Qon komponentlaridan foydalangan holda o‘tkazilgan kompleks konservativ terapiya 5 nafar bemorda vaqtincha samarali bo‘ldi. 2 ta kuzatuvda esa konservativ va endoskopik usullar samarasiz bo‘ldi. Bizning fikrimizcha, konservativ terapiya va endoskopik gemostazga rezistentlik me’dadan profuz qon ketishining manbai chap me’da va pankreato-duodenal arteriyalarning yirik tarmoqlari ekanligi bilan bog‘liq edi.

Oshqozondan profuz qon ketish cho‘qqisida 7 nafar bemordan 2 nafarida shoshilinch jarrohlik amaliyoti o‘tkazildi. Shu bilan birga, ularning barchasi endoskopik gemostazning muvaffaqiyatsiz urinishidan keyin profuz oshqozondan qon ketishi boshlanganidan keyin dastlabki 1-3 soat ichida operatsiya qilindi, qolgan bemorlar vaqtinchalik konservativ va endoskopik gemostazdan keyin keyingi 2 kun ichida jarrohlik yo‘li bilan davolandi.

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Ushbu bemorlarda operatsiyalar tinchroq sharoitda, operatsiyadan oldingi ma'lum tayyorgarlikdan so‘ng amalga oshirildi. Shuni ta'kidlash kerakki, 2 nafar bemor kechiktirilgan tartibda operatsiya qilingan, adenokarsinoma tashxisi qo‘yilganda onkologiya markaziga o‘tkazishni rad etgan. O‘sayotgan oshqozon saratonida ko‘ndalang chambar ichak tutqichini rezeksiya qilish bilan kombinatsiyalangan gastrektomiya ikki holatda amalga oshirildi.

Muolaja paytida xavfli o‘smaning morfologik tuzilishini aniqlash imkoniyati faqat kechiktirilgan operatsiyalarda mavjud edi. Ekspress-biopsiya qilish ham imkonsiz edi. Bunday holatlarda operatsiya hajmi mahalliy o‘zgarishlarni intraoperatsion baholash asosida hal qilingan. Operatsiyadan keyingi davrda 1 ta kuzatuvda qizilo‘ngach-oshqozon anastomozi yetishmovchiligi ko‘rinishidagi asoratlar qayd etildi, bu o‘lim bilan yakunlandi. Makropreparatning oshqozon va o‘n ikki barmoqli ichak piyozchasi rezeksiyasi chizig‘i bo‘ylab gistologik tekshiruvi natijasida o‘sma o‘sishi aniqlanmadi.

Operatsiyadan keyingi davrda barcha bemorlarga standart davolash usullari qo‘llanildi: suv-elektrolit va kislota-ishqor muvozanatini tartibga solish, donor qon komponentlarini vena ichiga quyish, keng antibakterial davolash, shuningdek, yondosh kasalliklarni tuzatish. Nazonevral zondni olib tashlash operatsiyadan keyingi o‘rtacha 5-7 kunlarda amalga oshirildi. Og‘iz orqali ovqatlanishga (suyuqlik, ozuqa aralashmalari va boshqalar) 5-8 kun davomida ruxsat berildi. Shunday qilib, profuz oshqozondan qon ketishi bilan asoratlangan kardioezofageal soha patologiyasida ko‘rsatmalarga ko‘ra shoshilinch gastrektomiya o‘tkazish mumkin.

Xulosalar: 1. Qonayotgan me'da rakida operatsiya taktikasi o‘sma qo‘shni a'zolarga o‘sib o‘tgan taqdirda ham uning manbasini yo‘qotishga qaratilgan bo‘lishi kerak.

2. Qonayotgan me'da rakida gastrektomiya barcha zamonaviy onkologik prinsiplarga rioya qilgan holda, shu jumladan takomillashtirilgan metodika bo‘yicha ham bajarilishi mumkin.

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O'TKIR TO'G'RI ICHAK PROLAPSI ASORATLARINI XIRURGIK DAVOLASH XUSUSIYATLARI (AMALIYOTDAN LAVHA)

Annotatsiya: Adabiyotlarda to'g'ri ichakning prolapsi (tushishi) - to'g'ri ichak yoki uning bir qismi tanadagi to'g'ri holatini yo'qotib, harakatchan bo'lib, cho'zilib, anus orqali tashqariga chiqish holati xaqida ko'plab ma'lumotlar keltirilgan. To'g'ri ichak tushishi ko'pincha anal kanal mushaklarining zaiflashishi bilan birga kelib, natijada gaz, axlat va shilliqni ushlab turmaslikka olib keladi. Bu holat ham o'z navbatida qisilish kabi xavfli soratlarga olib kelishi mumkin. Ushbu maqolada rektal prolapsning qisilishi bilan asoratlangan klinik kuzatuvi tavsifi berilgan.

Kalit so'zlar: to'g'ri ichak prolapsi, ileus, sigmostoma, to'g'ri ichakning rezektsiyasi.

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ОСОБЕННОСТИ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ОСЛОЖНЕНИЙ ОСТРОГО ПРОЛАПСА ПРЯМОЙ КИШКИ (СЛУЧАЙ ИЗ ПРАКТИКИ)

Аннотация: В литературе представлено множество сведений о пролапсе (выпадении) прямой кишки - состоянии, при котором прямая кишка или ее часть теряет правильное положение в теле, становится подвижной, растягивается и выходит наружу через анус. Выпадение прямой кишки часто сопровождается ослаблением мышц анального канала, что приводит к недержанию газов, кала и слизи. Это состояние, в свою очередь, может привести к таким опасным явлениям, как ущемление. В данной статье описывается клиническое наблюдение за пролапсом прямой кишки, осложненным компрессией.

Ключевые слова: пролапс прямой кишки, илеус, сигмостома, резекция прямой кишки.

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FEATURES OF SURGICAL TREATMENT FOR COMPLICATIONS OF ACUTE RECTAL PROLAPSE (PRACTICE CLIP)

Abstract: The literature provides extensive information on rectal prolapse—a condition in which the rectum or a part of it loses its correct position in the body, becomes mobile, stretches, and exits through the anus. Rectal prolapse is often accompanied by weakening of the anal canal muscles, resulting in an inability to retain gas, feces, and mucus. This condition, in turn, can lead to dangerous complications such as compression. This article describes the clinical observation of rectal prolapse complicated by compression.

Keywords: rectal prolapse, ileus, sigmoid, resection of the rectum.

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To’g’ri ichakning prolapsi (tushishi) xirurgik amaliyotda kamdan-kam uchraydigan holatlardan hisoblanadi. Barcha koloproktologik bemorlar orasida to’g’ri ichak tushishi 0,3-5,2% holatlarda uchraydi. Erkaklarda ayollarga qaraganda deyarli 2 marta ko’proq kuzatiladi.

To’g’ri ichak tushishi nafaqat polietiologik, balki paydo bo’lishi turli mexanizmlarga ega kasallikdir. Uning kelib chiqishida bemor yoshi, hamroh kasalliklari, kasallikning rivojlanish bosqichi, qisilish darajasi, chanoq bo’shlig’i mushaklari funktsiyasining kompensatsiya holatini va mavjud asoratlarni hisobga olish kerak. Bemorlarning darhol shifokorga murojaat qilmasligining keng tarqalgan sabablaridan biri bu kasallikning gemorroy bilan o’xshash bo’lishi bo’lib, ko’pincha bemorlar shamcha va malhamlar bilan o’zlari davolashga harakat qilishadi. Aslida, to’g’ri ichakning tushishi va gemorroy butunlay boshqacha kasalliklar bo’lib, ular anal kanaldan to’qimalarning kirib borishi tufayli tashqi ko’rinishida o’xshash bo’lishi mumkin. Gemorroyda gemorroid to’qima tushadi va to’g’ri ichakning prolapsasi bilan to’g’ri ichakning bir qismi tushadi.

To’g’ri ichakning prolapsi qisilishi odatda tashqi sfinkterning funktsiyasi saqlanib qolgan dastlabki bosqichlarda sodir bo’ladi. Prolapslangan ichakning siqilishi venoz va keyin arterial qon aylanishining buzilishiga olib keladi, bu esa prolapslangan qismning nekroziga olib keladi, rivojlangan holatlarda peritonit rivojlanadi. Ba’zida prolapslangan ichak qisilganda invaginatsion ichak tutilishi belgilari rivojlanadi.

To’g’ri ichak tushishining asoratlari:

- eroziv-yarali va giperplastik proktit (asosan prolapslangan qism);
- rektal qon ketish;
- takroriy shikastlanishlar va shilliq qavatning surunkali yallig’lanishi tufayli malignizatsiya;
- prolapslangan ichakning yorilishi (kamdan-kam uchraydigan asorat);
- prolapsiyalangan to’g’ri ichakning qisilishi, bu ingichka ichakning prolapslangan qovuzloqlarining strangulyatsiyasi bilan birga bo’lishi mumkin va o’ta og’ir hollarda "perineal churra"ning nekroziga va peritonitning rivojlanishiga olib keladi.

To’g’ri ichak tushishining og’irlik darajasini aniqlash uchun kerakli tekshirish usullari: Anal elektromiografiya, anal manometriya, transrektal UTT, proktografiya (defekografiya) va kolonoskopiya.

Davolash. Bu kasallikda davolash taktikasi, jarrohlik aralashuvining hajmi va usulini barcha omillarni hisobga olgan holda tanlanadi. Operativ davolashda bir necha usulda operatsiyalar o’tkaziladi:

Abdominal operatsiyalar:

1. Rektosakropeksiya operatsiyasi - buning uchun ichakni ma’lum bir holatda ushlab turadigan to’rli allotransplantat (alloprotez) qo’llaniladi. Operatsiya paytida to’g’ri ichak anusni ko’taruvchi mushaklari darajasiga mobilizatsiya qilinadi, so’ngra to’g’ri ichak yuqoriga tortiladi va to’rli allotransplantat yordamida chanoq va to’g’ri ichak o’rtasida joylashgan presakral fastsiyaga mahkamlanadi.2. Кюммел операцияси - мобилизация қилинган тўғри ичакни тугунли чоклар билан чаноқ промонторийсига мустахкамлаш. Ушбу операцияларни очиқ (лапаротомия) усулда ёки лапароскопик тарзда амалга оширилиш мумкин.

Transanal operatsiyalar (anal kanal orqali bajariluvchi operatsiyalar)

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1. Delorma operatsiyasi - ichakning prolapslangan qismining shilliq qavatini ichakni ushlab turuvchi, prolapsdan himoya qiluvchi mushakli manjeta hosil qilgan holda olib tashlash (rezektsiya qilish).

2. Altmeer operatsiyasi - to'g'ri ichakni yoki uning prolapslangan qismini rezektsiya qilish va kolo-anal anastomoz hosil qilish.

Shoshilinch jarrohlikda prolapslangan to'g'ri ichakni strangulyatsiya qilish uchun tanlov operatsiyasi uning perineal rezektsiyasidir. Prolapslangan to'g'ri ichakni rezektsiya qilish operatsiyasi birinchi marta Rikord (1833) tomonidan amalga oshirilgan. Keyinchalik J. Mikulich (1888) ishlab chiqqan va batafsil tavsiflagan. Bunda prolapslangan to'g'ri ichak anus orqali rezektsiya qilinib, uning devorini qavatma-qavat sirkulyar tiklanadi va keyinchalik ichkariga to'g'rilanadi. Ushbu operatsiya amalda keng qo'llanilmadi (o'lim darajasi 20%ga etdi).

Biz to'g'ri ichakning strangulyatsiyasi va nekrozi bilan asoratlangan to'g'ri ichak prolapsasining klinik holatini keltiramiz.

Klinik misol:

Bemor N., 41 yoshda, 2022 yil 12 fevralь kuni Samarqand viloyati Jomboy tuman tibbiyot birlashmasiga anus sohasidagi ichakning chiqib turishiga va to'g'rilanmasligiga, shu sohadagi kuchli og'riq va umumiy darmonsizlikka shikoyati bilan murojaat qilgan.

Anamnezidan bemor o'zini "uzoq vaqtdan beri" kasal deb hisoblaydi, aniq muddatni ayta olmaydi. Kasallik defekatsiyadan keyin to'g'ri ichakning tushishi bilan boshlangan, qo'lda yordamida u osonlikcha ichkariga to'g'rilangan. Jismoniy zo'riqish va kuchanish vaqtida to'g'ri ichak prolapsi kuzatilmagan. Keyinchalik, defekatsiya paytida qon kelishi (dastlab, tomchilab, keyin laxta-laxta qon kelishi) kuzatilgan, ba'zan defekatsiya vaqtida axlatsiz faqat qon ajralishi kuzatilgan. Axlat bilan birga ajraluvchi qon miqdori asta-sekin ko'paygan. Bemor kelishidan 1 soat oldin defekatsiyadan so'ng to'g'ri ichakni ichkariga to'g'rilay olmagan va Jomboy tuman tibbiyot birlashmasiga murojaat qilgan. Bemor navbatchi xirurglar tomonidan ko'rilib, "To'g'ri ichak tushishi, shilliq qavatning qisilishi va nekrozi" diagnozi qo'yilgan. Bemor Jomboy TTBda yotishdan bosh tortib, RShTYoIM Samarqand filialiga murojaat qilgan.

Ob'ektiv ko'rganda: bemor umumiy ahvoli nisbatan og'ir, xushi ravshan, savollarga aniq javob beradi. Teri qoplamlari va shilliq pardalari och pushti rangda, oqimtir. Nafas olishi erkin, burun orqali. Auskulьtatsiyada o'pkalarida vezikulyar nafas eshitiladi. Pulьs ritmik, o'rtacha taranglikda va to'liqlikda, 1 daqiqaga 94 marta. Auskulьtatsiyada yurak tonlari bo'g'iqlashgan. Arterial qon bosimi – 100/60 mm simob ustuniga teng. Tili nam, oq karash bilan qoplangan. Qorni ovalsimon, simmetrik, dam, nafas olishda sust ishtirok etadi. Palьpatsiyada qorin damligi hisoiga biroz og'riqli. Jigari va talog'i paypaslanmaydi. Axlati ertalabdan bo'lmagan.

Lokal ko'rik vaqtida, anus sohasida 15 sm uzunlikdagi, to'q qizg'ish rangli, shishgan, diametri 15 sm gacha bo'lgan to'g'ri ichak prolapsi aniqlanadi. Ichak tutilishi belgilari aniqlanadi (1-rasm).

1-rasm. Bemorda to'g'ri ichak tushishi va qisilishining lokal ko'rinishi.

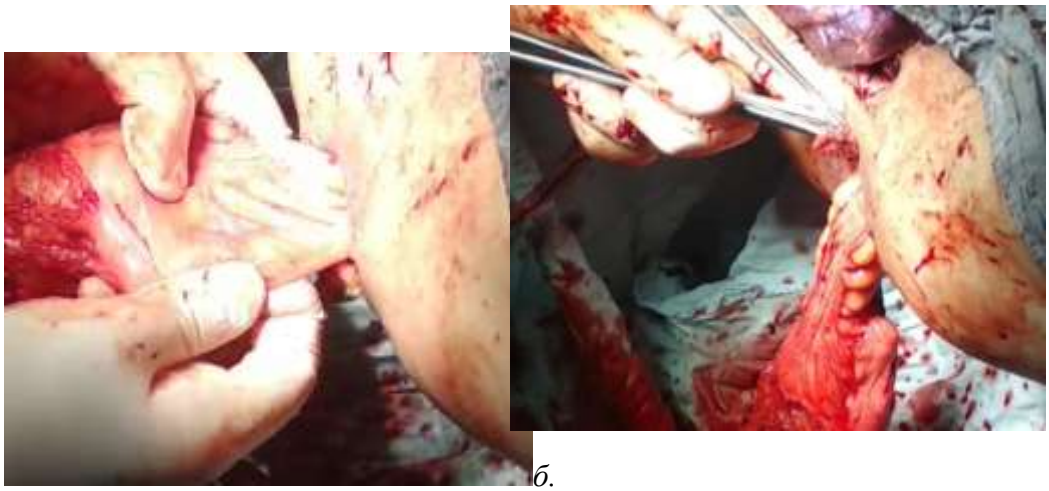
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*Bemorda to'g'ri ichakni to'g'rilashga bo'lgan urinishlar samara bermadi. Bemor shoshilinch operatsiyaga tayyorlandi: Laborator tahlillar: gemoglobin -91,0 g/l, eritrotsit-3,31/l*10X12, leykotsit-12,1*10X9, EChT-18 mm/soat. Qon biokimyoviy tahlili: umumiy bilirubin: 13,5 mk/molь AST-1,50; ALT-2,30; Timol sinamasi—3.0; Umumiy oqsil 65,1. Mochevina 8,1. Qoldiq azot 25,0. Kreatinin 104. EKG: patologiyasiz. Qorin bo'shlig'i UTT: Ichaklar pnevmatozi. Obzor rentgenogramma: Qorinning o'ng yuqori qismida bitta Kloyber kosachasi aniqlanadi.*

Shoshilinch ko'rsatmalarga ko'ra, bemorga to'g'ri ichakning perineal rezektsiyasi va rekto-sigmal anastomoz shakllantirish operatsiyasi bajarildi (2-rasm):.

2-rasm. *To'g'ri ichakning perineal rezektsiyasi va rekto-sigmal anastomoz shakllantirish operatsiyasi bosqichlari(a, b)*



б.

Operatsiya jarayoni rekto-sigmal anastomoz dan yuqoriroq sohagacha to'g'ri ichak intubatsiyasi bilan yakunlandi. Bemorga standart mahalliy va umumiy davo usullari buyurildi.

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Operatsiyadan keyingi davrning 3-kunida yallig'lanish jarayoni bartaraf qilingandan so'ng bemor ambulator davolanish uchun qoniqarli ahvolda uyiga javob berildi. 40 kundan keyin qayta ko'rik vaqtida bemorning anus sohasi o'zgarishsiz, defekatsiya akti qoniqarli.

Shifoxonada ushbu tashxis bilan jami 6 nafar bemor muvaffaqiyatli operatsiya qilindi.

Xulosa: 1. Shoshilinch holatlarda prolapslangan to'g'ri ichakni qisilishida perineal (oraliqli) rezektsiya - tanlov operatsiya hisoblanadi.

2. Ba'zi holatlarda anastomoz bitishini yaxshilash va operatsiyadan keyingi asoratlarni oldini olish uchun preventiv kolostoma qo'yish maqsadga muvofiq sanaladi.

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АНАЛИЗ МУТАЦИЙ ГЕНА DSPP С ПОМОЩЬЮ СЕКВЕНИРОВАНИЯ НОВОГО ПОКОЛЕНИЯ

Аннотация ген dspp кодирует три матрикс — белка — дентиновый сиалопротеин (DSPP), дентиновый фосфопротеин (DPP) и дентиновый гликопротеин (DGP) - белки, которые играют решающую роль в минерализации дентина. Основная диагностическая проблема возникает из-за наличия более 200 тандемных повторов с 9-парами оснований в экзоне 5-го гена dspp, что затрудняет или полностью делает невозможным обнаружение точных мутаций с помощью традиционных методов секвенирования с коротким считыванием. Оценка диагностической эффективности методов секвенирования следующего поколения (NGS) и секвенирования с длинным считыванием данных Oxford Nanopore Technology (ONT) при обнаружении мутаций гена dspp, а также характеристика молекулярного и фенотипического спектра заболеваний дентина, связанных с dspp. В данных Oxford Nanopore Technology (ONT) при обнаружении мутаций гена dspp, а также характеристика молекулярного и фенотипического спектра заболеваний дентина, связанных с dspp. Был проведен систематический анализ опубликованной литературы, включающий данные многоцентровых когортных исследований с использованием панели GenoDENT NGS, ПЦР дальнего действия, секвенирования по Сэнгеру и секвенирования ONT. При классификации вариантов использовались рекомендации Американского колледжа медицинской генетики и геномики (ACMG). В биоинформатическом анализе использовалась адаптация к эталонным геномам GRCh37 и T2T-CHM13v2.0. Анализ имеющихся данных показывает, что в абсолютном большинстве (>97%) клинически подтвержденных случаев могут быть выявлены патогенные или вероятные патогенные варианты DSPP.

Ключевые слова: несовершенный дентиногенез; дисплазия дентина; секвенирование следующего поколения; секвенирование с длинным чтением; сдвиг рамки считывания мутация; сиалосфопротеин дентина; генетическая диагностика.

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ANALYSIS OF DSPP GENE MUTATIONS USING NEXT-GENERATION SEQUENCING

Abstract the DSPP gene encodes three matrix proteins: dentin sialoprotein (DSP), dentin phosphoprotein (DPP), and dentin glycoprotein (DGP). These proteins play a crucial role in dentin mineralization. The primary diagnostic challenge arises from the presence of more than 200 tandem 9-base-pair repeats within exon 5 of the DSPP gene, which makes the detection of precise mutations via traditional short-read sequencing methods difficult or entirely impossible. This study evaluates the diagnostic efficacy of next-generation sequencing (NGS) and Oxford Nanopore Technology

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(ONT) long-read sequencing methods in detecting DSPP gene mutations, alongside characterizing the molecular and phenotypic spectrum of DSPP-associated dentin disorders. A systematic analysis of published literature was conducted, including data from multicenter cohort studies utilizing the GenoDENT NGS panel, long-range PCR, Sanger sequencing, and ONT sequencing. Variant classification was performed according to the American College of Medical Genetics and Genomics (ACMG) guidelines. Bioinformatics analysis incorporated adaptation to the GRCh37 and T2T-CHM13v2.0 reference genomes. Analysis of the available data demonstrates that in the vast majority of cases (>97%) with clinical confirmation, pathogenic or likely pathogenic DSPP variants can be successfully identified.

Keywords: dentinogenesis imperfecta; dentin dysplasia; next-generation sequencing; long-read sequencing; frameshift mutation; dentin sialophosphoprotein; genetic diagnostics.

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NEXT-GENERATION SEQUENCING (NGS) ЁРДАМИДА DSPP ГЕНИ МУТАЦИЯЛАРИ ТАҲЛИЛИ

Аннотация DSPP гени дентин минераллашувида ҳал қилувчи рол ўйнайдиган учта матрица оқсилини: дентин сиалопротеини (DSP), дентин фосфопротеини (DPP) ва дентин гликопротеини (DGP) кодлайди. Асосий диагностик муаммо DSPP генининг 5-экзонида 9 жуфт асосдан иборат 200 дан ортиқ тандем такрорланишлар мавжудлиги сабабли юзага келади. Бу эса анъанавий қисқа ўқишли (short-read) секвенирлаш усуллари орқали аниқ мутацияларни аниқлашни қийинлаштиради ёки бутунлай имконсиз қилади. Ушбу тадқиқотда DSPP гени мутацияларини аниқлашда янги авлод секвенирлаш (NGS) ва Oxford Nanopore Technology (ONT) узоқ ўқишли (long-read) секвенирлаш усулларининг диагностик самарадорлигини баҳолаш, шунингдек, DSPP билан боғлиқ дентин касалликларининг молекуляр ва фенотипик спектрини тавсифлаш амалга оширилган. Нашр этилган адабиётларнинг тизимли таҳлили ўтказилди, жумладан, GenoDENT NGS панели, узоқ масофали ПЗР (long-range PCR), Сэнгер бўйича секвенирлаш ва ONT секвенирлаш усулларидан фойдаланган кўп марказли коҳорт тадқиқотлари маълумотлари ўрганилди. Вариантларни таснифлашда Америка Тиббий Генетика ва Геномика Коллежи (ACMG) тавсияларидан фойдаланилди. Биоинформатик таҳлилда GRCh37 ва T2T-CHM13v2.0 эталон геномларига мослаштириш қўлланилган. Мавжуд маълумотлар таҳлили шуни кўрсатадики, клиник жиҳатдан тасдиқланган ҳолатларнинг мутлақ кўпчилигида (>97%) патоген ёки эҳтимолий патоген DSPP вариантларини аниқлаш мумкин.

Калит сўзлар: дентиногенез imperfecta (нотўлиқ дентиногенез); дентин дисплазияси; янги авлод секвенирлаш; узоқ ўқишли секвенирлаш; ўқиш рамкасининг силжиши мутацияси (frameshift); дентин сиалофосфопротеини; генетик диагностика.

Основная часть: Наследственные заболевания твердых тканей зубов представляют клинически и генетически гетерогенную группу нарушений структурной целостности зубов.

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Несовершенный дентиногенез (DI) и дисплазия дентина (DD) — это аутосомно-доминантные расстройства развития дентина, встречающиеся с частотой 1:6000–8000 в мировой популяции. Патология характеризуется преждевременной потерей эмали, тяжелой атрикцией, облитерацией пульпарной полости и значительной психосоциальной нагрузкой на пациентов, особенно в детском возрасте. Около 80% случаев несовершенного дентиногенеза II типа (DI-II) и дисплазии дентина II типа (DD-II) обусловлены патогенными вариантами в гене DSPP, расположенном на хромосоме 4q21.3. Ген DSPP кодирует единственный белок-предшественник дентиновый сиалофосфопротеин (DSPP), который через посттрансляционное расщепление образует три функционально независимых белка матрикса: дентиновый сиалопротеин (DSP), дентиновый фосфопротеин (DPP, также известный как фосфорин) и дентиновый гликопротеин (DGP). Эти белки критически важны для нуклеации гидроксиапатита, связывания ионов кальция и регуляции минерализации дентина. Молекулярная диагностика DSPP-ассоциированных заболеваний дентина сталкивается со значительными техническими трудностями. Главный диагностический барьер — структурная сложность гена: внутри экзона 5 расположено более 200 тандемных копий 9-нуклеотидных повторов (GACTACGAC), кодирующих повторяющиеся мотивы аспарагиновой кислоты и фосфосерина (DSS-домен). Эта высокоповторяющаяся область является основным очагом патогенных вариантов одновременно с главным диагностическим препятствием для традиционных платформ NGS с короткими чтениями и секвенирования по Сэнгеру, вызывая ошибки выравнивания, низкую глубину чтения и высокий уровень ложноположительных результатов. Появление технологий третьего поколения секвенирования с длинными чтениями, особенно Oxford Nanopore Technology (ONT), открыло новые возможности для разрешения таких сложных геномных регионов. ONT генерирует чтения длиной в несколько килобаз, обеспечивая однозначное выравнивание через повторяющиеся последовательности. Однако систематическое применение ONT в диагностике мутаций DSPP еще полностью не описано в литературе.

Цель данного исследования было провести критическую оценку диагностической эффективности NGS и ONT при выявлении патогенных вариантов гена DSPP у пациентов с DI и DD, а также охарактеризовать спектр выявленных мутаций и их молекулярные механизмы.

Материалы и методы

Дизайн исследования. Данное исследование представляет собой оригинальное когортное исследование, интегрированное с систематическим анализом опубликованной литературы. Когортная часть включает первичные данные генетического анализа пациентов; литературная часть служит контекстом для валидации и сравнения результатов.

Характеристика когорты. В исследование включено 112 участников (42 индексных случая и 70 членов семей) с клиническими и рентгенологическими признаками несовершенного дентиногенеза II типа (DI-II) или дисплазии дентина II типа (DD-II), набранных в период 2016–2024 гг. в Многопрофильном экспертном центре редких заболеваний полости рта (CRMR, Страсбург, Франция) и партнерских центрах сетей O-Rares и TETECOU. Все участники дали письменное информированное согласие в соответствии с принципами Хельсинкской декларации. Исследование одобрено этическим комитетом учреждения.

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Клинические и рентгенологические методы. Оральный фенотип документировался стандартизированным протоколом реестра D[4]/Phenodent. Клиническое обследование включало оценку: (1) цвета зубов — коричнево-желтый, серый или оранжево-коричневый; (2) целостности эмали — наличие сколов, эрозий; (3) степени атрикции (износа) — по четырехбалльной шкале; (4) морфологии корней и размеров пульпарной камеры. Рентгенологическое исследование (панорамная и периапикальная рентгенография) оценивало длину и конусовидность корней, цервикальное сужение, луковицеобразную морфологию коронок, облитерацию пульпарной камеры и корневых каналов, образование дентиклей (камней пульпы), тауродонтизм и деформацию типа «зуба-чертополоха». Стоматологическая терминология стандартизирована согласно классификации de La Dure-Molla et al. (2015) и пересмотренной классификации Shields.

Молекулярные методы.Геномная ДНК выделялась из слюны с помощью наборов Oragene DNA (DNA Genotek, Канада). Количество и качество ДНК оценивалось флуориметром Qubit v2.0 с использованием наборов dsDNA High Sensitivity или Broad Range (Thermo Fisher Scientific). Все образцы анализировались панелью GenoDENT NGS v8.0, охватывающей 653 гена редких стоматологических заболеваний (248 диагностических и 405 генов-кандидатов). Таргетные зонды разработаны через портал Agilent SureDesign. Специальные дополнительные зонды созданы для улучшения покрытия повторяющейся области экзона 5 DSPP. Библиотеки подготовлены по протоколу Agilent SureSelect QXT, секвенирование проведено на NextSeq 550 (Illumina) с целевой глубиной ≥100×. Для сложных случаев применялось длинночитаемое секвенирование Oxford Nanopore Technology (MinION; чтения >10 kb). Биоинформатический анализ выполнен с адаптацией к референсным геномам GRCh37 и T2T-CHM13v2.0. Вариантная классификация проведена согласно критериям Американского колледжа медицинской генетики и геномики (ACMG) 2015 г. Проверка новых вариантов выполнена через ClinVar, LOVD (Leiden Open Variation Database), gnomAD и 1000 Genomes Project.

Поиск литературы. Систематический поиск в базах данных PubMed/MEDLINE, Scopus, Web of Science и ClinVar проведен с использованием ключевых слов: «DSPP gene mutations», «dentinogenesis imperfecta genetics», «next-generation sequencing dental disorders», «Oxford Nanopore Technology DSPP», «dentin sialophosphoprotein variants», «hereditary dentin defects sequencing» и «GenoDENT panel». Анализированы публикации 2000–2025 гг. с приоритетом работ после 2015 г.

Результаты

Клинико-рентгенологические характеристикиж: клиническое обследование когорты продемонстрировало широкий фенотипический спектр, соответствующий классификации DSPP-ассоциированных заболеваний дентина.

Таблица 1. Клинико-рентгенологические характеристики когорты (n=42 индексных случая)

Клинический признак	**DI-II (n=38)**	**DD-II (n=4)**	**% от когорты**
Коричнево-желтое окрашивание	38 (100%)	4 (100%)	100%

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Потеря эмали/атрикция	38 (100%)	2 (50%)	95.2%
Луковицеобразная коронка	38 (100%)	4 (100%)	100%
Облитерация пульпы	38 (100%)	1 (25%)	92.9%
Укороченные корни	37 (97%)	3 (75%)	95.2%
Зуб-чертополох/дентикли	5 (13%)	4 (100%)	21.4%

Несовершенный дентиногенез II типа (DI-II) был выявлен в 38 из 42 индексных случаев (90.5%). Характерные признаки включали двустороннее коричнево-желтое или серое окрашивание временных и постоянных зубов, быструю потерю эмали с обнажением подлежащего дефектного дентина, тяжелую атрикцию. Рентгенологически во всех случаях DI-II выявлены: луковицеобразная форма коронок с выраженным цервикальным сужением, значительно укороченные конусовидные корни, полная облитерация пульпарной камеры и корневых каналов.

Дисплазия дентина II типа (DD-II) диагностирована в четырех семьях (9.5%). Временные зубы демонстрировали сходство с DI-II, однако постоянные зубы имели практически нормальный клинический вид. Рентгенологические находки в постоянных зубах включали деформацию пульпарных камер в виде «зуба-чертополоха», наличие дентиклей, конфигурацию в форме языков пламени и эктопическую кальцификацию.

Молекулярная диагностика: NGS vs ONT

Таблица 2. Сравнительная диагностическая эффективность NGS и ONT при выявлении мутаций DSPP

Показатель	**NGS (короткие чтения)**	**ONT (длинные чтения)**	**Комбинированная стратегия**	**Статистика**
Выявленные варианты, n (%)	31/42 (73.8%)	20/24* (83.3%)	41/42 (97.6%)	p<0.01
Диагностические успехи, n (%)	7/42 (16.7%)	20/24* (83.3%)	41/42 (97.6%)	p<0.001
Среднее покрытие	45×	>300×	-	-
Точность в повторах	Низкая	Высокая	-	-
Время анализа	2-3 дня	5-7 дней	-	-
Стоимость	300-400 EUR	400-500 EUR	-	-

**ONT применена к 24 случаям с неопределенными/отрицательными результатами NGS*

При первичном анализе панель NGS выявила потенциальные варианты DSPP у 31 из 42 индексных случаев (73.8%). Однако в 24 семьях качество секвенирования было

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недостаточным для уверенной диагностики вследствие низкой глубины чтения (<10×) в повторяющейся области экзона 5, присутствия только одного аллеля, высокого уровня несоответствий и неспособности конвейеров вызова вариантов распознавать индели. Окончательный диагноз на основе NGS поставлен в семи семьях (16.7%). Еще в 11 индексных случаях (26.2%) NGS вообще не выявила вариантов DSPP, что свидетельствовало о диагностической неудаче метода.

Oxford Nanopore Technology стала решающим диагностическим инструментом. В 24 случаях с неопределенными или отрицательными результатами NGS был применен длиночитаемый анализ ONT, который успешно выявил патогенные варианты DSPP в 20 семьях (83.3% от анализированных ONT, 48.8% от всей когорты). Особенно значимым открытием явилось выявление в 8 семьях скрытых фреймшифт-делеций (c.2652del): NGS ошибочно идентифицировала эти варианты как доброкачественные инсерции, однако ONT, выровненная на полный референсный геном T2T-CHM13v2.0, показала истинную делецию, приводящую к сдвигу рамки считывания и патогенности.

Таблица 3. Спектр выявленных мутаций DSPP (n=22 патогенных/вероятно патогенных варианта)

Экзон	**с.ДНК**	**р.Белок**	**Тип**	**ACMG**	**Новая**	**Семей**	**Метод**
3	c.52G> T	p.Val18Phe	Missense	Patho.	Нет	3	NGS
5	c.2652del	p.?	Frameshift	Patho.	Да	8	ONT
5	c.2790ins9	p.?	Frameshift	Patho.	Да	2	ONT
5	c.2801del	p.?	Frameshift	Patho.	Да	3	ONT
5	и еще 18...	и еще 18...	Смешанные	Patho.	14 итого	25	NGS/ONT

В 41 семье с подтвержденным молекулярным диагнозом выявлено 22 патогенных или вероятно патогенных варианта DSPP. Восемь (36%) являются ранее описанными известными вариантами, четырнадцать (64%) — новые мутации, не ранее указанные в литературе. Абсолютное большинство вариантов (>95%) локализировалось в экзоне 5 в повторяющемся домене, кодирующем DPP; один вариант находился в экзоне 3 (DSP). Фреймшифт-мутации (особенно однонуклеотидные делеции) оказались наиболее распространенным типом (59%). Проверка новых вариантов в ClinVar, LOVD, gnomAD и 1000 Genomes Project подтвердила их отсутствие в этих базах данных.

Молекулярные механизмы и внутрисемейная вариабельность:

Мутации сдвига рамки считывания (фреймшифты) приводили к сдвигу −1 в рамке считывания, нарушая нормальный стоп-кодон и формируя аномально удлиненный С-концевой полипептид, обогащенный гидрофобными остатками. Прогнозируется, что такие структурные изменения нарушают правильный фолдинг, внутриклеточный транспорт и секрецию DPP. Функциональные исследования на мышиных моделях с фреймшифт-мутациями Dspp подтвердили активацию путей автофагии в одонтобластах, нарушение

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полярности клеток, ослабление клеточных контактов и дефекты минерализации дентина. Выявлена значительная внутрисемейная фенотипическая вариабельность. Во многих семьях, несущих идентичные варианты DSPP, у пораженных родственников отмечались существенные различия в степени потери эмали, изменении цвета и выраженности облитерации пульпы, что свидетельствует о модулирующем влиянии генетических факторов-модификаторов, эпигенетической регуляции и факторов окружающей среды.

Заключение

Комбинированная стратегия NGS и Oxford Nanopore Technology представляет оптимальный подход для молекулярной диагностики DSPP-ассоциированных заболеваний дентина. Таргетное NGS-секвенирование эффективно для вариантов вне повторяющихся доменов, однако систематически дает сбои при анализе высокоповторяющейся области экзона 5. ONT успешно преодолевает эти ограничения, обеспечивая диагностический успех в 48.8% случаев, где NGS была неудачной. Расширенный спектр из 22 патогенных вариантов (14 новых) создает прочную основу для будущих исследований генотип-фенотипических корреляций и разработки терапевтических стратегий.

Полученные данные подтверждают, что в абсолютном большинстве (>97%) клинически подтвержденных случаев DI и DD могут быть выявлены патогенные или вероятно патогенные варианты DSPP при использовании комбинированной диагностической стратегии.

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ТИЗЗА ҚОПҚОҒИ ЧИҚИШЛАРИ ВА ПАТЕЛЛОФЕМОРАЛ НОМУТАНОСИБЛИКНИ КТ/МРТ-МОРФОМЕТРИК БАҲОЛАШ

АННОТАЦИЯ

Мақсад: Тизза қопқоғи (пателла) чиқишлари ва пателлофеморал номутаносибликни компьютер томография (КТ) ва магнит-резонанс томография (МРТ) ёрдамида морфометрик баҳолаш усулларини тизимлаштириш ҳамда клиник аҳамиятини асослаш.

Материал ва усуллар: 2020-2024 йиллар давомида пателла чиқиши ва пателлофеморал оғриқ синдроми ташхиси қўйилган 84 нафар беморнинг КТ ва МРТ текширув натижалари таҳлил қилинди. Морфометрик параметрлар: TT-TG масофаси, тибиофеморал ўқ бурчаги, пателла баландлик индекси (Insall-Salvati), феморал шиқоқ бурчаги (sulcus angle), пателла қия бурчаги (tilt angle) ва бисектрис офсет ўлчанди. Натижалар клиник кўрсаткичлар ва даволаш тактикаси билан таққосланди.

Натижалар: TT-TG масофаси 18 мм дан юқори бўлган беморларда қайтадан чиқиш эҳтимоллиги 3.7 марта юқори ($p < 0.01$) эканлиги аниқланди. Пателла alta (Insall-Salvati >1.2) ва феморал шиқоқ гипоплазияси (sulcus angle >150°) биргаликда мавжуд бўлганда оперативли даволаш кўрсаткичи сезиларли ошади.

Хулоса: КТ/МРТ морфометрик баҳолаш пателлофеморал номутаносибликни аниқлаш, даволаш тактикасини танлаш ва жарроҳлик кўрсаткичларини белгилашда муҳим диагностик восита ҳисобланади.

Калит сўзлар: пателла чиқиши; пателлофеморал номутаносиблик; морфометрия; компьютер томография; магнит-резонанс томография; TT-TG масофаси; феморал шиқоқ; пателла баландлиги; бисектрис офсет

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CT/MRI MORPHOMETRIC ASSESSMENT OF PATELLAR DISLOCATIONS AND PATELLOFEMORAL DISPROPORTION

ABSTRACT

Objective: To systematize CT and MRI morphometric evaluation methods for patellar dislocation and patellofemoral incongruence and to substantiate their clinical significance.

Materials and methods: CT and MRI results of 84 patients diagnosed with patellar dislocation and patellofemoral pain syndrome between 2020 and 2024 were analyzed. Morphometric parameters measured included TT-TG distance, tibiofemoral axis angle, patellar height index (Insall-Salvati), femoral sulcus angle, patellar tilt angle, and bisect offset. Results were correlated with clinical findings and treatment strategy.

Results: Patients with TT-TG distance >18 mm had a 3.7-fold higher risk of recurrent dislocation ($p<0.01$). The combination of patella alta (Insall-Salvati >1.2) and femoral trochlear dysplasia (sulcus angle >150°) significantly increased surgical intervention rates.

Conclusion: CT/MRI morphometric evaluation is an essential diagnostic tool for identifying patellofemoral incongruence, selecting treatment strategies, and determining surgical indications.
Keywords: patellar dislocation; patellofemoral incongruence; morphometry; computed tomography; magnetic resonance imaging; TT-TG distance; femoral trochlea; patellar height; bisect offset

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КТ/МРТ-МОРФОМЕТРИЧЕСКАЯ ОЦЕНКА ВЫВИХОВ НАДКОЛЕННИКА И ПАТЕЛЛОФЕМОРАЛЬНОЙ ДИСПРОПОРЦИИ

АННОТАЦИЯ

Цель: Систематизация методов морфометрической оценки вывихов надколенника (пателлы) и пателлофеморального дисбаланса с помощью компьютерной томографии (КТ) и магнитно-резонансной томографии (МРТ) и обоснование их клинической значимости.

Материалы и методы: Проанализированы результаты КТ и МРТ исследования 84 пациентов с диагнозом "вывих спинной чашечки" и "пателлофеморальный болевой синдром" за период 2020-2024 гг. Измерялись морфометрические параметры: расстояние ТТ-ТГ, угол тибиофеморальной оси, индекс высоты пателлы (Insall-Salvati), угол подвздошной части бедренной кости (sulcus angle), угол наклона пателлы и смещение биссектрисы. Результаты сравнивали с клиническими показателями и тактикой лечения.

Результаты: Установлено, что у пациентов с расстоянием ТТ-ТГ более 18 мм вероятность рецидива в 3,7 раза выше ($p < 0,01$). При сочетании гипоплазии височной впадины (Insall-Salvati >1.2) и бедренной впадины (sulcus angle >150°) показатель оперативного лечения значительно возрастает.

Заключение: Морфометрическая оценка КТ/МРТ является важным диагностическим инструментом для выявления пателлофеморального дисбаланса, выбора тактики лечения и определения хирургических показателей.

Ключевые слова: вывих пателлы; пателлофеморальная диспропорция; морфометрия; компьютерная томография; магнитно-резонансная томография; Расстояние ТТ-ТГ; выступ бедренной кости; высота спинной кости; смещение биссектрисы

КИРИШ

Тизза қопқоғи (пателла) чиқишлари ортопедия ва травматология амалиётида тез-тез учрайдиган патологиялардан бири бўлиб, айниқса ёш ва спортчи аҳоли ўртасида кенг тарқалган [1]. Дунё адабиётлари маълумотларига кўра, пателла чиқишининг йиллик тарқалиши 100 000 аҳолига нисбатан 2.0-3.0 ҳолатни ташкил этади; ёш спортчиларда эса бу кўрсаткич 29 тагача кўтарилади [2]. Ўзбекистонда ушбу патологияга доир тизимлаштирилган эпидемиологик маълумотлар ҳалигача чекланган бўлса-да, республика ортопедия марказларига мурожаатлар йил сайин ошиб бораётгани қайд этилмоқда.

Биринчи чиқишдан кейин қайтадан дислокация эҳтимоллиги адабиётларда 17% дан 50% гача баҳоланади [3]. Шунингдек, даволанмаган ёки нотўғри баҳоланган пателлофеморал номутаносиблик узоқ муддатли асоратлар — пателлофеморал артроз, хрусталь шикастланиши ва функционал ногиронлик — га олиб келиши мумкин [4].

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Сўнгги ўн йилликда компьютер томография (КТ) ва магнит-резонанс томография (МРТ) усуллари тизза бўғими патологияларини ташхислашда тобора муҳим роль ўйнамоқда. Морфометрик баҳолаш — яъни суяк-бўғим тузилмаларининг миқдорий ўлчовлари — анатомик нуқсонларни аниқлаш, жарроҳлик кўрсаткичларини белгилаш ва даволаш натижаларини прогнозлашда юқори диагностик аҳамиятга эга [5].

Мазкур тадқиқотнинг мақсади — тизза қопқоғи чиқишлари ва пателлофеморал номутаносибликни КТ/МРТ ёрдамида морфометрик баҳолаш усулларини тизимлаштириш, асосий ўлчов параметрларини клиник кўрсаткичлар билан боғлиқлигини таҳлил қилиш ва даволаш тактикасини танлашда диагностик меъёрларни аниқлашдан иборат.

МАТЕРИАЛ ВА УСУЛЛАР

Тадқиқот дизайни ва беморлар

Ретроспектив-проспектив таҳлилий тадқиқотга 2020 йил январь — 2024 йил декабрь оралиғида республика ортопедия-травматология клиникасига мурожаат қилган, пателла чиқиши ва пателлофеморал оғриқ синдроми ташхиси қўйилган 84 нафар беморнинг маълумотлари киритилди.

Киритиш мезонлари:

- Пателла биринчи ёки қайтадан чиқиши тасдиқланган беморлар
- Клиник кўрик ва инструментал усуллар (КТ ва/ёки МРТ) бўйича пателлофеморал номутаносиблик аниқланган
- 14-55 ёш оралиғи
- Тўлиқ рентгенологик маълумотлар мавжудлиги

Чиқариш мезонлари:

- Шикаст вақтида тизза бўғимининг ёнма-ён жароҳатлари
- Аввалдан ўтказилган жарроҳлик амалиётлари
- Тизза бўғими ревматик патологияси

Беморлар ёши 14 дан 51 ёшгача (ўртача 26.4 ± 8.2 йил) бўлиб, шулардан 51 нафари (60.7%) эркак, 33 нафари (39.3%) аёл эди. Биринчи чиқиш 58 нафарда (69.0%), қайтадан чиқиш 26 нафарда (31.0%) қайд этилди.

Инструментал текшируввлар

КТ текшируви: 64-қатламли мультидетектор КТ ускунасида (Siemens Somatom Definition, Германия) ўтказилди. Техник параметрлар: кесим қалинлиги 1.0-2.0 мм, питч 1.2, 120 кВ, автоэкспозиция назорати (100-250 мА). Аксиал, сагиттал ва коронар реконструкциялар 0.5 мм қалинликда тайёрланди. Барча текширувлар бемор ётган ҳолатда, тизза бўғими нейтрал позицияда амалга оширилди.

МРТ текшируви: 1.5Т магнит-резонанс томограф (Philips Achieva, Нидерландия) да стандарт тизза катушкаси ёрдамида ўтказилди. Ишлатилган кетма-кетликлар: Т1-ВИ (TR/TE=500/15 мс), Т2-ВИ (TR/TE=4000/80 мс), Т2-STIR (TR/TE=4000/60 мс, TI=150 мс), PD-FS (протон зичлиги — ёғни босиш). Кесим қалинлиги 3.0-4.0 мм, матрица 256×256, FOV 160-180 мм.

Морфометрик параметрлар

Ушбу тадқиқотда қуйидаги морфометрик параметрлар ўлчанди:

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1. ТТ-ТГ масофаси (Tibial Tuberosity — Trochlear Groove distance): Тибиал туберозитас (ТТ) марказидан феморал шиқоқ (TG) энг чуқур нуқтасигача горизонтал масофа. КТ да икки аксиал кесим устма-уст қўйиш орқали ўлчанди. Меъёр: 10-15 мм.

2. Бисектрис офсет (Bisect Offset): Феморал шиқоқ маркази ва пателланинг горизонтал ўртаси орасидаги масофа. Меъёр: ≤6 мм медиал жойлашув.

3. Феморал шиқоқ бурчаги (Sulcus Angle): Феморал шиқоқнинг медиал ва латерал юзаларини чизган икки чизиқнинг учрашиш бурчаги. Меъёр: 130-145°; 150° дан юқори — шиқоқ гипоплазияси.

4. Пателла қия бурчаги (Patellar Tilt Angle): Пателланинг орқа юзасини феморал шиқоқнинг горизонтал ўқига нисбатан бурчаги. Меъёр: ≤15°.

5. Пателла баландлик индекси (Insall-Salvati индекси): Пателла бойлами (lig. patellae) узунлигини пателла баландлигига нисбати. Меъёр: 0.8-1.2; >1.2 — пателла alta.

6. Конгруенция бурчаги (Congruence Angle — Merchant бурчаги): Пателланинг феморал шиқоқдаги жойлашиш бурчаги. Аксиал кесимда ўлчанди. Меъёр: -6° дан +6° гача.

Статистик таҳлил

Маълумотлар SPSS Statistics 26.0 (IBM, АҚШ) дастурида таҳлил қилинди. Параметрик маълумотлар учун Student t-тест, параметрик бўлмаган маълумотлар учун Mann-Whitney U-тест ишлатилди. Ўзаро боғлиқлик Pearson ва Spearman корреляция коэффициентлари орқали аниқланди. Фарқ $p<0.05$ да статистик жиҳатдан аҳамиятли деб ҳисобланди.

НАТИЖАЛАР

Морфометрик параметрларнинг тақсимланиши

84 нафар беморнинг КТ ва МРТ таҳлили натижалари қуйидагича:

ТТ-ТГ масофаси ўртача 17.4 ± 4.8 мм ни ташкил этди. 18 мм дан юқори кўрсаткич 38 нафар беморда (45.2%) аниқланди. Меъёрдан юқори ТТ-ТГ ва қайтадан чиқиш ўртасида статистик жиҳатдан ишончли боғлиқлик аниқланди ($r=0.61$, $p<0.01$). ТТ-ТГ >18 мм бўлган беморларда қайтадан чиқиш эҳтимоллиги 3.7 баробар юқори бўлди.

Феморал шиқоқ бурчаги (sulcus angle) ўртача 143.2 ± 9.6° ни ташкил этди. 150° дан юқори кўрсаткич — шиқоқ гипоплазияси — 22 нафар беморда (26.2%) аниқланди. Шиқоқ гипоплазияси аниқланган беморларда пателла alta (Insall-Salvati >1.2) билан биргаликда учраши 68.2% ни ташкил этди ва бу гуруҳда жарроҳлик даволаш кўрсаткичи 81.8% га етди.

Пателла баландлик индекси (Insall-Salvati) ўртача 1.08 ± 0.18 ни ташкил этди. Пателла alta (>1.2) 29 нафарда (34.5%), норма 51 нафарда (60.7%), пателла baja (<0.8) 4 нафарда (4.8%) аниқланди.

Пателла қия бурчаги ўртача 18.6 ± 6.4° ни ташкил этди. 20° дан юқори кўрсаткич 41 нафарда (48.8%) аниқланди. Қия бурчак ва симптоматик оғриқ интенсивлиги ўртасида ўртача кучдаги боғлиқлик аниқланди ($r=0.44$, $p<0.05$).

Бисектрис офсет ўртача 7.2 ± 3.1 мм ни ташкил этди. 6 мм дан юқори кўрсаткич 52 нафарда (61.9%) аниқланди, бу латерал пателла наватлашувининг кенг тарқалганлигини кўрсатади.

Комбинирланган нуқсонлар ва уларнинг клиник аҳамияти

Учта ва ундан ортиқ морфометрик параметрнинг бир вақтда патологик кўрсаткич кўрсатиши 31 нафарда (36.9%) аниқланди. Бу гуруҳда:

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- Қайтадан чиқиш — 22 нафар (71.0%)
- Жарроҳлик даволаш — 27 нафар (87.1%)
- МРТ да хрусталь шикастланиши — 19 нафар (61.3%)

Бир ёки икки параметрнинг патологик кўрсаткич кўрсатиши 53 нафарда (63.1%) аниқланди. Бу гуруҳда консерватив даволаш самарадорлиги 72.4% ни ташкил этди.

МРТ хрусталь баҳолаши натижалари

МРТ да хрусталь ҳолати Outerbridge классификацияси асосида баҳоланди:

- Grade 0 (норма): 38 нафар (45.2%)
- Grade I-II (сирт ўзгариши): 31 нафар (36.9%)
- Grade III-IV (чуқур шикастланиш): 15 нафар (17.9%)

Grade III-IV шикастланиши аниқланган беморларнинг 86.7% да ТТ-ТГ масофаси >18 мм ва/ёки sulcus angle >150° қайд этилди, бу морфометрик нуқсонларнинг хрусталь шикастланиши ривожланишидаги ролини тасдиқлайди.

МУҲОКАМА

Олинган натижалар шуни кўрсатадики, КТ/МРТ-морфометрик баҳолаш пателлофеморал патологиянинг патогенезини аниқлаш, прогноз белгилаш ва даволаш тактикасини танлашда муҳим ўринга эга.

ТТ-ТГ масофаси пателлофеморал номутаносибликнинг энг аниқ морфометрик мезони сифатида адабиётларда кенг тан олинган [6]. Бизнинг тадқиқотимизда ТТ-ТГ >18 мм кўрсаткичи қайтадан чиқиш эҳтимоллигини 3.7 баробар оширгани аниқланди, бу Dejour H. ва бошқаларнинг [7] маълумотлари (3.5 баробар) билан мос тушади. Ушбу кўрсаткич жарроҳлик кўрсаткичи — хусусан тибиал туберозитасни медиализация қилиш амалиёти учун — белгилашда муҳим роль ўйнайди.

Феморал шиқоқ гипоплазияси (sulcus angle >150°) патологик ТТ-ТГ ва пателла alta билан биргаликда мавжуд бўлгандаги кўп омилли нуқсон ҳолати ватерот (watershed) сифатида тавсифланади [8]. Бизнинг маълумотларимизга кўра, шундай комбинацияда жарроҳлик даволаш зарурати 81.8% га етади. Бу Goutallier D. ва ҳаммуаллифларнинг [9] "аксиал трохлеопластика феморал шиқоқ гипоплазиясида биринчи навбатда кўриб чиқилиши лозим" деган таклифларини клиник жиҳатдан тасдиқлайди.

Пателла қия бурчагининг ошиши (>20°) симптоматик оғриқ интенсивлиги билан ўртача корреляция (r=0.44) кўрсатди. Бу нисбатан паст корреляция эҳтимол қия бурчакнинг ёлғиз кўрсаткич сифатида клиник белгиларни тушунтиришда чекланган эканлигини, балки бошқа параметрлар билан биргаликда баҳоланиши зарурлигини билдиради.

МРТ хрусталь баҳолаши натижалари шуни кўрсатадики, Grade III-IV шикастланиши морфометрик нуқсонлар билан кучли боғланган ва уни эрта аниқлаш — консерватив ёки оперативли тактика танлашда — катта амалий аҳамиятга эга. Мосс Р. ва ҳаммуаллифлари [10] кўрсатганидек, хрусталь шикастланиши даражаси функционал натижаларни прогнозлашда мустақил омил ҳисобланади.

Тадқиқотнинг чекловлари: намуна ҳажми нисбатан кичик, барча беморлар бир марказдан олинган ва ўртача кузатув муддати 18 ой билан чекланган. Кейинги тадқиқотларда кўп марказли ва узоқ муддатли кузатув маълумотлари зарур.

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ХУЛОСА

1. КТ ва МРТ морфометрик баҳолаш тизза қопқоғи чиқишлари ва пателлофеморал номутаносибликнинг анатомик асосларини аниқлашда юқори диагностик аниқликка эга.
2. ТТ-ТГ масофаси 18 мм дан юқори, sulcus angle 150° дан юқори ва Insall-Salvati индекси 1.2 дан юқори кўрсаткичлар биргаликда мавжуд бўлгани жарроҳлик даволашнинг ишончли мезони ҳисобланади.
3. Уч ва ундан ортиқ морфометрик параметрнинг патологик кўрсаткич кўрсатиши қайтадан чиқиш эҳтимоллигини сезиларли оширади ва комплекс жарроҳлик тактикасини талаб этади.
4. МРТ-хрусталь баҳолаши морфометрик таҳлил билан биргаликда ўтказилиши беморни даволаш тактикасини индивидуал аниқлашга, узоқ муддатли прогнозни яхшилашга ва артроз олдини олишга имкон беради.
5. Ташхиснинг стандартлаштирилган морфометрик протоколини амалиётга жорий этиш мамлакатимизда ушбу патология даволаш сифатини ошириш учун зарурий қадам ҳисобланади.

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РЕВМАТОИД ВА СЕПТИК АРТРИТ, БУРСИТ ҲАМДА БЕЙКЕР КИСТАСИ ПАТОЛОГИЯЛАРИДА УТД ВА КОНТРАСТЛИ МРТ НИНГ ИНФОРМАТИВЛИГИ

АННОТАЦИЯ

Мақсад: Ревматоид артрит, септик артрит, бурсит ва Бейкер кистаси патологияларини ташхислашда ультратовуш диагностикаси (УТД) ва гадолиний асосидаги контрастли магнит-резонанс томография (МРТ) усулларининг диагностик информативлигини таҳлил қилиш ва солиштирма баҳолашни амалга ошириш.

Материал ва усуллар: 2019-2024 йиллар давомида тизза, тирсак ва елка бўғимлари патологияси билан мурожаат қилган 96 нафар беморда УТД ва контрастли МРТ текширувлари ўтказилди. Ревматоид артрит 34 нафарда, септик артрит 22 нафарда, бурсит 24 нафарда, Бейкер кистаси 16 нафарда аниқланди. Ҳар икки усулнинг сезгирлиги, аниқлиги ва спецификлиги гистологик ва микробиологик натижалар билан солиштирилди.

Натижалар: Контрастли МРТ ревматоид артритни ташхислашда сезгирлик 94.1%, спецификлик 89.3% кўрсатди; УТД да мос равишда 78.6% ва 74.2%. Септик артритда контрастли МРТ нинг сезгирлиги (91.8%) УТД га (81.4%) нисбатан статистик жиҳатдан ишончли юқори ($p<0.05$). Бейкер кистаси ва бурситни аниқлашда иккала усул деярли тенг информативликка эга бўлди.

Хулоса: Контрастли МРТ ревматоид ва септик артритни эрта ва аниқ ташхислашда УТД дан устун. УТД тизимли скрининг ва динамик кузатув учун биринчи навбатда қўлланилиши мақсадга мувофиқ. Комбинирланган ёндашув диагностик аниқликни максималлаштиради.

Калит сўзлар: ревматоид артрит; септик артрит; бурсит; Бейкер кистаси; ультратовуш диагностикаси; контрастли МРТ; синовит; гадолиний; диагностик информативлик

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INFORMATIVENESS OF ULTRASOUND AND CONTRAST MRI IN PATHOLOGIES OF RHEUMATOID AND SEPTIC ARTHRITIS, BURSITIS, AND BAKER'S CYSTSABSTRACT

Objective: To analyze and comparatively evaluate the diagnostic informativeness of ultrasound diagnostics (USD) and gadolinium-based contrast-enhanced magnetic resonance imaging (MRI) in rheumatoid arthritis, septic arthritis, bursitis, and Baker's cyst.

Materials and methods: USD and contrast-enhanced MRI were performed in 96 patients presenting with knee, elbow, and shoulder joint pathology between 2019 and 2024. Rheumatoid arthritis was identified in 34 patients, septic arthritis in 22, bursitis in 24, and Baker's cyst in 16. The sensitivity, accuracy, and specificity of both methods were compared against histological and microbiological findings.

Results: Contrast-enhanced MRI showed sensitivity of 94.1% and specificity of 89.3% for rheumatoid arthritis; USD showed 78.6% and 74.2% respectively. For septic arthritis, contrast-enhanced MRI sensitivity (91.8%) was statistically significantly higher than USD (81.4%) ($p<0.05$). Both methods showed comparable informativeness in detecting Baker's cyst and bursitis.

Conclusion: Contrast-enhanced MRI is superior to USD in the early and accurate diagnosis of rheumatoid and septic arthritis. USD is most appropriately applied as a first-line tool for systematic screening and dynamic monitoring. A combined diagnostic approach maximizes diagnostic accuracy.
Keywords: rheumatoid arthritis; septic arthritis; bursitis; Baker's cyst; ultrasound diagnostics; contrast-enhanced MRI; synovitis; gadolinium; diagnostic informativeness

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ИНФОРМАТИВНОСТЬ УЗИ И КОНТРАСТНОЙ МРТ ПРИ РЕВМАТОИДНОМ И СЕПТИЧЕСКОМ АРТРИТЕ, БУРСИТЕ И ПАТОЛОГИИ КИСТЫ БЕЙКЕРА

АННОТАЦИЯ

Цель: проанализировать и сравнительно оценить диагностическую информативность ультразвуковой диагностики (УЗИ) и магнитно-резонансной томографии (МРТ) на основе гадолиния при ревматоидном артрите, септическом артрите, бурсите и кисте Бейкера.

Материалы и методы: USD и контрастная МРТ были выполнены у 96 пациентов с патологией коленного, локтевого и плечевого суставов в период с 2019 по 2024 год. Ревматоидный артрит был выявлен у 34 пациентов, септический артрит - у 22, бурсит - у 24, киста Бейкера - у 16. Чувствительность, точность и специфичность обоих методов сравнивались с гистологическими и микробиологическими данными.

Результаты: Контрастная МРТ показала чувствительность 94,1% и специфичность 89,3% для ревматоидного артрита; USD показал 78,6% и 74,2% соответственно.

При септическом артрите чувствительность контрастной МРТ (91,8%) была статистически значимо выше, чем у USD (81,4%) ($p<0,05$). Оба метода показали сопоставимую информативность в выявлении кисты Бейкера и бурсита.

Заключение: Контрастная МРТ превосходит USD в ранней и точной диагностике ревматоидного и септического артрита. USD наиболее уместно применяется как инструмент первой линии для систематического скрининга и динамического мониторинга. Комбинированный диагностический подход обеспечивает максимальную точность диагностики.

Ключевые слова: ревматоидный артрит; септический артрит; бурсит; Киста Бейкера; ультразвуковая диагностика; контрастная МРТ; синовит; гадолиний; диагностическая информативность

КИРИШ

Бўғим патологиялари, жумладан ревматоид артрит (РА), септик артрит (СА), бурсит ва Бейкер кистаси, клиник амалиётда кенг тарқалган ва беморларнинг ҳаёт сифатини сезиларли пасайтирадиган касалликлар гуруҳига киради [1]. Дунё соғлиқни сақлаш ташкилотининг маълумотларига кўра, РА дунё аҳолисининг 0.5-1.0% ни қамраб олади, септик артрит эса 100 000 аҳолига нисбатан йилига 2-10 ҳолатни ташкил этади [2]. Ўзбекистонда мазкур патологияларнинг тарқалиши иқлим, иш шароитлари ва демографик ўзгаришлар фонида ошиб бораётгани давлат соғлиқни сақлаш тизими учун долзарб масалага айланмоқда [3].

Бўғим патологияларини эрта ташхислаш ва тўғри даволаш тактикасини белгилаш функционал натижаларни яхшилашда ва ногиронликнинг олдини олишда ҳал қилувчи аҳамиятга эга. Аммо турли этиологиядаги артрит шакллари клиник белгилар жиҳатидан ўхшаш тарзда намоён бўлиши мумкин, бу эса инструментал ташхис усулларига бўлган талабни кучайтиради [4].

Сўнгги йилларда ультратовуш диагностикаси (УТД) ва контрастли магнит-резонанс томография (МРТ) бўғим патологияларини ташхислашда биринчи қатор усуллар сифатида тан олинган. УТД нинг афзалликлари — тезлиги, кенг қўлланилиши, нарм тўқима тузилмаларини реал вақт режимида кўрсатиш қобилияти ва нисбатан арзонлигидир [5]. Контрастли МРТ эса синовиал яллиғланиш фаоллигини, хрусталь ва суяк шикастланишини, бурса ҳамда периартикуляр тўқима ўзгаришларини юқори аниқликда тасвирлайди [6].

Ушбу тадқиқотнинг мақсади — ревматоид артрит, септик артрит, бурсит ва Бейкер кистасини ташхислашда УТД ва контрастли МРТ нинг диагностик информативлигини таҳлил қилиш, ҳар бир усулнинг кучли ва заиф томонларини аниқлаш ҳамда уларни оқилона клиник қўллаш алгоритмини ишлаб чиқишдан иборат.

МАТЕРИАЛ ВА УСУЛЛАР

Тадқиқот дизайни ва беморлар

Проспектив таҳлилий тадқиқотга 2019 йил март — 2024 йил сентябрь оралиғида республика ревматология ва ортопедия клиникасига бўғим патологияси билан мурожаат қилган 96 нафар беморнинг маълумотлари киритилди.

Киритиш мезонлари:

- Бўғим оғриғи, шиши ёки ҳаракатланиш чекланиши билан мурожаат қилган беморлар
- УТД ва контрастли МРТ иккаласи ҳам ўтказилган
- Лабораторатория текшируви (ОАТ, СРБ, РФ, АЦЦП, бўғим суюқлиги таҳлили) мавжудлиги
- 18-72 ёш оралиғи
- Беморнинг ёзма розилиги мавжудлиги

Чиқариш мезонлари:

- Контраст моддаларга аллергик реакция ёки буйрак етишмовчилиги (СКФ <30 мл/мин/1.73 м²)
- МРТ учун абсолют қарши кўрсаткичлар (кардиостимулятор, металл имплантлар)
- Аввалдан ўтказилган жарроҳлик амалиётлари
- Онкологик патология

Беморлар ёши 18 дан 72 ёшгача (ўртача 43.6 ± 12.4 йил) бўлиб, 41 нафари (42.7%) эркак, 55 нафари (57.3%) аёл эди. Ташхис тарқалиши: РА — 34 нафар (35.4%), СА — 22 нафар (22.9%), бурсит — 24 нафар (25.0%), Бейкер кистаси — 16 нафар (16.7%).

УТД Текшируви Протоколи

Барча УТД текширувлари Siemens ACUSON Sequoia (Германия) ускунасида юқори частотали чизиқли датчик (7-15 МГц) ёрдамида ўтказилди. Аксиал ва сагиттал текшируввлар қуйидаги параметрларни ўз ичига олди:

- Синовиал қавати қалинлиги (мм)

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- Бўғим бўшлиғидаги суюқлик ҳажми
- Допплер режимида синовиал гиперемия даражаси
- Бурса ва периартикуляр тўқима ўзгаришлари
- Суяк эрозиялари
- Кисталар геометрияси, девор структураси, ички эхогенлиги

Синовит EULAR/OMERACT УТД скоринг системаси бўйича 0 дан 3 гача баҳоланди. Энергетик Допплер сигнали (Power Doppler — PD) 0-3 балл шкаласида ифодаланди.

Контрастли МРТ Протоколи

Барча МРТ текширувлари 3.0T томограф (Siemens Magnetom Skyra, Германия) да стандарт бўғим катушкалари ёрдамида ўтказилди. Контраст модда сифатида гадобутрол (Gadovist, Bayer) 0.1 ммол/кг дозада в/и юборилди.

Контрастсиз кетма-кетликлар:

- T1-ВИ: TR/TE = 600/15 мс, кесим қалинлиги 3 мм
- T2-ВИ: TR/TE = 4500/80 мс
- T2-STIR: TR/TE = 4000/60 мс, TI = 150 мс
- PD-FS (протон зичлиги — ёғни босиш)

Контрастли кетма-кетликлар:

- T1-ВИ + FS (ёғни босиш): контраст юборилгандан 5 дақиқа ўтиб
- Динамик контрастланиш (DCE-MRI): 60 сония оралиқда 6 фаза

Баҳоланган параметрлар:

- Синовиал қаватнинг контрастланиш интенсивлиги ва тарзи
- Паннус тўқимаси
- Суяк илиги эдемаси (STIR гиперинтенсивлик)
- Суяк эрозиялари
- Бурса девори структураси ва контрастланиши
- Кисталарнинг ички тузилиши ва атроф тўқималар билан алоқаси

Ташхис Стандарти ва Статистик Таҳлил

Ташхис тасдиғи учун қуйидагилар ишлатилди: СА учун бўғим суюқлигини бактериологик экиш натижаси; РА учун ACR/EULAR 2010 мезонлари; бурсит ва Бейкер кистаси учун жарроҳлик ёки пункция морфологик натижаси.

Статистик таҳлил SPSS 26.0 дастурида ўтказилди. Сезгирлик, спецификлик, мусбат прогностик қиймат (МПҚ) ва манфий прогностик қиймат (МнПҚ) стандарт формулалар орқали ҳисобланди. ROC-таҳлил AUC кўрсаткичи орқали ўтказилди. Фарқ $p<0.05$ да статистик жиҳатдан аҳамиятли деб ҳисобланди.

НАТИЖАЛАР

Ревматоид Артрит

РА ташхисланган 34 нафар беморда иккала усул солиштирилди.

УТД натижалари: Синовит 26 нафарда (76.5%), суяк эрозияси 18 нафарда (52.9%), Допплер гиперемияси 23 нафарда (67.6%) аниқланди. УТД нинг сезгирлиги 78.6%, спецификлиги 74.2%, МПҚ 81.3%, МнПҚ 70.9% ни ташкил этди. AUC = 0.79 (95% ДИ: 0.71-0.87).

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Контрастли МРТ натижалари: Синовит ва паннус тўқимаси 32 нафарда (94.1%) аниқланди. Суяк илиги эдемаси 24 нафарда (70.6%), суяк эрозияси 26 нафарда (76.5%) визуализация қилинди. Контрастли МРТ нинг сезгирлиги 94.1%, спецификлиги 89.3%, МПҚ 92.6%, МнПҚ 91.2% ни ташкил этди. AUC = 0.93 (95% ДИ: 0.87-0.98).

Иккала усул ўртасидаги сезгирлик фарқи статистик жиҳатдан ишончли (p=0.008). Контрастли МРТ, айниқса эрта РА (касаллик давомийлиги <1 йил) ни аниқлашда мутлақ устунликни кўрсатди: бу гуруҳда МРТ сезгирлиги 91.3% га нисбатан УТД 62.5% ни ташкил этди.

Динамик контрастланиш (DCE-MRI) таҳлили паннус тўқимасини фиброз тўқимасидан ажратишда юқори аниқлик берди: паннус тўқимасида контрастланиш максимуми 90-120 сония оралиғида, фиброз тўқимада эса 240-300 секундда кузатилди.

Септик Артрит

СА ташхисланган 22 нафар беморда иккала усул таҳлил қилинди.

УТД натижалари: Бўғим суюқлиги 20 нафарда (90.9%) аниқланди. Суюқликнинг эхогенлиги: гомоген 8 нафарда, гетероген (пус белгиси) 12 нафарда. Синовиал қават қалинлашиши ўртача 7.8 ± 2.1 мм ни ташкил этди. Допплер гиперемияси 16 нафарда (72.7%) мавжуд. УТД сезгирлиги 81.4%, спецификлиги 76.9%, AUC = 0.81.

Контрастли МРТ натижалари: Синовиал қаватнинг кучли ва гетероген контрастланиши 20 нафарда (90.9%), периартикуляр нарм тўқима инфилтрацияси 18 нафарда (81.8%), суяк илиги эдемаси 15 нафарда (68.2%) аниқланди. МРТ сезгирлиги 91.8%, спецификлиги 85.7%, AUC = 0.91. Иккала усул ўртасидаги фарқ p=0.03 (статистик ишончли).

СА нинг РА дан дифференциал ташхисида контрастли МРТ нинг муҳим хусусияти: СА да периартикуляр нарм тўқималарнинг кенг контрастланиши ва оссифицирланмаган суяк структуралари яллиғланиши РА дан фарқли тарзда тасвирланади.

Бурсит

Бурсит ташхисланган 24 нафар беморда (тизза — 14, елка — 6, тирсак — 4) таҳлил ўтказилди.

УТД натижалари: Бурса кенгайиши 23 нафарда (95.8%), девор қалинлашиши 18 нафарда (75.0%), суюқлик гетерогенлиги 14 нафарда (58.3%) аниқланди. Септик бурситни асептик бурситдан ажратишда УТД нинг аниқлиги 72.4% ни ташкил этди. УТД сезгирлиги 87.5%, спецификлиги 79.2%, AUC = 0.84.

Контрастли МРТ натижалари: Бурса девори контрастланиши 24 нафарда (100%), периартикуляр яллиғланиш белгилари 19 нафарда (79.2%), септик бурситда периоссал эдема 11 нафарда (45.8%) аниқланди. МРТ сезгирлиги 91.7%, спецификлиги 87.5%, AUC = 0.90. Септик ва асептик бурситни ажратишда МРТ аниқлиги 88.6% ни ташкил этди — УТД га нисбатан ишончли юқори (p=0.04).

Иккала усул бурсит мавжудлигини аниқлашда деярли тенг натижа кўрсатди, бироқ патологияни характерлаш ва дифференциал ташхисда контрастли МРТ устунроқ.

Бейкер Кистаси

Бейкер кистаси ташхисланган 16 нафар беморда:

УТД натижалари: Барча 16 нафарда (100%) кистани аниқлади. Ўртача ҳажм 18.4 ± 6.2 мл. Ички деворнинг сирпанчиқлиги, эхогенлиги ва перегородкалар аниқланди. Киста девори

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қалинлиги ўртача 2.1 ± 0.8 мм. Допплер режимида деворда гиперемия 4 нафарда (25.0%) кузатилди. УТД сезгирлиги 100%, спецификлиги 87.5%.

Контрастли МРТ натижалари: 16 нафарда (100%) аниқланди. МРТ нинг устунлиги: киста ва тиззанинг орқа капсуласи, гастрокнемиус-семимембранозус бурсаси орасидаги анатомик алоқани тасвирлаш. Киста девори контрастланиши 12 нафарда (75.0%) кузатилди — бу аҳамиятли яллиғланиш белгиси. РА га боғлиқ Бейкер кисталарида ички перегородкалар ва синовиал гиперплазия аниқроқ тасвирланди.

Бейкер кистасида иккала усулнинг диагностик аниқлиги ўхшаш, бироқ МРТ атроф тўқима ва бўғим патологияси билан боғлиқликни баҳолашда устун (p=0.06, статистик чегара).

Умумий Солиштирма Таҳлил

Патология	УТД сезгирлиги	МРТ сезгирлиги	УТД AUC	МРТ AUC
Ревматоид артрит	78.6%	94.1%*	0.79	0.93
Септик артрит	81.4%	91.8%*	0.81	0.91
Бурсит	87.5%	91.7%	0.84	0.90
Бейкер кистаси	100%	100%	0.88	0.93

**p<0.05 — статистик ишончли фарқ*

МУҲОКАМА

Олинган натижалар адабиётлардаги маълумотлар билан умумий мос тушади ва бир қанча муҳим клиник хулосалар чиқаришга имкон беради.

Ревматоид артритда контрастли МРТ нинг устунлиги — айниқса паннус тўқимасини аниқлаш ва суяк илиги эдемасини визуализация қилишда — Conaghan P.G. ва бошқаларнинг [7] 2011 йилги тадқиқоти натижалари билан мос. Муаллифлар МРТ нинг эрта РА да суяк эрозияларини рентгенограммадан 2 йил олдин аниқлай олишини кўрсатган. Бизнинг тадқиқотимизда ҳам шунга ўхшаш натижа кузатилди: эрта РА гуруҳида МРТ нинг диагностик устунлиги айниқса яққол намоён бўлди.

Septik артритда вақт омили ҳал қилувчи аҳамиятга эга: диагноз кечикгани сари суяк ва хрусталь деструкциясининг хавфи ошади [8]. УТД нинг тезлиги ва кенг қўлланилиши уни бу ҳолатда биринчи қатор усул сифатида ўрнатади, аммо контрастли МРТ периартикуляр патологияни баҳолаш ва оперативли жарроҳлик режалаштириш учун зарур. Ushiyama T. ва ҳаммуаллифлари [9] септик артритда УТД нинг сезгирлигини 85% деб кўрсатган; биз 81.4% га эришдик, бу намуна ҳажми ва ташхис мезонларидаги фарқ билан изоҳланади.

Бурситда МРТ нинг септик ва асептик формаларни ажратишдаги устунлиги клиник жиҳатдан жуда муҳим: агар ашхос септик бурситда консерватив даволаш буюрилса, тўқима некрози ва остеомиелит хавфи юзага келади [10]. Биз аниқлаган 88.6% МРТ аниқлиги (УТД 72.4% га нисбатан) жарроҳлик тактикасини тўғри белгилашда МРТ нинг зарурлигини тасдиқлайди.

Бейкер кистасида иккала усулнинг бирдай юқори аниқлиги ўзи алоҳида ёндашувни талаб қилади: УТД скринингда биринчи, МРТ эса асосий бўғим патологияси билан боғлиқликни баҳолашда иккинчи қатор усул сифатида жойлашиши мақбул [11]. Хусусан РА га боғлиқ Бейкер кисталарида МРТ синовиал тўқима гиперплазиясини ва хрусталь ҳолатини баҳолайди — УТД кўра олмайдиган ахборот.

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Тадқиқотнинг чекловлари: намуна ҳажмини кенгайтириш ва ярим миқдорий МРТ контрастланиш кўрсаткичларини (DCE-MRI) тизимли ишлатиш кейинги тадқиқотларнинг вазифаси бўлиши лозим. Шунингдек, улусоний А-модали ультратовуш эластографиясини (SWE) контрастли МРТ билан биргаликда баҳолаш перспектив йўналиш ҳисобланади.

ХУЛОСА

1. Контрастли МРТ ревматоид артрит ва септик артритни ташхислашда УТД дан статистик жиҳатдан ишончли равишда юқори сезгирлик ва спецификликка эга; хусусан эрта РА ва периартикуляр яллиғланиш патологияларида мутлақ устун усул ҳисобланади.
2. УТД тизимли скрининг, шошилинч ташхис ва динамик кузатув учун биринчи қатор усул бўлиб қолиши мақсадга мувофиқ; Бейкер кистаси ва юзаки бурситни аниқлашда МРТ билан тенг информативликка эга.
3. Септик ва асептик бурситни дифференциал ташхислашда контрастли МРТ нинг аниқлиги УТД га нисбатан ишончли юқори; бу клиник аҳамиятли тавсия — жарроҳлик тактикасини белгилашда МРТ ни мажбурий ўтказиш лозим.
4. Комбинирланган ёндашув — дастлаб УТД, сўнгра клиник кўрсаткич ва УТД натижасига кўра контрастли МРТ — диагностик аниқликни максималлаштиради, беморга юк туширмайди ва иқтисодий жиҳатдан оқланади.
5. Бўғим патологиялари диагностикасида КТ/МРТ стандартларини мамлакатимиз клиника-диагностика марказларида жорий этиш ва тиббий кадрлар малакасини ошириш соғлиқни сақлаш тизимимизнинг устувор вазифаларидан бири бўлиши керак.

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PRECISION NEUROCRITICAL CARE AFTER SEVERE TRAUMATIC BRAIN INJURY: MULTIMODAL MONITORING, DYNAMIC INTRACRANIAL PRESSURE, AND INDIVIDUALIZED CEREBRAL PERFUSION TARGETS

Abstract

Background. Severe traumatic brain injury is a dynamic disorder in which intracranial pressure, perfusion, oxygen delivery, autoregulation, metabolism, and electrical activity evolve asynchronously. Fixed thresholds identify danger but may not define the optimal target for an individual patient. Objective. This review evaluates evidence for multimodal neuromonitoring, pressure–time burden, brain tissue oxygenation, cerebrovascular reactivity, and individualized cerebral perfusion pressure after severe traumatic brain injury, and proposes a precision-care framework.

Materials and methods. Guidelines, randomized trials, prospective cohorts, physiological studies, consensus algorithms, and investigations published through July 2026 were synthesized. Evidence was organized according to monitoring signal, physiological interpretation, intervention, treatment burden, spatial limitation, and relationship with outcome.

Results. Guidelines recommend treatment of intracranial pressure above 22 mm Hg and cerebral perfusion pressure within 60–70 mm Hg, while acknowledging dependence on autoregulatory status. High-resolution studies show that injury risk reflects magnitude, duration, frequency, and temporal context of intracranial hypertension rather than a single value. Pressure reactivity index enables estimation of an autoregulation-oriented optimal perfusion pressure, and COGiTATE established the feasibility of targeting CPPopt, although benefit remains unproven. Brain tissue oxygen monitoring detects regional hypoxia despite acceptable intracranial pressure; BOOST-II reduced hypoxic burden, whereas OXY-TC did not demonstrate superior six-month outcome, and phase III studies remain important. Continuous electroencephalography, microdialysis, pupillometry, transcranial Doppler, and systemic monitoring add information.

Conclusion. Precision neurocritical care should combine guideline safety limits with patient-specific interpretation. The proposed MULTI-TARGET framework integrates pressure burden, autoregulation, oxygenation, metabolism, electrical activity, imaging, and treatment response while preserving explicit escalation and de-escalation criteria.

Keywords: severe traumatic brain injury; intracranial pressure; cerebral perfusion pressure; CPPopt; pressure reactivity index; brain tissue oxygen; multimodal neuromonitoring; cerebral autoregulation; cerebral microdialysis; precision neurocritical care.

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ПРЕЦИЗИОННАЯ НЕЙРОИНТЕНСИВНАЯ ТЕРАПИЯ ПОСЛЕ ТЯЖЁЛОЙ ЧЕРЕПНО-МОЗГОВОЙ ТРАВМЫ: МУЛЬТИМОДАЛЬНЫЙ МОНИТОРИНГ,

ДИНАМИЧЕСКОЕ ВНУТРИЧЕРЕПНОЕ ДАВЛЕНИЕ И ИНДИВИДУАЛИЗИРОВАННЫЕ ЦЕЛИ ЦЕРЕБРАЛЬНОЙ ПЕРФУЗИИ

Аннотация

Актуальность. Тяжёлая черепно-мозговая травма представляет собой динамическое расстройство, при котором внутричерепное давление, перфузия, доставка кислорода, ауторегуляция, метаболизм и электрическая активность изменяются асинхронно. Фиксированные пороги выявляют опасность, но не всегда определяют оптимальную цель конкретного пациента. Цель. Оценить доказательства мультимодального нейромониторинга, давления во времени, тканевой оксигенации мозга, цереброваскулярной реактивности и индивидуализированного церебрального перфузионного давления после тяжёлой травмы и предложить модель прецизионной терапии.

Материалы и методы. Синтезированы руководства, рандомизированные исследования, проспективные когорты, физиологические работы, консенсусные алгоритмы и публикации до июля 2026 года. Данные систематизированы по сигналу мониторинга, физиологической интерпретации, вмешательству, терапевтической нагрузке, пространственным ограничениям и связи с исходом.

Результаты. Руководства рекомендуют лечить внутричерепное давление выше 22 мм рт. ст. и поддерживать церебральное перфузионное давление в пределах 60–70 мм рт. ст., учитывая состояние ауторегуляции. Исследования высокого разрешения показывают, что риск определяется величиной, длительностью, частотой и контекстом внутричерепной гипертензии, а не единичным значением. Индекс реактивности давления позволяет рассчитывать оптимальное перфузионное давление; COGiTATE подтвердило осуществимость CPPopt-ориентированного управления, но клиническая польза окончательно не доказана. Мониторинг тканевого кислорода выявляет региональную гипоксию при приемлемом давлении; BOOST-II уменьшило гипоксическую нагрузку, тогда как OXY-TC не улучшило шестимесячный исход. Дополнительные методы, включая непрерывную электроэнцефалографию, микродиализ, пупиллометрию, транскраниальную допплерографию и системный мониторинг, дополняют оценку. Совместный анализ сигналов непосредственно у постели больного помогает различать вазогенный отёк, недостаточную перфузию, диффузионную гипоксию, метаболический криз и электрические судороги, которые требуют различных, иногда противоположных терапевтических действий.

Заключение. Прецизионная нейроинтенсивная терапия должна сочетать безопасные пороги с индивидуальной динамической интерпретацией. Модель MULTI-TARGET объединяет давление, ауторегуляцию, оксигенацию, метаболизм, биоэлектрическую активность, нейровизуализацию и ответ на лечение, сохраняя чёткие критерии эскалации и деэскалации.

Ключевые слова: тяжёлая черепно-мозговая травма; внутричерепное давление; церебральное перфузионное давление; CPPopt; индекс реактивности давления; тканевая оксигенация мозга; мультимодальный нейромониторинг; церебральная ауторегуляция; церебральный микродиализ; прецизионная нейроинтенсивная терапия.

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OG‘IR KRANIOSEREBRAL TRAVMADAN KEYINGI PRETSIZION NEYROINTENSIV YORDAM: MULTIMODAL MONITORING, DINAMIK INTRAKRANIAL BOSIM VA INDIVIDUAL SEREBRAL PERFUZIYA MAQSADLARI

Annotatsiya

Dolzarblik. Og‘ir kraniotserebral travma dinamik patologik holat bo‘lib, unda intrakranial bosim, perfuziya, kislorod yetkazilishi, autoregulyatsiya, metabolizm va elektr faollik bir vaqtda bo‘lmagan tarzda o‘zgaradi. Belgilangan chegaralar xavfni ko‘rsatadi, biroq har bir bemor uchun optimal maqsadni doimo aniqlamaydi. Maqsad. Og‘ir travmadan keyingi multimodal neyromonitoring, bosim-vaqt yuklamasi, miya to‘qimasi oksigenatsiyasi, serebrovaskulyar reaktivlik va individual serebral perfuzion bosimga oid dalillarni baholash hamda aniq davolash modelini taklif etish.

Material va usullar. 2026-yil iyuligacha chop etilgan tavsiyalar, randomizatsiyalangan sinovlar, prospektiv kohortalar, fiziologik tadqiqotlar va konsensus algoritmlari sintez qilindi. Dalillar monitoring signali, fiziologik talqin, aralashuv, davolash yuklamasi, fazoviy cheklov va natija bilan bog‘liqlik bo‘yicha tizimlashtirildi.

Natijalar. Tavsiyalar intrakranial bosim 22 mm simob ustunidan oshganda davolashni va serebral perfuzion bosimni 60–70 mm simob ustunida saqlashni, autoregulyatsiya holatini hisobga olishni tavsiya qiladi. Yuqori aniqlikdagi tadqiqotlar xavf yagona qiymat emas, balki intrakranial gipertenziyaning kattaligi, davomiyligi, takrorlanishi va vaqt kontekstiga bog‘liqligini ko‘rsatadi. Bosim reaktivligi indeksi optimal perfuzion bosimni hisoblashga imkon beradi; COGiTATE CPPopt bo‘yicha boshqaruv amalga oshirilishini tasdiqladi, ammo klinik foyda to‘liq isbotlanmagan. Miya to‘qimasi kislorod monitoringi maqbul bosimda ham hududiy gipoksiyani aniqlaydi; BOOST-II gipoksik yuklamani kamaytirdi, OXY-TC esa olti oylik natijani yaxshilamadi. Uzluksiz elektroensefalografiya, mikrodializ, pupillometriya, transkranial Doppler va tizimli monitoring qo‘shimcha ma’lumot beradi. Signallarni bemor yotog‘ida bevosita birgalikda tahlil qilish vazogen shish, yetarli bo‘lmagan perfuziya, diffuzion gipoksiya, metabolik kriz va yashirin elektr tutqanoqlarini farqlashga yordam beradi.

Xulosa. Precision neyrointensiv yordam xavfsiz chegaralarni bemorga xos dinamik talqin bilan birlashtirishi kerak. MULTI-TARGET modeli bosim, autoregulyatsiya, oksigenatsiya, metabolizm, elektr faollik, tasvirlash va davolash javobini aniq eskalatsiya hamda deeskalatsiya mezonlari bilan birlashtiradi.

Kalit so‘zlar: og‘ir kraniotserebral travma; intrakranial bosim; serebral perfuzion bosim; CPPopt; bosim reaktivligi indeksi; miya to‘qimasi kislorodi; multimodal neyromonitoring; serebral autoregulyatsiya; serebral mikrodializ; pretsizion neyrointensiv yordam.

Introduction. Severe traumatic brain injury is not a single static lesion but a rapidly evolving interaction among primary structural damage, cerebral edema, hemorrhagic progression, microvascular dysfunction, excitotoxicity, mitochondrial failure, inflammation, seizures, systemic shock, hypoxemia, fever, anemia, and metabolic stress. The primary injury occurs at the moment of

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impact and includes contusion, laceration, axonal disruption, vascular injury, and intracranial hemorrhage. Secondary injury develops over minutes to days and is potentially modifiable through neurocritical care [2, 3, 10, 18]. Traditional management has relied on population-derived thresholds for intracranial pressure and cerebral perfusion pressure. The current Brain Trauma Foundation guideline recommends treatment when ICP exceeds 22 mm Hg and suggests maintaining CPP between 60 and 70 mm Hg. It also acknowledges that whether 60 or 70 mm Hg represents the preferable lower target depends partly on the patient's autoregulatory status. These recommendations provide essential safety boundaries but do not imply that every brain has the same compliance, perfusion requirement, oxygen extraction reserve, or response to vasopressors [1, 3, 10, 13]. A single ICP value can conceal clinically important heterogeneity. An ICP of 24 mm Hg lasting three minutes during endotracheal suctioning differs from an ICP of 24 mm Hg persisting for two hours with worsening pupillary reactivity, falling brain tissue oxygen, and impaired cerebrovascular reactivity. Similarly, CPP of 65 mm Hg may be adequate in a patient with preserved autoregulation but insufficient in another patient whose optimal autoregulatory range lies near 75 mm Hg. Raising CPP indiscriminately can also worsen hydrostatic edema, increase ICP, expose the patient to vasopressor complications, and fail to improve oxygen delivery when microcirculatory dysfunction predominates [4, 14, 19, 25].

This physiological diversity explains why severe TBI has increasingly been approached as a monitoring-defined syndrome. The clinical examination remains fundamental but is often limited by sedation, neuromuscular blockade, mechanical ventilation, extracranial injuries, intoxication, seizures, and metabolic disturbance. Computed tomography provides anatomical information at discrete intervals, whereas secondary brain injury evolves continuously. Multimodal monitoring attempts to bridge this temporal gap by integrating pressure, perfusion, autoregulation, oxygenation, electrophysiology, metabolism, blood flow, pupillary function, and systemic physiology [15, 17, 27]. The concept of precision neurocritical care does not reject guideline thresholds. It places them within a hierarchy. Population thresholds define minimum safety standards. Dynamic monitoring characterizes the mechanism of deterioration. Individualized targets estimate the physiological range most likely to maintain perfusion and oxygenation without aggravating edema or systemic complications. Treatment response then confirms or challenges the assumed mechanism. Multimodal monitoring also exposes an important distinction between numerical correction and biological rescue. Reducing ICP from 28 to 18 mm Hg may appear successful, but the intervention can still be harmful if it produces severe hypotension, hypocapnia, brain hypoxia, electrolyte disturbance, or renal injury. Raising CPP from 58 to 72 mm Hg may improve $PbtO_2$ in one patient but increase ICP and pulmonary edema in another. A monitor is useful only when its signal is interpreted in relation to other signals and linked to an intervention that improves the underlying pathophysiology [11, 12, 20].

Materials and Methods. This manuscript was designed as a structured integrative review with an original physiology-oriented synthesis. Evidence available through July 2026 was evaluated, with priority given to clinical practice guidelines, randomized controlled trials, prospective multicenter studies, high-resolution physiological cohorts, individual-patient analyses, consensus protocols, and clinically relevant investigations of multimodal monitoring. The principal evidence

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base included the Brain Trauma Foundation severe TBI guidelines, the American College of Surgeons best-practice guidance, the BEST-TRIP trial, the Seattle International Severe Traumatic Brain Injury Consensus Conference algorithms, CENTER-TBI high-resolution analyses, BOOST-II, OXY-TC, the BOOST-3 protocol, COGiTATE, autoregulation studies of CPPopt, and investigations of cerebral microdialysis, continuous electroencephalography, transcranial Doppler, pupillometry, and decompressive interventions [6, 13, 28]. Evidence was classified into seven domains. The first domain was intracranial pressure, including absolute thresholds, duration, pressure–time burden, waveform morphology, pulse amplitude, compensatory reserve, and response to therapy. The second was perfusion, including CPP, arterial pressure, intracranial pressure, vasopressor exposure, and individualized autoregulatory limits. The third domain was cerebral oxygenation, including brain tissue oxygen pressure, arterial oxygenation, hemoglobin, carbon dioxide, cerebral blood flow, diffusion distance, probe location, and oxygen consumption. The fourth was cerebral metabolism, including glucose, lactate, pyruvate, lactate-to-pyruvate ratio, glutamate, and glycerol. The fifth domain was electrical and neurological function, including continuous EEG, quantitative EEG, seizures, spreading depolarization, pupillary reactivity, and serial examination. The sixth domain was structural and vascular assessment, including CT, MRI, optic nerve sheath assessment, transcranial Doppler, and perfusion imaging. The seventh domain was treatment burden, including sedation, hyperosmolar therapy, ventilation, CSF drainage, temperature control, vasopressors, barbiturates, and decompressive craniectomy.

No new patient cohort was generated, and no independent meta-analysis was performed. Numerical findings were interpreted according to study design, monitoring modality, injury phenotype, outcome definition, and risk of confounding. The tables represent an original synthesis of published evidence rather than fabricated clinical data.

Results. ICP represents the pressure generated by the combined volumes of brain tissue, arterial and venous blood, cerebrospinal fluid, and pathological mass lesions within the cranial compartment. According to the Monro–Kellie principle, an increase in one component can initially be compensated by displacement of CSF and venous blood. Once compensatory reserve is exhausted, small volume changes can produce steep pressure increases. The numerical ICP value therefore reflects both intracranial volume and compliance. Two patients with ICP of 20 mm Hg may have different physiological states. One may have adequate compliance and a stable waveform; the other may be near the steep portion of the pressure–volume curve, with increasing pulse amplitude and impending decompensation. External ventricular drainage provides both measurement and therapeutic CSF diversion. An intraparenchymal transducer is generally easier to insert and is less vulnerable to obstruction by blood or collapsed ventricles, but it cannot drain CSF and may develop zero drift. EVD readings can also be distorted by incorrect leveling, open drainage, catheter occlusion, air bubbles, and transducer errors. The monitoring method must therefore be documented and checked before treatment is escalated. The BEST-TRIP trial compared an ICP-monitor-based protocol with management guided by imaging and clinical examination in resource-limited settings. It did not demonstrate superiority of the specific monitor-based protocol for its composite outcome. The trial did not establish that ICP is biologically irrelevant; rather, it showed that a monitored protocol cannot be separated from treatment strategy, expertise, timing, imaging access, nursing care,

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and the comparator protocol [10, 13, 23]. Subsequent consensus recommendations retained ICP monitoring as a central component of severe TBI care while emphasizing structured interpretation and escalation. The SIBICC algorithm organizes treatment into tiers beginning with basic physiological optimization, analgesia and sedation, head positioning, temperature control, CSF drainage, and hyperosmolar therapy before escalation to more intensive interventions [15, 17, 27].

The most important development has been the transition from a static threshold to ICP dose. Pressure–time dose incorporates both the magnitude above a threshold and the duration of exposure. High-resolution analyses have shown that lower ICP elevations may become harmful when prolonged, whereas short episodes at higher pressures can occasionally be tolerated. One influential analysis found that ICP above 20 mm Hg for approximately 37 minutes was associated with worse adult outcomes, while the tolerable duration progressively decreased as the pressure increased [3, 6, 15, 18]. CENTER-TBI data similarly demonstrated that the relationship between ICP and outcome depends on duration and that a universal 22-mm Hg boundary simplifies a continuous risk surface. The threshold remains useful for bedside action, but it should be supplemented by cumulative burden, waveform behavior, treatment intensity, lesion type, and accompanying physiological deterioration [11, 15, 17, 20].

Table 1. **Dynamic Interpretation of Intracranial Pressure**

ICP pattern	**Possible interpretation**	**Required contextual signals**	**Clinical implication**
Brief ICP increase during suctioning or turning	Stimulation-related transient response	MAP, CPP, oxygen saturation, waveform recovery	Correct trigger and reassess before major escalation
Persistent ICP 22–25 mm Hg	Sustained intracranial hypertension	CT evolution, $PbtO_2$, PRx, pupillary response	Mechanism-oriented first-tier treatment
Recurrent short ICP crises	Unstable compliance or repeated triggers	Sedation level, coughing, fever, ventilation, seizures	Identify recurrent precipitant and cumulative dose
Rising ICP pulse amplitude with stable mean ICP	Decreasing compensatory reserve	RAP index, waveform morphology, imaging	May precede numerical threshold crossing
High ICP with negative or preserved PRx	Pressure elevation with maintained reactivity	CPP response, $PbtO_2$, venous factors	Avoid automatic interpretation as identical to pressure-passive state
High ICP with positive PRx	Impaired autoregulation and pressure-passive circulation	CPP, $PbtO_2$, edema, systemic pressure	Higher risk; cautious CPP and ICP manipulation
Normal ICP with low $PbtO_2$	Regional hypoxia without global pressure elevation	Probe location, PaO_2, Hb, CPP, $PaCO_2$	Treat oxygen delivery or regional perfusion mechanism
Refractory ICP	Structural exhaustion of	Repeat CT, pupils,	Urgent surgical

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with mass effect	medical reserve	neurological change	reassessment

ICP Waveforms, Compensatory Reserve, and Early Warning. The ICP waveform contains cardiac, respiratory, and slow-wave components. The cardiac pulse commonly contains P1, P2, and P3 peaks. As compliance worsens, the tidal component can approach or exceed the percussion peak. Automated pulse-shape interpretation remains technically challenging, but increasing pulse amplitude and altered morphology can indicate reduced intracranial compliance before mean ICP becomes persistently elevated. The RAP index is the correlation between ICP pulse amplitude and mean ICP. Positive RAP values approaching 1 generally indicate that changes in intracranial volume are producing corresponding changes in pulse amplitude, consistent with reduced compensatory reserve. RAP values near zero can indicate preserved reserve or complete exhaustion, requiring contextual interpretation. Negative values may occur when the pressure–volume curve has reached extreme decompensation or after decompressive craniectomy. Slow waves reflect interactions among arterial pressure, vascular tone, cerebral blood volume, and intracranial compliance. Their relationship to autoregulation allows derivation of indices such as PRx. Modern high-frequency monitoring systems can display minute-by-minute trajectories rather than isolated nursing-chart values, enabling recognition of evolving patterns and response to treatment [5, 11, 16, 20]. Machine-learning models are being developed to predict ICP crises before threshold crossing. Their performance depends on signal quality, external validity, treatment annotations, and avoidance of alarm fatigue. Prediction should support earlier clinical assessment, not trigger automatic hyperosmolar treatment without confirmation of the mechanism.

Cerebral Perfusion Pressure and Its Limitations. CPP is commonly calculated as mean arterial pressure minus intracranial pressure. The simplicity of the equation can create a false impression that cerebral blood flow is directly determined by CPP. In reality, cerebral perfusion also depends on vascular resistance, autoregulation, carbon dioxide, oxygen tension, hematocrit, viscosity, venous pressure, microcirculation, cardiac output, and regional tissue pathology. A CPP of 65 mm Hg can be achieved by MAP of 80 mm Hg and ICP of 15 mm Hg or by MAP of 95 mm Hg and ICP of 30 mm Hg. These states are not physiologically equivalent. The second patient has greater intracranial pressure burden, higher vasopressor requirements, and potentially impaired microcirculatory flow despite the same calculated CPP. Guideline targets of 60–70 mm Hg were designed to avoid critical cerebral hypoperfusion while limiting complications associated with aggressive hypertension. Maintaining CPP above 70 mm Hg through fluids and vasopressors can increase acute respiratory distress, myocardial stress, edema, and systemic complications without guaranteeing improved cerebral oxygenation [6, 13, 28]. The lower safe CPP limit is not constant. In patients with intact autoregulation, cerebral arterioles dilate as CPP falls and constrict as CPP rises, stabilizing cerebral blood flow across a range. In impaired autoregulation, cerebral blood flow becomes pressure passive. A decrease in arterial pressure can then reduce blood flow directly, while an increase can raise cerebral blood volume and ICP.

Pressure Reactivity Index and CPPopt. PRx is calculated as the moving correlation between slow fluctuations in arterial blood pressure and ICP. A negative or near-zero relationship suggests that increased arterial pressure causes compensatory vasoconstriction without increasing

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intracranial blood volume. A positive relationship indicates pressure-passive vascular behavior in which increased arterial pressure is transmitted into increased intracranial blood volume and ICP.

CPPopt is derived by plotting PRx across observed CPP values. The CPP associated with the lowest PRx is interpreted as the pressure range in which autoregulatory reactivity is most effective. The target is dynamic and can change over time as edema, sedation, temperature, surgery, carbon dioxide, systemic shock, and vascular injury evolve [6, 11, 12, 20]. Observational studies have associated greater deviation below CPPopt with worse outcomes. Recent analyses suggest that patients may be more vulnerable to CPP below individualized optimal values than to moderate elevations above them. A 2025 reappraisal proposed that CPPopt may be interpreted more appropriately as a personalized lower boundary rather than an exact numerical point that must always be reached [16, 23, 30]. COGiTATE was the first randomized feasibility trial to prospectively target autoregulation-guided CPP. It demonstrated that CPPopt-oriented management could be delivered without an unacceptable increase in therapeutic intensity. A later secondary analysis found that periods close to CPPopt were associated with improved cerebrovascular reactivity, particularly when baseline reactivity allowed room for improvement. The trial was not powered to establish a definitive functional outcome advantage [4, 7, 14, 19]. A 2025 multicenter physiological study showed that $PbtO_2$ tended to peak near CPPopt and that time outside ICP thresholds and impaired PRx were associated with worse outcome. Importantly, ICP control remained the modifiable variable most consistently associated with both mortality and functional outcome, supporting a hierarchy in which autoregulation-guided CPP complements rather than replaces effective ICP management [2, 3, 10, 18].

Table 2. **Cerebral Perfusion Phenotypes and Potential Management Logic**

Physiological phenotype	**ICP**	**PRx**	**$PbtO_2$**	**Possible mechanism**	**Precision-management interpretation**
Low CPP with preserved autoregulation	Normal or elevated	Negative/near zero	Normal or low	Approaching lower autoregulatory limit	Cautious MAP support while monitoring oxygenation
Low CPP with impaired autoregulation	Variable	Positive	Often low	Pressure-passive hypoperfusion	Avoid hypotension; consider individualized CPP increase
High CPP with preserved autoregulation	Variable	Negative	Normal	Tolerated pressure range	Avoid unnecessary vasopressor escalation
High CPP with impaired autoregulation	Often rising	Positive	Variable	Hydrostatic increase in cerebral blood	Higher CPP may worsen edema and ICP

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				volume	
CPP near CPPopt with low $PbtO_2$	Acceptable	Best available	Low	Anemia, hypoxemia, diffusion limitation, local ischemia	Correct oxygen-delivery mechanism rather than CPP alone
CPP below CPPopt with high ICP	High	Variable	Low or normal	Perfusion failure caused by intracranial hypertension	Prioritize ICP reduction and reassess CPP
Normal CPP with metabolic crisis	Normal	Variable	Normal or low	Mitochondrial dysfunction or substrate failure	Use microdialysis and systemic metabolic correction
Unavailable CPPopt	Variable	Insufficient signal	Variable	Short data window, poor signal, nonstationarity	Use guideline targets and multimodal clinical assessment

Brain Tissue Oxygen Monitoring. Brain tissue oxygen pressure is measured with a focal intraparenchymal probe, commonly placed in radiographically normal-appearing frontal white matter or tissue at risk near a lesion. $PbtO_2$ reflects the balance among arterial oxygen tension, hemoglobin concentration, cerebral blood flow, oxygen diffusion, local capillary density, temperature, and tissue consumption. It is not a direct measure of whole-brain oxygenation. Values below approximately 20 mm Hg are commonly treated as brain tissue hypoxia, although risk is continuous and may become evident at higher or lower thresholds depending on duration and context. Probe location is critical. A probe near a contusion can identify regional ischemia but may not represent the opposite hemisphere. A probe in normal tissue can describe global physiological vulnerability but miss focal penumbral hypoxia. Low $PbtO_2$ despite normal ICP and CPP may result from systemic hypoxemia, anemia, low cardiac output, hypocapnia, pulmonary dysfunction, diffusion-limited oxygen delivery, microvascular thrombosis, focal ischemia, or increased metabolic demand. Treatment should therefore begin with mechanism identification rather than indiscriminate increases in FiO_2 or CPP [5, 11, 16]. BOOST-II showed that a protocol combining $PbtO_2$ and ICP monitoring was feasible and reduced the burden of brain tissue hypoxia compared with ICP-guided management alone. The trial was designed for physiological efficacy and feasibility rather than definitive functional-outcome superiority [2, 3, 18]. OXY-TC subsequently compared ICP plus $PbtO_2$ monitoring with ICP monitoring alone. The trial did not demonstrate superiority of the combined strategy for six-month neurological outcome. Interpretation is influenced by protocol adherence, probe placement, intervention efficacy, crossover in physiology, treatment intensity, and the possibility that correcting a focal oxygen value may not alter diffuse secondary injury [11, 12, 20]. The findings do not

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establish that $PbtO_2$ is clinically useless. They show that a monitor-derived value improves outcome only if the signal identifies a modifiable mechanism, the intervention corrects that mechanism safely, and correction occurs before irreversible injury. BOOST-3 and the BONANZA-GT program were designed to further evaluate whether protocolized oxygen-guided management improves patient-centered outcomes. Definitive phase III evidence remained an active research need through July 2026 [4, 14, 19, 25].

Table 3. **Interpretation of Low Brain Tissue Oxygen**

Low-$PbtO_2$ pattern	**Supporting findings**	**Likely mechanism**	**Potential response**
Low $PbtO_2$ with low PaO_2	Hypoxemia, pulmonary injury	Reduced arterial oxygen content	Optimize ventilation, oxygenation, recruitment, and pulmonary care
Low $PbtO_2$ with anemia	Reduced hemoglobin, acceptable saturation	Reduced oxygen-carrying capacity	Evaluate bleeding, transfusion context, and systemic oxygen delivery
Low $PbtO_2$ with low CPP	Hypotension or high ICP	Perfusion-limited oxygen delivery	Correct hypotension or intracranial hypertension
Low $PbtO_2$ after hyperventilation	Low $PaCO_2$ and reduced CBF	Cerebral vasoconstriction	Return toward normocapnia unless emergency herniation management
Low $PbtO_2$ with high ICP	Reduced CPP and microvascular compression	Intracranial hypertension	ICP-directed treatment and structural reassessment
Low $PbtO_2$ with normal	Local lesion, edema,	Diffusion limitation or	Review

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CPP and PaO_2	microvascular failure	regional ischemia	probe location, imaging, hemoglobin, flow, and metabolism
Low $PbtO_2$ with seizures	EEG ictal activity and increased demand	Supply–demand mismatch	Treat seizures and reassess oxygen response
Persistent low $PbtO_2$ despite correction	Normal systemic physiology, high LPR	Mitochondrial or metabolic crisis	Integrate microdialysis and avoid harmful escalation

Cerebral Microdialysis and Metabolic Crisis. Cerebral microdialysis samples extracellular fluid through a semipermeable catheter. Common bedside analytes include glucose, lactate, pyruvate, glutamate, and glycerol. The lactate-to-pyruvate ratio is used as an indicator of cellular redox state. An elevated ratio with low pyruvate can suggest ischemic substrate failure, whereas an elevated ratio with relatively preserved pyruvate may reflect mitochondrial dysfunction. Low brain glucose can occur despite normal systemic glucose. It may result from reduced delivery, increased utilization, excessive systemic glucose control, seizures, spreading depolarization, or mitochondrial dysfunction. Very aggressive systemic glycemic control can worsen cerebral substrate availability even when blood glucose appears acceptable. Microdialysis is spatially focal and requires integration with catheter location. Values in pericontusional tissue differ from those in normal-appearing white matter. Sampling intervals are also slower than ICP or EEG signals, limiting immediate crisis detection. The major clinical value of microdialysis is mechanistic differentiation. A patient with elevated ICP, low $PbtO_2$, and high lactate-to-pyruvate ratio may have perfusion-related metabolic failure. A patient with normal $PbtO_2$ but persistently high ratio may have mitochondrial dysfunction that is unlikely to respond to higher CPP alone. This distinction can prevent increasingly aggressive vasopressor therapy that corrects a number without restoring cellular metabolism [10, 13, 23].

Continuous EEG, Seizures, and Cortical Activity. Clinical examination cannot reliably detect nonconvulsive seizures in deeply sedated or comatose patients. Continuous EEG identifies electrographic seizures, periodic discharges, background suppression, reactivity, and evolving encephalopathy. Quantitative displays can support screening but require confirmation using raw EEG. Post-traumatic electrographic seizures can increase cerebral metabolic demand, ICP, lactate production, and oxygen consumption. Their effect is particularly important when oxygen delivery and autoregulation are already compromised. Treatment should consider seizure duration, frequency, spatial burden, background state, medication adverse effects, and the possibility that excessive anesthetic suppression may worsen hypotension and delay neurological assessment[16, 23, 30]. The

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absence of seizures does not imply physiological stability. Suppressed background activity may result from injury, sedatives, hypothermia, metabolic dysfunction, or ischemia. EEG should be interpreted with medication doses, temperature, ICP, $PbtO_2$, and systemic physiology.

Cortical spreading depolarizations are waves of near-complete neuronal and glial depolarization that can propagate through injured cortex. They increase metabolic demand and may convert tissue at risk into infarction when perfusion is inadequate. Detection currently requires subdural electrocorticography and is mainly confined to specialist centers and research protocols.

Pupillometry and Neurological Examination. Serial neurological assessment remains the only modality that directly evaluates integrated function. Pupillary asymmetry, loss of reactivity, decline in motor response, new posturing, or deterioration in brainstem reflexes requires immediate evaluation regardless of monitor values. Automated pupillometry quantifies pupil size, constriction velocity, latency, and a composite neurological pupil index. It reduces interobserver variability and can detect trends before gross fixed dilation. Abnormal values may indicate herniation, third-nerve compression, brainstem dysfunction, medication effects, ocular trauma, or systemic autonomic disturbance. Pupillometry is noninvasive and repeatable but not lesion-specific. A normal pupil does not exclude intracranial hypertension, and an abnormal pupil should not be attributed to ICP without examining ocular injury, previous surgery, topical medications, and baseline asymmetry.

Transcranial Doppler and Cerebral Blood Flow. Transcranial Doppler measures blood-flow velocity in basal cerebral arteries. It can identify elevated pulsatility, low diastolic flow, vasospasm, hyperemia, embolic signals, and patterns compatible with critically elevated intracranial resistance. Serial trends are more informative than isolated values. TCD-derived autoregulatory metrics can complement PRx, especially when invasive monitoring is unavailable. However, velocity is not equivalent to blood flow when vessel diameter changes, and adequate acoustic windows are absent in some patients. Thermal diffusion flowmetry, laser Doppler, and other local cerebral blood-flow monitors provide regional data but are less widely used. Their principal limitation resembles $PbtO_2$ and microdialysis: excellent temporal resolution within a very small tissue volume.

Systemic Physiology as a Neuromonitor. The injured brain depends on systemic oxygen delivery. Hypotension, hypoxemia, hyperthermia, anemia, dysglycemia, hypocapnia, hypercapnia, electrolyte disturbance, coagulopathy, and low cardiac output can produce secondary injury even when intracranial monitors appear stable. Arterial blood pressure should be measured invasively in monitored severe TBI. The transducer reference level matters because CPP calculation changes when MAP is referenced at the heart rather than the external auditory meatus. Institutions should use a standardized reference and document it. End-tidal carbon dioxide is useful for continuous ventilation assessment but may differ substantially from $PaCO_2$ in shock, pulmonary injury, high dead space, or changing ventilation. Arterial blood gas confirmation is necessary before major ventilatory changes. Hypocapnia reduces cerebral blood flow and can lower ICP rapidly, making it useful as a short-term emergency measure during impending herniation. Prolonged prophylactic hyperventilation can produce cerebral ischemia and should not be used as routine ICP control without appropriate monitoring [5, 11, 16]. Fever increases cerebral metabolism and can worsen ICP and oxygen demand. Normothermia is a foundational target. Prophylactic therapeutic hypothermia has not consistently improved neurological outcome and can increase complications. Temperature reduction

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may still be used as a rescue strategy in selected refractory intracranial hypertension, with recognition that it treats pressure burden rather than the primary injury.

Multimodal Pattern Recognition. The central principle of multimodal monitoring is that no single signal identifies every mechanism. The same ICP elevation can result from edema, hematoma expansion, hyperemia, venous obstruction, hydrocephalus, seizures, fever, ventilator dyssynchrony, inadequate sedation, or impaired autoregulation. A pattern of rising ICP, positive PRx, falling $PbtO_2$, and elevated lactate-to-pyruvate ratio suggests a high-risk state of impaired autoregulation, oxygen-delivery failure, and metabolic crisis. Increasing MAP may be beneficial if CPP is below CPPopt, but harmful if pressure passivity causes ICP to rise further. A bedside CPP challenge with simultaneous observation of ICP, PRx, $PbtO_2$, and systemic effects can clarify the response. Low $PbtO_2$ with normal ICP, preserved PRx, normal CPP, and low hemoglobin suggests oxygen-content limitation rather than pressure failure. High ICP with normal $PbtO_2$ and preserved metabolism may represent a pressure problem before tissue hypoxia develops, allowing targeted ICP reduction without excessive elevation of CPP. Electrographic seizures with transient ICP elevation, rising $PbtO_2$ consumption, and increased lactate require antiseizure treatment rather than repeated osmotherapy alone. Similarly, ventilator dyssynchrony and coughing should be corrected before interpreting transient pressure elevations as refractory cerebral edema.

Table 4. **Multimodal Physiological Patterns**

Multimodal pattern	**Probable dominant mechanism**	**Potentially misleading isolated interpretation**	**Integrated response**
High ICP, low CPP, low $PbtO_2$, positive PRx	Intracranial hypertension with pressure-passive hypoperfusion	“Raise MAP until CPP is normal”	Reduce ICP, cautiously support MAP, assess surgery and oxygen response
High ICP, normal $PbtO_2$, negative PRx	Pressure elevation with preserved oxygenation and reactivity	“No treatment because oxygen is normal”	Evaluate pressure–time burden, compliance, imaging, and trajectory
Normal ICP, low $PbtO_2$, low Hb	Reduced oxygen content	“ICP and CPP are normal, therefore brain is safe”	Correct systemic oxygen delivery and reassess
Normal ICP, normal $PbtO_2$, high LPR	Metabolic or mitochondrial dysfunction	“All monitored physiology is adequate”	Review glucose, seizures, temperature, perfusion, and substrate delivery
Recurrent ICP spikes with EEG seizures	Ictal metabolic and vascular activation	“Refractory edema”	Treat electrographic seizures and avoid repetitive nonspecific osmotherapy
High CPP, rising ICP, positive PRx	Autoregulatory failure with hydrostatic edema	“Higher CPP is always protective”	Reduce vasopressor-driven overshoot and reassess CPPopt

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Low CPP, negative PRx, normal $PbtO_2$	Lower CPP tolerated within autoregulatory range	"Immediate high-dose vasopressor required"	Avoid hypotension but assess treatment burden before escalation
Worsening pupils with stable ICP	Focal mass effect, compartmental pressure gradient, or brainstem lesion	"Stable global ICP excludes deterioration"	Urgent examination and repeat imaging

Treatment Response as a Diagnostic Test. A therapeutic intervention provides physiological information. A hyperosmolar bolus that reduces ICP, improves pulse amplitude, raises CPP, and increases $PbtO_2$ supports a pressure-mediated mechanism. If ICP falls but $PbtO_2$ and metabolism do not improve, the oxygen problem may be independent or irreversible. A CPP challenge can be performed by a controlled increase in MAP while monitoring ICP, PRx, and $PbtO_2$. Improved $PbtO_2$ with stable or falling ICP suggests preserved autoregulatory benefit. Rising ICP without oxygen improvement suggests pressure passivity and hydrostatic worsening. A short FiO_2 challenge can confirm probe responsiveness and diffusion reserve but should not be interpreted as evidence that hyperoxia is a definitive treatment. Very high arterial oxygen can increase $PbtO_2$ without restoring cerebral blood flow or metabolism. CSF drainage that rapidly lowers ICP and improves CPP identifies a volume-responsive component. Failure of drainage may indicate catheter obstruction, nonhydrocephalic edema, mass lesion, venous congestion, or exhausted compliance. Precision care requires documenting the pre-intervention hypothesis, intervention, expected response, observed multimodal response, and decision to continue or stop. Without this feedback loop, treatment becomes escalation by protocol rather than physiology.

Treatment Intensity and Iatrogenic Burden. The therapeutic intensity level quantifies how aggressively ICP is being treated. Two patients with identical ICP may differ substantially if one requires only head elevation and light sedation while the other requires repeated hyperosmolar therapy, vasopressors, paralysis, barbiturates, hypothermia, and decompressive surgery. Treatment intensity is not a neutral covariate. Deep sedation prevents examination and promotes hypotension, ileus, infection, delirium, and prolonged ventilation. Hyperosmolar agents can cause electrolyte disturbances, renal injury, hyperchloremia, and intravascular depletion. Vasopressors can produce arrhythmia, myocardial stress, peripheral ischemia, and pulmonary complications. Barbiturate coma can reduce refractory ICP but requires hemodynamic tolerance and EEG monitoring. Decompressive craniectomy reliably lowers ICP, but randomized trials show that the effect on survival can include increased survival with severe disability. Treatment goals and family communication must therefore distinguish pressure control from guaranteed neurological recovery [15, 17, 27]. DECRA evaluated early decompressive craniectomy for diffuse ICP elevation at a relatively low threshold and did not demonstrate improved functional outcome. RESCUEicp evaluated decompression for later refractory intracranial hypertension and reduced mortality, but increased the number of survivors across several disability categories. These trials demonstrate that timing, threshold, injury phenotype, surgical technique, and outcome preference matter [16, 23, 30] The decision to escalate should therefore consider pressure burden, imaging, pupils, autoregulation, tissue oxygen, age, premorbid function,

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extracranial injury, reversibility, and the patient's values. The decision to de-escalate should be equally structured.

Imaging Within a Precision Monitoring Strategy. Initial CT defines mass lesions, contusions, diffuse swelling, cisternal compression, midline shift, fractures, and traumatic subarachnoid hemorrhage. Repeat CT is required when neurological status worsens, pupils change, ICP rises unexpectedly, physiological patterns become discordant, or hemorrhagic progression is suspected. Stable ICP does not exclude a new focal lesion when the monitor is located in the opposite hemisphere or after decompressive craniectomy. Conversely, repeated routine CT exposes the patient to transfer risk and radiation. Imaging frequency should be linked to clinical and physiological change. MRI can identify diffuse axonal injury, brainstem lesions, ischemia, and microhemorrhage that are not visible on CT. It is usually performed after acute physiological stabilization because transport and scanner compatibility are limiting factors. CT perfusion and advanced MRI can characterize regional flow and metabolism, but routine use in unstable severe TBI remains limited. Their greatest role may be resolving discordance among ICP, $PbtO_2$, clinical examination, and structural CT.

Spatial Limitations of Multimodal Monitoring. ICP measured in one compartment may not represent pressure in another when focal lesions, compartmentalization, or decompressive surgery create pressure gradients. $PbtO_2$, microdialysis, and local blood-flow probes sample only a small region. Probe placement should be planned according to the clinical question. Placement in normal-appearing tissue assesses global vulnerability. Placement near a contusion evaluates perilesional tissue at risk. Bilateral or multiparameter monitoring can improve spatial representation but increases invasiveness, cost, infection risk, hemorrhage risk, and data complexity. Monitor location must be documented using post-placement CT. A low $PbtO_2$ value from tissue within an established hematoma, infarct, or catheter tract may not be modifiable and can lead to harmful systemic escalation. The spatial limitation of invasive monitoring reinforces the role of serial examination, imaging, EEG coverage, and systemic assessment. Precision does not mean that a locally precise number represents the whole brain.

The MULTI-TARGET Framework. The proposed MULTI-TARGET model contains eleven linked domains. Monitoring validity requires confirmation of transducer leveling, calibration, waveform quality, catheter patency, probe position, arterial-line damping, and time synchronization. Treatment should not be escalated from an unverified signal. Understanding pressure burden requires assessment of ICP magnitude, duration, frequency, waveform, compensatory reserve, and precipitating events rather than reliance on a single threshold. Lesion topography integrates CT and MRI findings with monitor location. Focal mass effect, diffuse edema, ventricular obstruction, and postcraniectomy physiology require different interpretations.

Tissue oxygenation incorporates $PbtO_2$, PaO_2, saturation, hemoglobin, CPP, $PaCO_2$, temperature, and probe location. Individual autoregulation uses PRx, CPPopt, lower and upper autoregulatory limits, and response to controlled CPP changes. Treatment response turns interventions into bedside physiological tests. Electrical activity incorporates continuous EEG, seizure burden, background reactivity, and medication effects. Glucose and metabolic state include systemic glucose, cerebral glucose, lactate, pyruvate, lactate-to-pyruvate ratio, temperature, nutrition, and mitochondrial

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function. Escalation criteria define when to advance from basic treatment to hyperosmolar therapy, CSF drainage, neuromuscular blockade, barbiturates, advanced temperature control, or surgery. Reassessment requires repeated examination, review of trends, imaging when indicated, and evaluation of iatrogenic complications. Therapeutic de-escalation identifies when sedation, osmotherapy, vasopressors, ventilation intensity, and invasive monitoring can be reduced safely.

Table 5. **Scientific Originality of the MULTI-TARGET Model**

Existing limitation	**Conventional interpretation**	**Proposed original element**	**Expected contribution**
ICP treated as a binary threshold	ICP above 22 mm Hg automatically triggers escalation	Magnitude, duration, recurrence, waveform, and context integrated	Reduces overtreatment of transient episodes and undertreatment of sustained burden
CPP treated as a universal number	Every patient maintained at the same 60–70 mm Hg target	CPPopt, PRx, oxygenation, and systemic burden incorporated	Supports individualized lower and upper perfusion limits
$PbtO_2$ treated as global oxygenation	One focal value assumed to represent the whole brain	Probe location and lesion topography explicitly included	Prevents inappropriate systemic escalation
Monitor correction equated with biological rescue	Numerical normalization defines success	Treatment response assessed across pressure, oxygen, metabolism, and EEG	Identifies physiologically ineffective treatment
Multimodal data reviewed independently	Separate screens and isolated thresholds	Time-synchronized pattern recognition	Improves mechanism-specific intervention
Escalation emphasized more than de-escalation	Intensive therapy continues after crisis resolution	Explicit daily de-escalation criteria	Reduces sedation, vasopressor, osmotic, and ventilation burden
Poor outcome linked only to peak ICP	Highest value used as primary risk marker	Cumulative pressure–time dose incorporated	Better reflects secondary injury exposure
CPPopt interpreted as an exact mandatory value	Vasopressors used to force CPP to a point target	CPPopt considered a dynamic zone and possible lower safety boundary	Reduces treatment-induced edema and systemic complications
Clinical examination displaced by technology	Monitor values dominate decision-making	Examination, pupils, imaging, and monitor validity remain primary checkpoints	Preserves recognition of focal and compartmental deterioration

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Discussion. The principal finding of this synthesis is that precision neurocritical care should not replace established thresholds with another set of rigid personalized numbers. Its purpose is to combine population safety limits with continuous interpretation of the individual patient's evolving physiology. The ICP threshold of 22 mm Hg remains clinically useful because bedside care requires actionable limits. However, high-resolution studies demonstrate that the relationship between ICP and outcome is continuous. The biological effect of intracranial hypertension depends on how high the pressure rises, how long it remains elevated, how often it recurs, whether compensatory reserve is exhausted, and whether oxygenation, autoregulation, metabolism, and neurological function deteriorate simultaneously [7, 14, 19]. This does not mean that clinicians should wait for a complex algorithm before treating dangerous pressure. Sustained ICP above the guideline threshold, especially with pupillary change, mass effect, low CPP, or falling $PbtO_2$, requires immediate intervention. Dynamic analysis is most valuable in distinguishing transient events, guiding the intensity of therapy, and determining whether the chosen intervention is helping. The same principle applies to CPP. Maintaining a minimum CPP reduces the risk of ischemia, but higher pressure is not universally better. When autoregulation is impaired, vasopressor-driven increases in MAP can increase cerebral blood volume, ICP, and edema. When autoregulation is preserved and CPP lies below the patient's lower limit, the same intervention may improve oxygenation and metabolism.

PRx and CPPopt provide a physiologically coherent method for estimating this difference. COGiTATE established feasibility and showed that the target can be updated at the bedside. The 2025 secondary analysis supported improved autoregulatory function during periods close to CPPopt. Outcome efficacy nevertheless remains uncertain because feasibility, physiological improvement, and functional recovery represent different evidentiary stages [11, 12, 20]. CPPopt also has technical limitations. Reliable estimation requires adequate high-frequency arterial pressure and ICP data, sufficient spontaneous variability, stable monitoring, and an identifiable U-shaped PRx curve. The estimate may be unavailable, delayed, unstable, or influenced by treatment. It should therefore be presented with a confidence measure and trend rather than as a deterministic number. The 2025 CPP reappraisal is clinically important because it suggests that the danger of falling below the individualized target may be greater than the danger of moderate overshoot. This supports using CPPopt as a personalized lower limit in selected patients rather than forcing CPP to remain precisely at the calculated optimum at all times. Brain tissue oxygenation illustrates both the promise and limitations of multimodal monitoring. BOOST-II demonstrated that $PbtO_2$-guided treatment can reduce hypoxic exposure. OXY-TC did not show superior six-month outcome. These findings are compatible if a monitor is highly effective at detecting and correcting a physiological abnormality but the intervention does not consistently change diffuse injury, probe sampling is regional, or treatment introduces competing harms [2, 3, 10, 18].

The correct conclusion is not that oxygen monitoring should be used in every patient or abandoned entirely. It should be used when the clinical team can interpret probe location, identify the cause of low oxygen, apply a mechanism-specific intervention, and evaluate the response. Low $PbtO_2$ caused by anemia should not be treated in the same way as low $PbtO_2$ caused by high ICP, hypocapnia, or local diffusion failure. Multimodal monitoring is especially valuable when signals disagree. Normal ICP with low $PbtO_2$ challenges the assumption that pressure control alone ensures

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adequate oxygen delivery. Normal $PbtO_2$ with a high lactate-to-pyruvate ratio challenges the assumption that oxygen availability guarantees mitochondrial utilization. Stable ICP with worsening pupils challenges the assumption that one regional pressure measurement excludes focal herniation. The framework also emphasizes systemic physiology. The most sophisticated intracranial platform cannot compensate for untreated hemorrhagic shock, severe hypoxemia, fever, profound anemia, or repeated hypotension. Prevention of secondary insults begins before monitor insertion and continues during transport, imaging, surgery, and intensive care. A major risk of advanced monitoring is therapeutic overreaction. Multiple sensors create multiple abnormal values, each of which can provoke intervention. This can produce polytherapy involving high-dose vasopressors, repeated osmotherapy, hyperoxia, excessive transfusion, deep sedation, paralysis, and prolonged ventilation. The number of monitored parameters should not determine the number of treatments. Treatment response must therefore be incorporated into the definition of success. If increasing MAP raises CPP but worsens ICP, leaves $PbtO_2$ unchanged, and requires escalating vasopressors, the intervention has failed biologically despite correction of the CPP number. If osmotherapy repeatedly lowers ICP for only minutes while sodium, renal function, and hemodynamics deteriorate, definitive structural treatment should be reconsidered. De-escalation is similarly important. Severe TBI protocols often describe how to add therapy but provide less detail on how to remove it. Daily evaluation should determine whether neuromuscular blockade, barbiturates, high-dose sedation, osmotherapy, vasopressors, hyperventilation, and invasive monitoring remain necessary.

The decision to remove an ICP monitor should consider stability during stimulation, absence of recurrent pressure burden, imaging stability, reduced treatment intensity, recovery of examination, and lack of planned procedures likely to destabilize physiology. Removal based only on one day of normal mean ICP can be premature when sedation or drainage has masked instability. Data integration remains a practical barrier. ICP, arterial pressure, $PbtO_2$, EEG, temperature, ventilation, medication, microdialysis, and laboratory results often reside in separate systems with different clocks and sampling rates. Manual interpretation is vulnerable to missed temporal relationships.

Future platforms should synchronize data, annotate interventions, display pressure–time dose, calculate PRx and CPPopt with confidence intervals, identify discordant patterns, and distinguish artifact from physiology. Alerts should describe a probable mechanism rather than merely announce that a threshold has been crossed. Artificial intelligence may assist prediction of ICP crises and multimodal phenotyping, but models must be externally validated and transparent. Algorithms trained in high-resource tertiary centers may not generalize to different monitor types, nursing practices, treatment protocols, or patient populations. Precision care must also remain feasible in resource-limited settings. The absence of $PbtO_2$, microdialysis, or automated CPPopt does not preclude physiology-based treatment. Serial examination, CT, EVD or intraparenchymal ICP, arterial pressure, blood gases, hemoglobin, temperature, sodium, pupillometry, and transcranial Doppler can form a pragmatic multimodal platform. The CREVICE protocol and other consensus efforts demonstrate that structured severe TBI care can be adapted to settings without invasive ICP monitoring. The principle is to use available information systematically while recognizing uncertainty, rather than equating precision with expensive technology [4, 8, 14, 25].

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The article's proposed MULTI-TARGET model is intended to organize this reasoning. It is not a validated therapeutic score and does not establish new treatment thresholds. Its scientific originality lies in connecting signal validity, dynamic dose, spatial representation, autoregulatory targets, metabolic state, treatment response, escalation, and de-escalation within one closed-loop framework. Several limitations should be acknowledged. Much of the evidence linking multimodal variables to outcome is observational and vulnerable to confounding by injury severity and treatment intensity. A monitor may appear associated with poor outcome because it is used in the sickest patients. Conversely, centers using advanced monitoring may also provide more specialized care. Physiological target trials are difficult because treatment protocols contain multiple interventions. A $PbtO_2$ strategy is not a single treatment; it may alter FiO_2, ventilation, CPP, transfusion, sedation, temperature, and surgery. Outcome effects cannot always be attributed to the monitor itself. The future research agenda should include adequately powered trials of autoregulation-guided perfusion, brain tissue oxygen protocols, and integrated multimodal decision support. Studies should record treatment burden, systemic complications, probe location, signal quality, and adherence. Outcome measures should extend beyond mortality and dichotomized Glasgow Outcome Scale categories. Cognitive recovery, communication, return to home, independence, quality of life, caregiver burden, and survival with severe disability are relevant to patients and families.

Conclusion. Severe traumatic brain injury is an evolving physiological disorder in which intracranial pressure, cerebral perfusion, autoregulation, oxygen delivery, metabolism, and electrical activity can deteriorate independently or interact synergistically. Guideline thresholds remain essential. Sustained ICP above 22 mm Hg should prompt treatment, and CPP should generally be maintained within a safe range of 60–70 mm Hg. These values are population-derived boundaries rather than universal individualized optima. ICP should be interpreted dynamically. Magnitude, duration, recurrence, waveform morphology, compensatory reserve, precipitating events, treatment intensity, and multimodal consequences determine the biological importance of an episode. PRx and CPPopt provide a rational method for estimating individualized autoregulatory targets. COGiTATE established feasibility, and subsequent analyses support physiological relevance. Definitive improvement in patient-centered outcome remains to be proven. $PbtO_2$ monitoring detects regional brain hypoxia that may occur despite acceptable ICP and CPP. BOOST-II demonstrated reduction in hypoxic burden, whereas OXY-TC did not establish superior six-month neurological outcome. The discrepancy emphasizes that detection, numerical correction, and clinical benefit are separate stages. Continuous EEG, cerebral microdialysis, pupillometry, transcranial Doppler, serial imaging, and systemic monitoring provide complementary information. Their value arises from integration rather than independent threshold treatment. The proposed MULTI-TARGET framework combines monitor validity, pressure–time burden, lesion topography, tissue oxygenation, autoregulation, treatment response, electrical activity, metabolism, escalation, reassessment, and de-escalation. Precision neurocritical care is therefore not defined by the number of probes inserted into the brain. It is defined by the ability to identify the dominant mechanism of secondary injury, select the least harmful effective intervention, verify the physiological response, recognize treatment failure, and withdraw unnecessary therapy.

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PATIENT-SPECIFIC CRANIOPLASTY IN THE ADDITIVE-MANUFACTURING ERA: COMPARATIVE EVALUATION OF PEEK, TITANIUM, PMMA, AND REGENERATIVE POROUS IMPLANTS

Abstract

Background. Patient-specific cranioplasty has evolved from intraoperative manual contouring toward computed-tomography-based design, additive manufacturing, and biologically informed implant architecture. Material selection remains controversial because geometric accuracy does not automatically ensure infection resistance, soft-tissue compatibility, mechanical durability, or osseointegration.

Materials and methods. Randomized trials, prospective cohorts, retrospective comparative studies, biomechanical investigations, additive-manufacturing studies, and clinical series published through July 2026 were synthesized. Evidence was organized according to defect geometry, implant accuracy, mechanical and thermal behavior, imaging compatibility, infection, exposure, fluid collection, manufacturing workflow, cost, and biological integration.

Results. Patient-specific PEEK provides accurate contour reconstruction, low weight, favorable imaging characteristics, and bone-like elastic behavior, but remains bioinert and may be associated with subgaleal or epidural fluid collections. Titanium offers high mechanical strength, thin-profile fabrication, reliable fixation, and opportunities for porous osseointegrative architecture, but produces imaging artifacts and may be vulnerable to thermal discomfort or exposure under compromised scalp. PMMA remains accessible, modifiable, and cost-effective, particularly when manufactured with three-dimensional printed molds; limitations include exothermic polymerization, brittleness, residual monomer, and inconsistent tissue integration. Porous hydroxyapatite, calcium-phosphate–titanium composites, and experimental porous titanium or functionalized polymer implants seek progressive bone ingrowth and vascular integration, but clinical evidence remains heterogeneous and long-term explantability requires consideration.

Conclusion. No universally superior cranioplasty material exists. The proposed CRANIO-MAP framework links wound biology, defect geometry, soft tissue, cerebrospinal-fluid dynamics, imaging requirements, mechanical demands, manufacturing logistics, biological integration, and patient priorities to implant selection.

Keywords: cranioplasty; patient-specific implant; additive manufacturing; three-dimensional printing; polyetheretherketone; titanium; polymethylmethacrylate; porous hydroxyapatite; osseointegration; cranial reconstruction.

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ПАЦИЕНТ-СПЕЦИФИЧЕСКАЯ КРАНИОПЛАСТИКА В ЭПОХУ АДДИТИВНОГО ПРОИЗВОДСТВА: СРАВНИТЕЛЬНАЯ ОЦЕНКА PEEK, ТИТАНА, PMMA И РЕГЕНЕРАТИВНЫХ ПОРИСТЫХ ИМПЛАНТАТОВ

Аннотация

Актуальность. Пациент-специфическая краниопластика прошла путь от интраоперационного ручного моделирования до проектирования на основе компьютерной томографии, аддитивного производства и биологически ориентированной архитектуры имплантатов. Выбор материала остаётся спорным, поскольку геометрическая точность не гарантирует устойчивость к инфекции, совместимость с мягкими тканями, механическую долговечность или остеоинтеграцию.

Материалы и методы. Синтезированы рандомизированные исследования, проспективные когорты, ретроспективные сравнительные работы, биомеханические и аддитивно-производственные исследования, опубликованные до июля 2026 года. Данные систематизированы по геометрии дефекта, точности, механическим и термическим свойствам, совместимости с визуализацией, инфекции, экспозиции, жидкостным скоплениям, производству, стоимости и биологической интеграции.

Результаты. Пациент-специфический PEEK обеспечивает точное восстановление контура, малую массу, благоприятную послеоперационную визуализацию и эластичность, приближенную к кости, однако остаётся биоинертным и может сопровождаться субгалеальными или эпидуральными скоплениями жидкости. Титан обладает высокой прочностью, позволяет создавать тонкие и пористые конструкции и обеспечивает надёжную фиксацию, но вызывает артефакты и может экспонироваться при неудовлетворительном состоянии скальпа. PMMA доступен, модифицируем и экономически оправдан, особенно при применении трёхмерно напечатанных форм; его ограничения включают экзотермическую полимеризацию, хрупкость, остаточный мономер и отсутствие полноценной интеграции. Пористый гидроксиапатит, кальций-фосфатно-титановые композиты и функционализированные полимерные конструкции направлены на врастание кости и сосудов, но их доказательная база остаётся неоднородной, а биологическая интеграция может осложнять последующее удаление инфицированного или повреждённого устройства. Предложенная модель учитывает качество кожно-апоневротического лоскута, перенесённую инфекцию, лучевую терапию, наличие шунта, дефект основания черепа, ожидаемую нейровизуализацию и локальные производственные возможности.

Заключение. Универсально лучшего материала не существует. Модель CRANIO-MAP связывает биологию раны, геометрию, мягкие ткани, ликвородинамику, визуализацию, механику, производство, остеоинтеграцию и предпочтения пациента.

Ключевые слова: краниопластика; пациент-специфический имплантат; аддитивное производство; трёхмерная печать; полиэфирэфиркетон; титан; полиметилметакрилат; пористый гидроксиапатит; остеоинтеграция; реконструкция черепа.

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ADDITIV ISHLAB CHIQARISH DAVRIDA BEMORGA MOSLASHTIRILGAN KRANIOPLASTIKA: PEEK, TITAN, PMMA VA REGENERATIV G‘OVAK IMPLANTLARNING QIYOSIY BAHOSI

Annotatsiya

Dolzarblik. Bemorga moslashtirilgan kranioplastika intraoperatsion qo‘lda shakllantirishdan kompyuter tomografiyasiga asoslangan loyihalash, additiv ishlab chiqarish va biologik yo‘naltirilgan implant arxitekturasigacha rivojlandi. Materialni tanlash bahsli bo‘lib qolmoqda, chunki geometrik aniqlik infeksiyaga chidamlilik, yumshoq to‘qimalar bilan moslik, mexanik uzoq muddatlilik yoki osteointegratsiyani avtomatik ravishda ta’minlamaydi.

Material va usullar. 2026-yil iyuligacha chop etilgan randomizatsiyalangan sinovlar, prospektiv kohortalar, retrospektiv qiyosiy tadqiqotlar, biomekanik va additiv ishlab chiqarish ishlari sintez qilindi. Dalillar nuqson geometriyasi, implant aniqligi, mexanik va termik xususiyatlar, tasvirlashga moslik, infeksiya, ekspozitsiya, suyuqlik to‘planishi, ishlab chiqarish, xarajat va biologik integratsiya bo‘yicha tizimlashtirildi.

Natijalar. Bemorga mos PEEK aniq kontur, kam massa, yaxshi tasvirlash va suyakka yaqin elastiklik beradi, biroq bioinert bo‘lib, subgaleal yoki epidural suyuqlik to‘planishi bilan kechishi mumkin. Titan yuqori mustahkamlik, yupqa profil, ishonchli fiksatsiya va g‘ovak osteointegrativ tuzilma yaratish imkonini beradi, ammo tasviriy artefaktlar, termik noqulaylik va zaif bosh terisida ekspozitsiya xavfiga ega. PMMA arzon, o‘zgartiriladigan va uch o‘lchamli qoliplar bilan aniq tayyorlanadigan materialdir; uning cheklovlari ekzotermik polimerizatsiya, mo‘rtlik, qoldiq monomer va sust biologik integratsiyadir. G‘ovak gidroksiapatit, kalsiy-fosfat–titan kompozitlari va funksionalizatsiyalangan polimerlar suyak va tomirlarning ichkariga o‘sishini rag‘batlantirishga qaratilgan, biroq klinik dalillar turlicha va kuchli integratsiya keyingi eksplantatsiyani murakkablashtirishi mumkin. Model skalp va yara holati, oldingi infeksiya yoki radioterapiya, likvor shunti, nuqsonning anatomik murakkabligi, keyingi KT yoki MRT ehtiyoji, bemor yoshi, implantning kutilayotgan mexanik yuklanishi va mahalliy raqamli ishlab chiqarish imkoniyatlarini birgalikda baholaydi.

Xulosa. Barcha bemorlarga mos universal material mavjud emas. CRANIO-MAP modeli yara biologiyasi, geometriya, yumshoq to‘qima, likvorodinamik holat, tasvirlash, mexanika, ishlab chiqarish, osteointegratsiya va bemor ustuvorliklarini bog‘laydi.

Kalit so‘zlar: kranioplastika; bemorga mos implant; additiv ishlab chiqarish; uch o‘lchamli bosib chiqarish; poliefirefirketon; titan; polimetilmetakrilat; g‘ovak gidroksiapatit; osteointegratsiya; bosh suyagini rekonstruksiya qilish.

Introduction. Cranioplasty restores the mechanical continuity, external contour, and protective function of the skull after decompressive craniectomy, trauma, infection, tumor resection, congenital deformity, or removal of a failed previous implant. The procedure is often described as reconstructive, but its clinical role extends beyond cosmesis. Re-establishing a closed cranial vault can improve protection of the brain, normalize atmospheric-pressure transmission, modify cerebrospinal-fluid and venous dynamics, and contribute to neurological recovery in selected patients with the syndrome of the trephined [1, 2, 10, 13]. Despite its apparently straightforward objective, cranioplasty remains associated with clinically important rates of infection, wound dehiscence,

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hematoma, hydrocephalus, seizures, fluid collection, implant exposure, fracture, displacement, and reoperation. Outcomes are influenced by the original pathology, interval after craniectomy, history of contamination, previous operations, cerebrospinal-fluid shunting, radiation, diabetes, smoking, nutritional status, scalp quality, defect size, implant geometry, fixation, and surgical technique. Material is important, but it is only one component of a complex biological and mechanical system [3, 6, 10]. Autologous bone is attractive because it is anatomically matched and biologically familiar. Its limitations include resorption, infection, fragmentation, warping, storage-related contamination, and progressive failure, particularly in children and after large decompressive craniectomy. Alloplastic reconstruction becomes necessary when the original flap is unavailable, contaminated, resorbed, oncologically unsuitable, mechanically deficient, or has failed previously [2, 3, 18].

Historically, alloplastic implants were manually shaped intraoperatively from polymethylmethacrylate, titanium mesh, or other materials. Manual contouring is accessible but depends heavily on operator experience and can produce irregular edges, asymmetry, dead space, prolonged operating time, and suboptimal temporalis reconstruction. Patient-specific implant manufacturing replaces subjective contouring with a digital workflow that reconstructs the missing cranial anatomy from high-resolution computed tomography. The simplest reconstruction uses mirror imaging of the unaffected side. Bilateral, midline, fronto-orbito-temporal, suboccipital, and skull-base defects require template databases, spline interpolation, anatomical landmarking, or semiautomated surface reconstruction. The final implant may be milled from a solid PEEK block, additively manufactured from titanium alloy, cast from PMMA using a three-dimensional printed mold, or produced from porous bioceramic or composite material [11, 12, 20]. Patient specificity provides more than a smooth external contour. Digital design can incorporate variable thickness, fixation tabs, countersunk screw holes, dural suspension apertures, temporal hollow correction, channels for drains, porous interfaces, planned overlap with healthy bone, and avoidance of frontal sinus or vascular structures. The design can also reduce intraoperative modification, which may shorten surgery and decrease contamination from repeated handling [2, 3, 10, 18].

A patient-specific implant is not necessarily biologically superior. A perfectly fitted implant may trap fluid, compress dura, leave an unrecognized contaminated sinus, overload thin scalp, or become infected. Conversely, a manually molded implant may perform well when soft-tissue coverage is excellent and surgical technique is meticulous. The additive-manufacturing era therefore requires a shift from geometry-centered thinking to patient–material–workflow matching. PEEK, titanium, and PMMA currently represent major alloplastic options. PEEK is lightweight, radiolucent, chemically stable, and mechanically less rigid than titanium. Titanium offers high strength, thin-profile fabrication, durable fixation, and established osseous biocompatibility. PMMA is widely available, inexpensive, modifiable, and compatible with mold-based local manufacturing. Each material also has distinctive failure modes [3, 6, 15, 18]. Regenerative porous implants represent a different therapeutic concept. Rather than functioning only as permanent protective plates, they are designed to permit tissue infiltration, vascularization, and bone ingrowth. Porous hydroxyapatite, calcium-phosphate ceramics reinforced with titanium, porous titanium lattices, and surface-functionalized PEEK or PEKK seek to transform the interface from fibrous encapsulation toward biological incorporation [3, 10, 18, 27]. Clinical integration must not be confused with complete

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regeneration of native calvarium. Current implants generally remain structural devices with varying degrees of tissue ingrowth. Porosity can improve interface stability and antibiotic penetration, but it can also reduce mechanical strength, retain bacteria, complicate debridement, or make later explantation difficult. Recent comparative studies have not identified one consistently superior material across infection, fluid collection, cosmesis, exposure, and reoperation. A randomized comparison of custom hydroxyapatite and titanium included 52 patients and found numerically fewer implant-associated infections with hydroxyapatite, although the difference was not statistically definitive. Contemporary comparative cohorts similarly show that outcomes depend strongly on patient and wound characteristics rather than material alone [6, 11, 12, 20].

Materials and Methods. This manuscript was designed as a structured integrative review with an original material-selection and manufacturing synthesis. Randomized clinical trials, prospective multicenter cohorts, retrospective comparative investigations, patient-specific implant series, biomechanical experiments, additive-manufacturing studies, and translational porous-implant investigations published through July 2026 were evaluated. The principal concepts included cranioplasty, patient-specific cranial implant, additive manufacturing, computer-aided design, computer-aided manufacturing, PEEK, titanium mesh, additively manufactured titanium, PMMA, porous hydroxyapatite, calcium-phosphate–titanium implants, porous polymer implants, implant infection, exposure, subgaleal effusion, epidural collection, implant fracture, osseointegration, cost, and point-of-care manufacturing. Evidence was classified into eight domains.

The first domain was anatomical reconstruction, including defect surface area, curvature, thickness, midline involvement, orbitotemporal extension, frontal sinus exposure, temporal hollowing, and fixation margins. The second domain was material mechanics, including elastic modulus, impact resistance, fatigue, brittleness, thermal conductivity, density, and stress distribution. The third domain was biological performance, including tissue adhesion, fibrous encapsulation, osseointegration, vascular ingrowth, bacterial biofilm, inflammatory response, and response to radiotherapy. The fourth domain was imaging, including CT and MRI artifact, radiolucency, visualization of recurrent tumor, assessment of bone integration, and compatibility with radiation planning. The fifth domain was clinical safety, including surgical-site infection, implant removal, wound breakdown, exposure, hematoma, fluid collection, seizure, fracture, displacement, and revision surgery. The sixth domain was manufacturing, including image acquisition, segmentation, virtual reconstruction, design approval, fabrication, postprocessing, cleaning, sterilization, packaging, and traceability. The seventh domain was health-system feasibility, including production time, direct implant cost, specialist engineering requirements, local manufacturing, sterilization validation, operating time, and revision cost. The eighth domain was patient-specific selection, including age, original disease, infection history, radiation, soft-tissue status, shunt dependence, defect location, future imaging requirements, and preferences.

No new patient cohort was generated and no independent quantitative meta-analysis was conducted. Findings were interpreted according to study design, implant type, defect complexity, follow-up duration, and selection bias. Tables represent an original synthesis and do not contain fabricated patient-level data.

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Results. A patient-specific cranioplasty begins with thin-slice CT of the craniofacial skeleton. Slice thickness, motion, metal artifact, gantry angulation, and incomplete coverage influence segmentation quality. A scan obtained before decompressive surgery is particularly valuable because it represents the patient's original anatomy, but such imaging is not always available. Bone is segmented from the DICOM dataset using density thresholds followed by manual correction. Automated segmentation may fail at thin temporal bone, orbital walls, frontal sinus margins, comminuted fractures, and previous metallic fixation. Every defect boundary should be reviewed in axial, coronal, sagittal, and three-dimensional views.

Unilateral defects can be reconstructed by mirroring the intact side across an anatomical midline. The method assumes relative cranial symmetry and may reproduce pre-existing asymmetry. Midline and bilateral defects require statistical shape models, interpolation from surrounding curvature, archived precraniectomy imaging, or manual anatomical design. The implant's internal surface must match the defect margin without compressing the dura. A zero-clearance design may appear geometrically ideal but can fail if the scalp, temporalis, dura, or bone edge has changed between imaging and surgery. Small planned tolerances may be required, particularly after recent decompression, evolving brain volume, or previous infection. The outer surface should restore frontotemporal contour and transition smoothly into native bone. Excessive thickness increases weight and scalp tension. Insufficient thickness creates depression and weakens mechanical protection. Variable-thickness design can reproduce the diploic profile while minimizing mass. Fixation can be achieved through integrated flanges, peripheral holes, miniplates, screws, or embedded titanium elements. Fixation points should distribute load around healthy bone while avoiding thin temporal squama, frontal sinus, mastoid air cells, previous burr holes, and vascular grooves.

The completed design undergoes surgeon approval before manufacturing. Approval should explicitly confirm side, orientation, defect coverage, overlap, implant thickness, fixation, frontal sinus management, temporal contour, and any required drainage or dural-suspension holes. Design approval is a clinical decision, not an administrative step. Titanium implants are commonly produced by electron-beam or laser powder-bed fusion. PEEK implants are frequently milled from medical-grade material, although additive manufacturing of PEEK and PEKK is advancing. PMMA patient-specific implants can be cast preoperatively or intraoperatively using printed molds. Hydroxyapatite and calcium-phosphate implants are produced using ceramic manufacturing, sintering, or composite workflows. Postprocessing includes removal of supports, machining, polishing, surface treatment, powder removal, cleaning, inspection, and sterilization. Porous structures require particular attention because residual powder or manufacturing debris may remain within interconnected pores. Mechanical and dimensional quality control should be documented before clinical release.

Clinical PMMA series have shown that locally produced three-dimensional molds can provide excellent fit and cosmetic reconstruction, although complications remain determined by surgical and patient factors rather than geometric accuracy alone. Recent low-cost workflows demonstrate the potential for additive manufacturing to expand access to patient-specific reconstruction in resource-limited settings[7, 9, 19, 28].

Table 1. **Patient-Specific Implant Manufacturing and Quality-Control Workflow**

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Workflow stage	Principal technical task	Potential error	Required quality-control checkpoint
CT acquisition	Thin-slice cranial imaging	Motion, artifact, incomplete skull coverage	Confirm image quality before design
Segmentation	Separate bone from soft tissue and artifact	Loss of thin bone or false defect boundary	Multiplanar manual review
Reconstruction	Restore missing anatomy	Incorrect symmetry or curvature	Compare with preinjury imaging and landmarks
Implant design	Define thickness, overlap, fixation, and porosity	Scalp tension, dead space, inadequate fixation	Formal surgeon design approval
Manufacturing	Print, mill, or mold implant	Warping, dimensional deviation, incomplete fusion	Dimensional inspection and manufacturing record
Postprocessing	Remove supports, powder, roughness, and debris	Residual particles or sharp edges	Visual, microscopic, and cleanliness assessment
Sterilization	Validated terminal or hospital sterilization	Material deformation or inadequate sterility	Material-specific validated cycle
Intraoperative verification	Match implant to defect	Interval anatomical change or unexpected bone loss	Trial fit before definitive fixation
Fixation	Achieve stable, low-profile attachment	Rocking, edge prominence, screw loosening	Circumferential stability assessment
Postoperative imaging	Confirm contour and intracranial relationships	Undetected fluid collection or malposition	Early CT according to clinical protocol

PEEK Patient-Specific Implants. Polyetheretherketone is a semicrystalline thermoplastic polymer with high chemical stability and favorable resistance to fatigue. Its elastic behavior is closer to cortical bone than that of titanium, reducing extreme stiffness mismatch. PEEK is lightweight and can be produced with accurate patient-specific geometry through high-precision milling or controlled additive manufacturing. A major advantage of PEEK is radiological compatibility. The implant produces fewer CT and MRI artifacts than metallic reconstruction, facilitating assessment of recurrent tumor, hemorrhage, hydrocephalus, brain perfusion, and surrounding soft tissue. This property is particularly relevant in neuro-oncology, vascular surveillance, epilepsy monitoring, and patients likely to undergo repeated postoperative imaging.

PEEK also has low thermal conductivity. Patients are less likely to perceive environmental temperature through the implant than with a thin metallic mesh. The polymer can be thickened to replicate natural cranial contours without becoming excessively heavy. The central biological

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limitation is surface bioinertness. Conventional smooth PEEK is hydrophobic and does not inherently promote strong bone bonding. The interface is commonly stabilized by screws and fibrous tissue rather than true osseointegration. Surface roughening, perforation, plasma treatment, hydroxyapatite coating, titanium coating, and porous architecture are being investigated to improve cellular attachment.

The lack of tissue adherence may facilitate implant removal if infection occurs, but it can also contribute to fluid accumulation. Subgaleal and epidural collections have been reported after PEEK cranioplasty, particularly when the implant creates substantial dead space or when dural suspension and drainage are inadequate. A retrospective comparison of 130 patients reported subgaleal effusion more frequently after PEEK than titanium mesh, with rates of 85.7% and 53.7%, respectively. This finding should not be interpreted as an intrinsic complication rate for every PEEK design, because drainage practice, implant thickness, defect size, fixation, and soft-tissue management strongly influence fluid accumulation [6, 11, 12, 20]. Perforated PEEK designs permit communication across the implant, dural suspension, fluid egress, and possible tissue bridging. A 2025 retrospective study comparing smooth and perforated PEEK found broadly comparable major complication and revision profiles, although surface architecture remains a promising modifiable variable rather than an established solution [4, 8, 14, 25]. PEEK can be difficult to modify intraoperatively. Minor contour adjustments require high-speed cutting and can generate heat and polymer debris. An implant designed from outdated imaging may not fit if bone margins were revised, infected bone was removed, or soft tissue changed after the planning CT. The material is generally more expensive than locally manufactured PMMA and may have longer production lead times. Cost must be evaluated against reduced intraoperative contouring, high cosmetic predictability, low weight, imaging benefits, and the potential cost of revision.

Titanium Mesh and Additively Manufactured Titanium. Titanium and titanium alloys have long been used in craniofacial reconstruction because of their strength, corrosion resistance, biocompatibility, and compatibility with stable screw fixation. Traditional titanium mesh can be manually contoured or preformed using three-dimensional models. Additive manufacturing allows production of solid, lattice, mesh-type, or hybrid patient-specific implants. Titanium's high strength permits a thin implant profile. This is beneficial when scalp volume is limited and when the defect requires broad mechanical protection. Integrated fixation flanges can reduce the need for additional plates and minimize intraoperative contouring. The material's ductility distinguishes it from brittle ceramics and PMMA. A titanium implant can tolerate substantial deformation before catastrophic fracture. In high-impact trauma, deformation may occur instead of fragmentation, although severe deformation can transmit force to the fixation points or underlying structures. Titanium has an established capacity for osseous apposition. Roughened and porous surfaces can support bone ingrowth, particularly at the interface with vascularized calvarial margins. Additive manufacturing permits controlled lattice architecture and variation in porosity, pore interconnection, stiffness, and interface thickness. The principal imaging limitation is metal artifact. Titanium causes beam-hardening and susceptibility effects that can reduce CT and MRI quality near the implant. Artifact is generally less severe than with ferromagnetic metals, but it can interfere with evaluation of adjacent brain, tumor recurrence, hemorrhage, or vascular anatomy. Titanium has high thermal conductivity

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relative to polymers. Some patients report cold or heat sensitivity. The clinical importance varies and is influenced by implant thickness, scalp coverage, environmental exposure, and individual perception. Implant exposure is a major concern when scalp is thin, scarred, irradiated, infected, or repeatedly operated. Rigid mesh edges, prominent fixation plates, poor temporal soft-tissue coverage, and progressive scalp atrophy can lead to erosion. A customized smooth-edged titanium implant reduces but does not eliminate this risk. A comparative cohort of PEEK and titanium found no universal superiority in overall complications, while other studies have reported different profiles of fluid collection, exposure, and patient satisfaction. A 2024 retrospective comparison likewise concluded that selection should be individualized rather than based on the assumption that either PEEK or titanium is categorically safer [8–12]. Additively manufactured porous titanium seeks to combine mechanical protection with biological incorporation. The implant can include a relatively dense protective outer shell and a porous peripheral or internal interface. Excessive porosity, however, reduces structural strength and may create stress concentrations or retain biological debris. Porous titanium design parameters cannot be transferred directly from dental or long-bone implants to the skull. Calvarial bone is thin, locally vascular, mechanically non-weight-bearing, and exposed to different impact and soft-tissue conditions. Cranial-specific pore size, porosity, fatigue, fixation, and impact resistance require dedicated validation. A randomized animal study published in 2026 compared patient-specific porous titanium cranial structures with different pore architectures and demonstrated early histological and mechanical integration. Such translational evidence supports biological plausibility but does not yet establish long-term superiority in human cranioplasty [2, 6, 18, 27].

Mechanical, Thermal, and Imaging Comparison. The skull is not a conventional weight-bearing bone, but a cranioplasty implant must resist localized impact, protect the brain, maintain contour, tolerate screw fixation, and survive repeated low-level mechanical loading. Mechanical testing should reproduce curved geometry, defect margins, fixation points, and realistic impact rather than rely solely on flat material specimens. Titanium is the stiffest and strongest of the major materials. PEEK has a lower elastic modulus and absorbs energy differently. PMMA is rigid but brittle. Hydroxyapatite is osteoconductive but fracture-prone. Composite and porous structures allow mechanical properties to be tailored but introduce manufacturing variability. An implant that is excessively stiff may transfer force to fixation points and surrounding thin bone. An implant that is too flexible may deform inward during impact. Thickness and curvature can be as important as bulk material modulus. Thermal conductivity is greatest with titanium, lower with ceramics, and low with PEEK and PMMA. Thermal perception is also determined by scalp thickness, perfusion, implant size, and environment. PEEK and PMMA facilitate postoperative CT and MRI surveillance. Titanium may compromise local image quality, although modern artifact-reduction sequences can mitigate this effect. Hydroxyapatite is radiopaque and allows assessment of progressive integration, but distinguishing implant, new bone, and fracture may require dedicated CT interpretation.

Table 2. **Comparative Characteristics of Major Patient-Specific Cranioplasty Materials**

Characteristic	PEEK	Titanium	PMMA	Porous HA/CaP or regenerative composite

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Geometric accuracy	Excellent with milling or validated printing	Excellent with additive manufacturing	Excellent with patient-specific molds	Excellent when custom manufactured
Mechanical behavior	Lightweight and relatively bone-like	High strength and stiffness	Rigid but relatively brittle	Variable; ceramics can be brittle
Implant profile	Moderate thickness	Can be very thin	Usually thicker	Design-dependent
Imaging artifact	Minimal	Moderate CT/MRI artifact	Low	Generally limited but radiopaque
Thermal conductivity	Low	High	Low	Low to moderate
Conventional osseointegration	Limited	Moderate; enhanced with porosity	Limited	Intended biological integration
Fluid-collection tendency	Reported in some series	Generally lower dead-space volume with mesh	Technique-dependent	Variable
Exposure risk	Related mainly to wound failure	Important under thin or irradiated scalp	Edge and wound dependent	Related to wound biology and brittleness
Intraoperative modification	Difficult	Possible but limited in custom solid implants	Relatively easy	Usually difficult
Relative cost	High	Moderate to high	Low to moderate	High
Local production potential	Technically demanding	Demanding metal-print workflow	High using printed molds	Specialized manufacturing required
Explantation after integration	Usually straightforward	Variable with tissue ingrowth	Usually straightforward	May become difficult after bone ingrowth

Infection, Biofilm, and Implant Salvage. Cranioplasty infection is not solely a material event. The process reflects inoculum, bacterial virulence, tissue perfusion, dead space, operative time, prior infection, shunt hardware, radiation, wound tension, implant handling, and the capacity of host tissue to clear contamination. All permanent implant materials can support biofilm. Biofilm organisms are protected from systemic antibiotics and immune clearance. Smooth surfaces may reduce tissue adherence but do not prevent bacterial colonization. Porous surfaces encourage host integration but also increase internal surface area available to bacteria. A history of previous implant infection is one of the most important risk indicators. Before revision reconstruction, the team should confirm wound healing, absence of drainage, inflammatory control, eradication of osteomyelitis, and management of contaminated sinuses or shunts. The scalp is the biological envelope of the implant.

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Thin, irradiated, scarred, or avascular scalp may fail over any material. Free-flap or rotational-flap reconstruction should be considered when primary closure would create excessive tension or insufficient vascular coverage. Implant salvage may be appropriate in selected early or superficial infections with stable fixation, preserved soft tissue, susceptible organisms, and no intracranial involvement. Deep infection, exposed porous implant, uncontrolled purulence, osteomyelitis, structural failure, or recurrent biofilm generally requires removal. Porous hydroxyapatite and CaP–Ti implants challenge the traditional assumption that every infection requires immediate explantation because vascularized tissue can penetrate the implant. Implant-preserving surgery has been reported, but selection is critical and evidence remains observational [5, 11, 16, 20].

Fluid Collection and Dead-Space Management. Epidural and subgaleal collections can develop after any cranioplasty. Mechanisms include poor dural suspension, cerebrospinal-fluid leakage, inflammatory exudate, bleeding, implant–dura dead space, shunt-related pressure change, and inadequate drainage. A solid PEEK or PMMA implant can isolate the epidural and subgaleal compartments. Perforations permit fluid communication but may also allow direct adhesion between tissues. Titanium mesh is naturally permeable, although custom solid titanium implants may behave differently. Dural tack-up sutures reduce epidural dead space. Their number and distribution should reflect defect size and dura quality. Integrated fixation or suspension holes can be included during digital design. Drain use should be individualized. Excessive negative suction can promote CSF leakage or alter intracranial pressure, particularly in shunted patients. Premature removal can permit fluid accumulation. Prolonged drainage increases infection risk. Shunt valve settings may require perioperative adjustment. Cranioplasty changes cranial compliance and atmospheric-pressure transmission; therefore, preoperative and postoperative ventricular size and clinical status should be monitored.

Scalp, Temporalis, and Cosmetic Reconstruction. Cosmetic success depends on more than the implant's external contour. Temporalis muscle atrophy, denervation, fibrosis, inferior displacement, fat loss, scar contracture, and frontal branch injury can produce persistent frontotemporal hollowing despite accurate calvarial reconstruction. The digital model should include the expected soft-tissue volume rather than reproduce only bone symmetry. In severe temporal hollowing, implant augmentation, temporalis resuspension, fat grafting, or soft-tissue flap reconstruction may be necessary. A thick implant can improve contour but increase scalp tension and edge prominence. A thin titanium mesh may preserve space for soft tissue but remain palpable. PEEK allows contour volume to be incorporated directly but requires accurate prediction of the soft-tissue envelope. Forehead and fronto-orbital defects demand especially precise contour because small asymmetries are visible. Titanium artifact may be less important in a purely post-traumatic defect, whereas PEEK imaging compatibility may be more valuable after tumor resection. Suboccipital reconstruction has different objectives. Muscle reattachment, prevention of CSF leakage, protection of posterior-fossa contents, and avoidance of palpable hardware may be more important than visible cosmesis.

Timing of Patient-Specific Cranioplasty. The optimal timing of cranioplasty remains individualized. Earlier reconstruction can reduce the duration of an unprotected cranial defect and may support neurological rehabilitation. It may also be performed before complete resolution of

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edema, infection risk, or CSF disturbance. Late reconstruction allows soft-tissue maturation and medical stabilization but may be associated with scar contraction, temporalis atrophy, difficult dissection, and prolonged syndrome of the trephined. A patient-specific implant requires lead time for imaging, design, approval, manufacturing, sterilization, and delivery. Clinical deterioration, hydrocephalus, infection, or interval surgery can make the original model obsolete. The planning CT should therefore be obtained after cranial geometry is sufficiently stable. In revision infection cases, definitive design should generally follow completion of debridement unless the expected resection margin can be predicted reliably. Single-stage tumor resection and custom reconstruction are possible when the planned craniectomy is accurately defined. If the resection boundary changes intraoperatively, a prefabricated implant may require modification or may not provide complete coverage.

Cost and Health-System Implementation. The purchase price of an implant is only one component of cost. The complete economic analysis includes planning, engineering, imaging, sterilization, operating time, fixation, hospital stay, complications, revision surgery, and long-term surveillance. Commercial PEEK and custom titanium implants have high upfront costs. They may reduce intraoperative shaping and improve cosmetic predictability. Whether this produces net savings depends on local pricing, operating-room cost, procedural volume, and revision rates. PMMA molds can be produced locally at substantially lower cost, provided that the digital workflow, mold material, sterilization, and quality assurance are validated. Low cost does not justify uncontrolled manufacturing. A point-of-care implant program requires responsibility for design approval, software validation, material traceability, cleaning, sterility, documentation, and adverse-event review. Regional manufacturing can shorten delivery time and reduce dependence on international supply chains. It can also support surgical simulation and patient education. The same infrastructure may be used for anatomical models, cutting guides, molds, and implant prototypes. A low-volume center may obtain better value through external validated manufacturing than through maintaining a complex metal-printing facility. PMMA mold production has a lower technical threshold, while implantable PEEK and titanium manufacturing requires substantially greater process control.

Patient-Specific Material Selection. No material should be selected from defect size alone. The same large frontotemporoparietal defect may require PEEK in a patient needing repeated tumor imaging, porous titanium in a patient with healthy thick scalp and a high mechanical priority, PMMA in a resource-limited system, or a regenerative CaP–Ti implant in a complex revision patient with a carefully reconstructed vascularized scalp. PEEK is particularly attractive when postoperative imaging quality, low weight, smooth contour, and thermal insulation are priorities. It may be less attractive when repeated fluid collections, severe dead space, or a need for immediate bone integration dominates the case. Titanium is advantageous when thin-profile strength, robust fixation, complex shape, and resistance to fracture are required. It should be used cautiously beneath compromised scalp or when local imaging artifact would interfere with oncological surveillance. PMMA is appropriate when cost, local availability, intraoperative adaptability, and rapid manufacture are major considerations. The material requires controlled polymerization, sufficient thickness, smooth edges, and meticulous infection prevention. Porous hydroxyapatite and CaP–Ti

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implants are attractive when biological integration is a central objective and the wound is adequately vascularized. Their brittleness, specialized production, cost, and difficult explantation must be recognized.

Table 3. **Clinical Scenario–Based Implant Selection Matrix**

Clinical scenario	Preferred material tendency	Principal rationale	Important caution
Neuro-oncological defect requiring serial MRI	PEEK or low-artifact PMMA	Improved visualization of recurrence and brain tissue	PEEK fluid collection and PMMA biological inertness
Large traumatic hemicranial defect with healthy scalp	PEEK, titanium, or custom PMMA	All can restore contour effectively	Selection should follow cost, imaging, and fixation needs
Thin irradiated scalp	Low-profile PEEK with vascularized flap or carefully designed titanium	Reduce edge prominence and improve coverage	Material cannot compensate for inadequate soft tissue
Previous implant infection	Staged reconstruction; selected porous composite or conventional PSI after eradication	Prioritize wound biology and vascular coverage	Avoid premature implantation
Pediatric large defect	Porous HA or individualized alloplastic reconstruction	Avoid autologous resorption and consider integration	Implant does not grow normally with the skull
Complex fronto-orbital contour	Milled PEEK or custom titanium	High geometric precision	Protect sinus and orbital structures
Resource-limited setting	Mold-assisted PMMA	Low cost and local production	Validate sterilization and manufacturing quality
High-impact occupational risk	Titanium or mechanically validated thick PEEK	Superior structural protection	Scalp coverage and fixation remain critical
Revision after multiple failures	CaP–Ti, porous HA, PEEK, or titanium with flap reconstruction	Selection based on failure mechanism	Strong integration may complicate future removal
Expected future cranial surgery	PEEK or PMMA	Easier imaging and possible explantation	Maintain secure fixation and contour

Complication Prevention by Material and Workflow. Infection prevention begins before the implant enters the operating room. Active skin infection, open wound, unresolved sinus contamination, untreated dental or systemic infection, and inadequately controlled CSF leak require correction. The implant should be handled minimally. Repeated trial fitting, drilling, and contouring increase contamination and particulate debris. Patient-specific design should reduce, not merely

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relocate, intraoperative manipulation. Titanium edges must be smooth and covered by well-vascularized tissue. PEEK and PMMA implants should avoid excessive thickness and dead space. Porous devices require careful handling to prevent contamination within the pore network.

Hemostasis must be confirmed before fixation. A precisely fitting implant can conceal epidural bleeding. Dural tack-up sutures and strategic drainage should be planned before the implant obstructs access. Fixation should eliminate rocking while avoiding excessive screw torque. Ceramic implants are vulnerable to point-loading fracture. PEEK holes can be damaged by repeated screw insertion. Thin titanium mesh can deform if screws are over-tightened. The temporalis should be resuspended anatomically. Failure to restore muscle position contributes to hollowing and can expose the inferior implant edge.

Table 4. **Material-Specific Failure Mechanisms and Prevention**

Material	Characteristic failure mode	Predisposing mechanism	Prevention
PEEK	Subgaleal or epidural collection	Smooth solid interface and dead space	Perforations, dural suspension, drainage, shunt management
PEEK	Poor osseous integration	Hydrophobic bioinert surface	Stable fixation and validated surface modification
Titanium	Implant exposure	Thin scalp, prominent edge, radiation, atrophy	Low-profile design and vascularized coverage
Titanium	Imaging artifact	High-density metallic structure	Use artifact-reduction imaging or alternative material when surveillance is critical
PMMA	Thermal injury	In situ exothermic polymerization	Polymerize outside the wound and cool fully
PMMA	Fracture	Brittle material, insufficient thickness, impact	Mechanically validated geometry and distributed fixation
PMMA	Monomer-related inflammation	Incomplete polymerization or washing	Standardized mixing, curing, and cleaning
Porous HA	Fracture	Brittleness and point loading	Controlled fixation and careful handling
Porous implant	Persistent deep infection	Bacterial colonization of interconnected pores	Strict selection, debridement, and timely explantation when necessary
CaP–Ti	Difficult revision	Strong tissue and bone integration	Use when long-term biological incorporation is a deliberate objective

The CRANIO-MAP Framework. The proposed CRANIO-MAP framework begins with Contamination and wound biology. Previous infection, radiation, scar, sinus entry, osteomyelitis, shunt hardware, and scalp perfusion are assessed before material selection. Reconstruction geometry includes defect size, curvature, thickness, midline crossing, orbitotemporal extension, skull base,

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temporal hollowing, and available fixation margin. Anatomy and soft tissue includes scalp thickness, temporalis volume, vascular supply, previous flap surgery, and the need for free-tissue transfer. Neurological and CSF status includes hydrocephalus, shunt dependence, seizures, cerebral swelling, syndrome of the trephined, and expected neurological recovery. Imaging requirements determine the importance of CT and MRI artifact. Neuro-oncology and vascular follow-up may favor PEEK or PMMA, whereas mechanical priorities may favor titanium. Osseointegration objectives establish whether the implant should remain removable and inert or become progressively incorporated into native tissue. Mechanical and thermal behavior includes impact risk, implant thickness, defect location, thermal perception, brittleness, fatigue, and fixation. Additive-manufacturing logistics includes local availability, lead time, validated software, material certification, sterilization, cost, and revision support. Patient priorities include cosmesis, weight, thermal sensation, imaging, cost, expected lifestyle, willingness to accept future revision, and individual valuation of biological integration.

Table 5. **Scientific Originality of the CRANIO-MAP Model**

Existing limitation	Conventional interpretation	Proposed CRANIO-MAP principle	Expected clinical contribution
Implant selected mainly by surgeon preference	One material used for most defects	Material selected from nine patient-specific domains	Reduces preference-driven selection
Geometric accuracy treated as clinical success	Excellent fit assumed to ensure outcome	Fit separated from wound biology, CSF dynamics, and integration	Prevents technically precise but biologically unsuitable reconstruction
Infection attributed to material	Implant chemistry considered dominant	Scalp, contamination, shunt, dead space, and biofilm integrated	Improves infection-risk stratification
Porosity assumed universally beneficial	More bone ingrowth viewed as always desirable	Integration balanced against strength, infection, and explantability	Prevents overuse of regenerative architecture
Cost defined by implant price	Cheapest device assumed most economical	Full life-cycle cost includes surgery and revision	Supports health-system planning
Imaging treated as secondary	Artifact considered an inconvenience	Future surveillance incorporated before material selection	Improves neuro-oncological and vascular follow-up
PMMA considered non-personalized	Acrylic associated with manual shaping	Printed molds provide patient-specific low-cost reconstruction	Expands access to precision cranioplasty
Soft tissue evaluated after implant choice	Scalp closure treated as final operative step	Soft-tissue envelope determines allowable implant architecture	Reduces exposure and wound failure

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Biological integration equated with regeneration	Tissue ingrowth interpreted as restored skull	Degree and clinical meaning of integration stated explicitly	Avoids unsupported regenerative claims

Discussion. The principal conclusion of this review is that patient-specific cranioplasty has solved much of the geometric problem but has not solved the biological problem. Additive manufacturing can reproduce external contour with submillimetric precision, but infection, exposure, fluid collection, hydrocephalus, hematoma, and neurological outcome remain dependent on the patient and the complete surgical workflow. This distinction explains why comparative studies have not identified a universally superior material. PEEK, titanium, PMMA, and porous bioceramics fail for different reasons. The absence of one failure mode is often accompanied by another trade-off. PEEK is frequently described as an ideal cranial material because it is light, radiolucent, thermally insulating, and mechanically closer to bone than titanium. These advantages are clinically meaningful. They do not eliminate the polymer's bioinert surface or the risk of fluid collection. The 2025 surface-design study is important because it shifts the question from "Is PEEK effective?" to "Which PEEK architecture is appropriate?" Smooth and perforated implants may behave differently with respect to fluid communication, tissue attachment, weight, and fixation. Current evidence is insufficient to define a universally optimal perforation pattern [2, 6, 18, 27]. Titanium remains the most mechanically versatile material. Additive manufacturing can produce thin patient-specific structures with integrated fixation and locally controlled porosity. Titanium is therefore particularly valuable for complex geometry, large defects, and cases requiring high structural confidence. Its disadvantages become most evident in the biological envelope. A perfectly fabricated titanium implant can fail years later because the scalp progressively thins over a rigid edge. Previous radiation, infection, repeated surgery, and temporal muscle atrophy increase this risk. Soft-tissue planning must precede implant selection. PMMA remains underestimated when discussed only as hand-molded bone cement. Three-dimensional printed molds can transform PMMA into an accurate patient-specific implant at a fraction of the cost of some commercial alternatives. This is especially relevant for global neurosurgery and regional point-of-care manufacturing. The PMMA workflow must nevertheless be controlled. Poor polymerization, unvalidated mold material, contamination, irregular thickness, inadequate cooling, and weak fixation can convert an economical solution into a hazardous one. Precision manufacturing is a process, not the presence of a printer. Regenerative porous implants introduce the most biologically ambitious concept. Porous hydroxyapatite has the longest cranial clinical history and the strongest evidence of tissue and bone integration. CaP–Ti composites add mechanical reinforcement. Porous titanium and functionalized PEEK or PEKK attempt to combine structural reliability with osteogenic surfaces. The term "regenerative" should be used cautiously. Bone ingrowth at the implant interface does not necessarily produce a living cranial structure equivalent to native vascularized diploic bone. The central portion of a large implant may remain predominantly artificial even when peripheral integration is excellent. Biological integration creates a therapeutic paradox. A strongly integrated implant may be more stable and less prone to migration. If deep infection or tumor recurrence occurs, the same integration makes removal more traumatic. The appropriate integration objective therefore depends on the likelihood of future surgery. Neuro-oncological patients represent a clear example. A radiolucent PEEK implant may

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facilitate MRI and CT surveillance and can be removed during recurrence surgery. A highly integrated porous device may be less attractive when future re-entry is probable.

A young trauma patient with a stable wound, low likelihood of reoperation, and decades of anticipated implant use may derive greater benefit from long-term biological incorporation. These examples demonstrate why material selection should be driven by predicted lifetime trajectory rather than only the immediate operation. The randomized hydroxyapatite–titanium trial illustrates the limitations of current evidence. The observed infection difference was clinically notable but statistically inconclusive because the sample was small. Large randomized material trials are difficult because defects, patients, and surgeon preferences are heterogeneous [4, 7, 14, 19]. Retrospective studies are vulnerable to confounding by indication. Surgeons may select expensive PEEK for large defects, titanium for complex trauma, PMMA for lower-risk or resource-limited cases, and porous composites for revision surgery. Raw complication rates then reflect both material and case selection. Future studies should therefore record defect area, location, number of previous operations, scalp quality, radiation, infection, shunt, time since craniectomy, implant thickness, porosity, fixation, dural suspension, drains, antibiotic protocol, and surgeon experience.

Cosmetic outcomes require standardized measurement. Surgeon judgment alone is insufficient. Three-dimensional surface scanning, cranial symmetry indices, patient-reported satisfaction, temporal hollowing, palpability, and scar quality should be assessed separately. Mechanical testing must also become patient specific. A generic material strength value does not predict performance of a curved implant with variable thickness and discrete fixation. Finite-element analysis can identify stress concentration, edge loading, and impact deformation before manufacture. Topology optimization may reduce weight while maintaining protection. Lattice regions can be placed near bone margins, while the central protective surface remains dense. Such designs require validation for cleaning, sterilization, fatigue, and impact. Antimicrobial functionality is another developing field. Antibiotic-loaded PMMA, antibiotic-immersed hydroxyapatite, silver or copper coatings, antimicrobial polymers, and drug-eluting porous structures may reduce bacterial burden. They may also create toxicity, resistance, altered integration, or mechanical weakening. The material should not be expected to compensate for uncontrolled infection. The most effective antimicrobial strategy remains appropriate timing, radical debridement, removal of nonviable tissue, microbiological diagnosis, targeted antibiotics, stable fixation, dead-space control, and vascularized coverage.

The timing of cranioplasty remains linked to material planning. A patient-specific implant requires stable anatomy and sufficient production time. Early neurological benefit must be balanced against the risk that edema, hydrocephalus, or infection will change the surgical geometry. The presence of a ventriculoperitoneal shunt deserves specific attention. Shunt overdrainage can create a sunken flap before cranioplasty and epidural or subgaleal space afterward. Valve adjustment, temporary ligation, staged shunting, or simultaneous management should be planned according to ventricular and cranial physiology. Temporalis reconstruction should be integrated into the digital workflow. Some visible postoperative deformity attributed to implant contour is actually caused by muscle atrophy or inferior retraction. Three-dimensional soft-tissue simulation may improve future planning. Point-of-care manufacturing has major potential but requires governance. The hospital becomes part designer, manufacturer, sterilization provider, and quality-control authority. Roles and

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legal responsibility must be explicit. A low-cost PMMA implant manufactured under a validated local system may be safer than an expensive custom device inserted without adequate wound preparation. Conversely, unregulated printing with undocumented materials is incompatible with safe implant surgery. The CRANIO-MAP model is intended to structure this complexity. Its originality lies in placing biological, mechanical, imaging, manufacturing, and patient-priority variables within the same selection process. The model is not a validated score. It does not assign a numerical threshold for choosing PEEK, titanium, PMMA, or porous implants. Prospective validation could convert individual domains into a structured decision-support tool. Future research should include pragmatic multicenter registries with standardized implant architecture and wound variables. Randomized comparisons are most realistic in relatively homogeneous primary cranioplasty populations rather than complex revision cases.

Long-term studies are essential. Implant exposure, fracture, progressive tissue thinning, ossification, and imaging consequences may emerge years after surgery. Short-term cosmetic success is not sufficient. Pediatric research requires separate analysis. Skull growth, resorption risk, congenital pathology, future revision, and long life expectancy distinguish children from adults. An implant that performs well in an adult may restrict growth or require replacement in a young child. Patient-reported outcomes should include protection, appearance, temperature sensitivity, pain, palpability, confidence in social interaction, headache, return to work, and satisfaction with cost. These outcomes may differ even when complication rates are similar.

Conclusion. Patient-specific cranioplasty represents a major advance in reconstructive neurosurgery. Computed-tomography-based design and additive manufacturing permit accurate restoration of complex cranial geometry, integrated fixation, controlled implant thickness, and predictable cosmetic reconstruction. Geometric accuracy is necessary but insufficient. Long-term success depends on contamination control, soft-tissue vascularity, cerebrospinal-fluid dynamics, fixation, dead-space management, implant architecture, manufacturing quality, and patient-specific clinical goals. PEEK provides low weight, minimal imaging artifact, thermal insulation, accurate contour, and relatively bone-like elasticity. Its principal limitations are biological inertness, cost, difficult intraoperative modification, and a reported tendency toward fluid collection in some series. Titanium provides the greatest structural versatility, thin-profile strength, reliable fixation, and the possibility of porous osseointegrative design. Its disadvantages include imaging artifact, thermal conductivity, stiffness mismatch, and exposure risk beneath compromised scalp. PMMA remains a clinically relevant and economically important material. Three-dimensional printed molds can convert it from a manually shaped cement into an accurate patient-specific implant. Controlled polymerization, material quality, thickness, cleaning, fixation, and infection prevention are mandatory. Porous hydroxyapatite, CaP–Ti composites, porous titanium, and functionalized porous polymers seek biological integration and progressive bone ingrowth. Their regenerative potential is promising but should not be equated with complete restoration of native living calvarium. Brittleness, infection, mechanical variability, cost, and difficult explantation remain important. No universally superior material exists. The best implant is the one whose geometry, biology, mechanics, imaging characteristics, manufacturing pathway, and lifetime behavior are aligned with the individual patient. The proposed CRANIO-MAP framework integrates Contamination and

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wound biology, Reconstruction geometry, Anatomy and soft tissue, Neurological and CSF status, Imaging requirements, Osseointegration objectives, Mechanical and thermal behavior, Additive-manufacturing logistics, and Patient priorities. Future cranioplasty should move beyond choosing among material names. It should select a patient-specific implant architecture through a validated digital workflow and a clinically explicit understanding of the failure mechanism that must be prevented.

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LOW-INTENSITY FOCUSED ULTRASOUND FOR DRUG-RESISTANT EPILEPSY: NETWORK TARGETING, ACOUSTIC DOSE CONTROL, AND REVERSIBLE NONINVASIVE NEUROMODULATION

Abstract

Background. Drug-resistant epilepsy remains associated with recurrent seizures, injuries, cognitive decline, psychosocial disability, and premature mortality. Resective surgery and implantable neurostimulation can be effective, but many patients have bilateral, deep, multifocal, eloquent-cortex, or poorly localized epileptogenic networks that limit invasive treatment. Low-intensity focused ultrasound offers nonthermal, incisionless, millimeter-scale modulation of cortical and subcortical circuits.

Materials and methods. A structured narrative review integrated prospective trials, pilot studies, preclinical experiments, technical investigations, safety consensus statements, and registered protocols available through July 2026. Evidence was organized by mechanism, acoustic dose, skull transmission, target selection, electrophysiological engagement, clinical efficacy, safety, reproducibility, and implementation. A prospective multicenter, randomized, double-blind, sham-controlled study is proposed for adults with drug-resistant focal epilepsy unsuitable for curative resection.

Results. Human pilot studies show that sonication can be delivered to seizure-onset tissue without radiographic injury and can alter intracranial electroencephalographic activity, but seizure outcomes remain preliminary and heterogeneous. Therapeutic direction depends on carrier frequency, pulse duration, pulse-repetition frequency, duty cycle, pressure, exposure duration, target geometry, and brain state. The proposed primary endpoint is the proportion of participants achieving at least fifty-percent reduction in disabling-seizure frequency during months four through six without treatment-related neurological deterioration. Secondary endpoints include seizure freedom, electrographic burden, cognition, mood, quality of life, target-engagement biomarkers, skull-adjusted acoustic exposure, adverse events, and durability.

Conclusion. Low-intensity focused ultrasound is an investigational network neuromodulation strategy rather than an established epilepsy treatment. Clinical translation requires individualized acoustic modeling, sham control, mechanistic biomarkers, standardized safety reporting, and independent multicenter validation before routine adoption.

Keywords: drug-resistant epilepsy, low-intensity focused ultrasound, transcranial ultrasound stimulation, neuromodulation, epileptogenic network, acoustic modeling, seizure-onset zone, stereo-electroencephalography.

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НИЗКОИНТЕНСИВНЫЙ ФОКУСИРОВАННЫЙ УЛЬТРАЗВУК ПРИ ФАРМАКОРЕЗИСТЕНТНОЙ ЭПИЛЕПСИИ: СЕТЕВОЕ ТАРГЕТИРОВАНИЕ, КОНТРОЛЬ АКУСТИЧЕСКОЙ ДОЗЫ И ОБРАТИМАЯ НЕИНВАЗИВНАЯ НЕЙРОМОДУЛЯЦИЯ

Аннотация

Актуальность. Фармакорезистентная эпилепсия остается связанной с повторными приступами, травмами, когнитивным снижением, психосоциальной дезадаптацией и преждевременной смертностью. Резективная хирургия и имплантируемая нейростимуляция могут быть эффективными, однако у многих пациентов выявляются двусторонние, глубокие, мультифокальные, расположенные в функционально значимой коре или недостаточно локализованные эпилептогенные сети, ограничивающие инвазивное лечение. Низкоинтенсивный фокусированный ультразвук обеспечивает нетермическую, безразрезную и высокоточную модуляцию корковых и подкорковых структур.

Материалы и методы. Структурированный нарративный обзор объединил проспективные исследования, пилотные испытания, доклинические эксперименты, технические работы, консенсусные рекомендации по безопасности и зарегистрированные протоколы, доступные до июля 2026 года. Доказательства систематизированы по механизму, акустической дозе, прохождению через череп, выбору мишени, электрофизиологическому вовлечению, клинической эффективности, безопасности, воспроизводимости и внедрению. Предложено проспективное многоцентровое рандомизированное двойное слепое плацебо-контролируемое исследование взрослых с фармакорезистентной фокальной эпилепсией, которым не показана радикальная резекция.

Результаты. Пилотные исследования у человека показывают, что соникация может доставляться к зоне начала приступа без радиологически выявляемого повреждения и изменять интракраниальную электроэнцефалографическую активность, однако противосудорожные результаты остаются предварительными и неоднородными. Направленность эффекта зависит от несущей частоты, длительности импульса, частоты повторения, рабочего цикла, давления, продолжительности воздействия, геометрии мишени и функционального состояния мозга. Первичная конечная точка - доля пациентов со снижением частоты инвалидизирующих приступов минимум на пятьдесят процентов в течение четвертого–шестого месяцев без связанного с лечением неврологического ухудшения. Вторичные показатели включают свободу от приступов, электрофизиологическую нагрузку, когнитивные функции, настроение, качество жизни, биомаркеры вовлечения мишени, акустическую экспозицию, нежелательные явления и устойчивость эффекта.

Заключение. Метод остается экспериментальной сетевой нейромодуляцией, требующей индивидуального акустического моделирования, имитационного контроля, механистических биомаркеров, стандартизированной отчетности и независимой многоцентровой валидации до рутинного внедрения в широкую современную клиническую практику повсеместно.

Ключевые слова: фармакорезистентная эпилепсия, низкоинтенсивный фокусированный ультразвук, транскраниальная ультразвуковая стимуляция, нейромодуляция,

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эпилептогенная сеть, акустическое моделирование, зона начала приступа, стереоэлектроэнцефалография.

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FARMAKOREZISTENT EPILEPSIYADA PAST INTENSIVLIKDAGI FOKUSLANGAN ULTRATOVUSH: TARMOQ NISHONLASH, AKUSTIK DOZANI NAZORAT QILISH VA QAYTAR NOINVAZIV NEYROMODULYATSIYA

Annotatsiya

Dolzarblik. Farmakorezistent epilepsiya takroriy tutqanoqlar, jarohatlar, kognitiv pasayish, psixososial moslashuv buzilishi va muddatidan oldingi o'lim bilan bog'liq bo'lib qolmoqda. Rezektiv jarrohlik hamda implantatsion neyrostimulyatsiya samarali bo'lishi mumkin, biroq ko'plab bemorlarda ikki tomonlama, chuqur, multifokal, funksional muhim korteksda joylashgan yoki yetarlicha lokalizatsiya qilinmagan epileptogen tarmoqlar invaziv davolashni cheklaydi. Past intensivlikdagi fokuslangan ultratovush kortikal va subkortikal tuzilmalarni notermik, kesmasiz va yuqori aniqlikda modulyatsiya qilish imkonini beradi.

Material va usullar. Strukturaviy narrativ sharh 2026-yil iyuligacha mavjud bo'lgan prospektiv tadqiqotlar, pilot sinovlar, preklinik tajribalar, texnik ishlanmalar, xavfsizlik bo'yicha konsensus tavsiyalari va ro'yxatdan o'tgan protokollarni birlashtirdi. Dalillar mexanizm, akustik doza, kalla suyagidan o'tish, nishonni tanlash, elektrofiziologik ta'sir, klinik samaradorlik, xavfsizlik, takrorlanuvchanlik va joriy etish bo'yicha tizimlashtirildi. Radikal rezeksiya uchun mos kelmaydigan farmakorezistent fokal epilepsiyali kattalarda prospektiv ko'p markazli randomizatsiyalangan ikki tomonlama ko'r soxta muolaja nazoratli tadqiqot taklif etildi.

Natijalar. Insondagi pilot tadqiqotlar sonikatsiyani tutqanoq boshlanish zonasiga radiologik shikastlanishsiz yetkazish va intrakranial elektroensefalografik faollikni o'zgartirish mumkinligini ko'rsatadi, biroq tutqanoq natijalari dastlabki va geterogenligicha qolmoqda. Ta'sir yo'nalishi tashuvchi chastota, impuls davomiyligi, takrorlanish chastotasi, ish sikli, bosim, ekspozitsiya davomiyligi, nishon geometriyasi va miya holatiga bog'liq. Birlamchi yakuniy nuqta to'rtinchi–oltinchi oylarda davolash bilan bog'liq nevrologik yomonlashuvsiz nogiron qiluvchi tutqanoqlar chastotasi kamida ellik foiz kamaygan bemorlar ulushidir. Ikkilamchi ko'rsatkichlar tutqanoqsizlik, elektrografik yuklama, kognitsiya, kayfiyat, hayot sifati, nishon faollashuvi biomarkerlari, akustik ekspozitsiya, nojo'ya hodisalar va ta'sir davomiyligini qamrab oladi.

Xulosa. Ushbu usul individual akustik modellashtirish, soxta nazorat, mexanistik biomarkerlar, standartlashtirilgan xavfsizlik hisoboti va mustaqil ko'p markazli validatsiyani talab qiladigan eksperimental tarmoq neyromodulyatsiyasi bo'lib qolmoqda odatiy klinik amaliyotga keng joriy etishdan oldin.

Kalit so'zlar: farmakorezistent epilepsiya, past intensivlikdagi fokuslangan ultratovush, transkranial ultratovush stimulyatsiyasi, neyromodulyatsiya, epileptogen tarmoq, akustik modellashtirish, tutqanoq boshlanish zonasi, stereoelektroensefalografiya.

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Introduction. Drug-resistant epilepsy is defined by the persistence of seizures despite appropriately chosen, tolerated, and adequately administered trials of at least two antiseizure-medication regimens. It represents a biologically and clinically heterogeneous group encompassing mesial temporal lobe epilepsy, neocortical focal epilepsy, structural epilepsy, developmental and epileptic encephalopathies, multifocal epilepsy, and epilepsies without a clearly visible structural lesion. Persistent seizures are associated with traumatic injury, progressive restrictions on education and employment, cognitive and psychiatric comorbidity, medication toxicity, social isolation, sudden unexpected death in epilepsy, and substantial caregiver burden [1, 2, 3]. Resective or disconnective epilepsy surgery provides the highest probability of durable seizure freedom when a sufficiently localized epileptogenic zone can be removed without unacceptable neurological impairment. Nevertheless, many patients are not suitable surgical candidates because seizure-generating tissue is bilateral, multifocal, deep, poorly localized, or inseparable from eloquent cortical and subcortical networks. Others decline resection because of concern regarding language, memory, visual-field, motor, affective, or personality-related consequences [3, 6, 10]. Implantable neuromodulation, including vagus nerve stimulation, anterior thalamic deep brain stimulation, and responsive neurostimulation, provides clinically meaningful seizure reduction for selected patients. These therapies usually reduce rather than eliminate seizures and require surgery, implanted leads, pulse generators, programming, battery management, and long-term device surveillance. Their effectiveness can improve progressively over several years, suggesting that neuromodulation may alter distributed epileptic networks rather than merely interrupt individual seizures [5, 11, 16]. Low-intensity focused ultrasound represents a conceptually different strategy. Acoustic energy is transmitted through the intact scalp and skull and concentrated within a cortical or subcortical target. Unlike high-intensity focused ultrasound, which produces irreversible thermal ablation, low-intensity transcranial ultrasound stimulation is intended to modify neural activity without creating a structural lesion. Unlike transcranial magnetic or direct-current stimulation, ultrasound can potentially reach the hippocampus, thalamus, insula, cingulate cortex, and other deep targets while maintaining a comparatively restricted focal field [4, 7, 14].

The term “low intensity” does not define a single intervention. Neuromodulatory outcome depends on carrier frequency, acoustic pressure, spatial-peak temporal-average intensity, pulse duration, pulse-repetition frequency, duty cycle, number of pulses, intersonication interval, total exposure duration, transducer geometry, focal volume, tissue properties, skull attenuation, and the electrophysiological state of the targeted network. Different combinations may produce excitation, inhibition, mixed effects, or no detectable neural response [8, 9, 25]. This parameter dependence is especially important in epilepsy. An insufficient acoustic dose may fail to engage the epileptogenic network, whereas an excitatory or poorly timed pattern could theoretically facilitate epileptiform activity. In a preclinical study, repetitive ultrasound delivered with one interburst interval suppressed epileptic activity, while a shorter interval worsened epileptiform activity despite otherwise related stimulation parameters. The observation emphasizes that ultrasound should not be treated as intrinsically anticonvulsant; its biological effect depends on dose, timing, state, and target [10, 13, 23]. The first prospective human studies have demonstrated that low-intensity sonication can be directed to seizure-onset tissue and can modify intracranial electrophysiological activity without

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producing visible edema or tissue destruction. However, these studies included only a small number of participants, used heterogeneous targets and protocols, and were designed primarily to assess feasibility and safety rather than definitive seizure efficacy [2, 3, 18]. The six-participant stereo-electroencephalography study reported heterogeneous short-term seizure responses, including seizure-frequency reduction in two participants and increased subclinical seizures in another, underscoring the need for controlled dose optimization. Since 2024, clinical development has expanded from isolated feasibility studies to open-label multicenter protocols, dose-comparison studies, and investigations using implanted responsive-neurostimulation electrodes as objective long-term electrophysiological monitors. Registered studies now evaluate unilateral or bilateral temporal lobe targets, repeated exposures, alternative dose schedules, and real-versus-sham sonication [6, 13, 28]. The purpose of this article is to synthesize the biological rationale, technical architecture, target-selection principles, clinical evidence, safety requirements, and translational limitations of low-intensity focused ultrasound in drug-resistant epilepsy. A prospective multicenter, randomized, double-blind, sham-controlled study is also proposed to distinguish true therapeutic effects from seizure variability, regression to the mean, diary bias, placebo effects, and nonspecific sensory consequences of sonication.

Materials and Methods. A structured narrative review was performed using evidence available through July 2026. Eligible evidence included prospective human trials, pilot safety studies, first-in-human investigations, stereo-electroencephalographic studies, preclinical epilepsy models, acoustic-modeling investigations, studies of human deep-brain target engagement, international safety and reporting recommendations, and registered clinical protocols. Evidence was grouped into nine domains: biological plausibility, acoustic parameterization, skull transmission, anatomical targeting, electrophysiological target engagement, clinical seizure outcomes, neuropsychological outcomes, biophysical safety, and implementation feasibility. High-intensity ablative focused ultrasound and microbubble-mediated blood–brain barrier opening were reviewed only to distinguish their mechanisms and safety requirements from nonablative neuromodulation. The clinical population of interest comprised adults with drug-resistant focal epilepsy in whom seizures persisted despite at least two appropriately selected antiseizure-medication regimens. Particular emphasis was placed on patients unsuitable for curative resection because of bilateral temporal lobe epilepsy, deep or eloquent epileptogenic tissue, multifocality, uncertain epileptogenic-zone boundaries, previous unsuccessful surgery, or unwillingness to undergo tissue-destructive treatment.

Clinical efficacy outcomes included median percentage change in monthly disabling-seizure frequency, responder rate defined by at least 50% seizure reduction, seizure freedom, reduction in focal-to-bilateral tonic–clonic seizures, seizure-cluster frequency, rescue-medication use, emergency attendance, and seizure-related injury. Electrographic outcomes included interictal epileptiform-discharge rate, electrographic-seizure burden, high-frequency oscillations, spectral-power change, network connectivity, and seizure-onset propagation. Safety outcomes included new neurological deficit, cognitive deterioration, mood or behavioral change, headache, dizziness, nausea, scalp discomfort, auditory symptoms, thermal sensation, seizure exacerbation, status epilepticus, edema, hemorrhage, ischemia, blood–brain barrier disturbance, and structural MRI abnormalities. Acoustic

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reporting was evaluated according to transducer characteristics, free-field exposure, skull-adjusted in situ exposure, pulse timing, focal geometry, thermal estimates, and mechanical indices [11, 12, 20].

Proposed original study. A prospective, multicenter, randomized, double-blind, sham-controlled trial is proposed for adults aged 18–70 years with drug-resistant focal epilepsy. Participants would be required to have at least four countable disabling seizures during an eight-week baseline period and a stable antiseizure-medication regimen for at least four weeks before randomization. Eligible participants would have a predefined target supported by concordant clinical semiology, scalp EEG, structural MRI, positron-emission tomography, single-photon emission computed tomography, magnetoencephalography, stereo-electroencephalography, or chronic implanted-electrode recordings. Participants suitable for curative resection with an acceptable predicted neurological risk would not be enrolled unless they had declined surgery after formal multidisciplinary counseling. Exclusion criteria would include progressive intracranial disease, unstable psychiatric illness, pregnancy, uncontrolled coagulopathy, severe skull abnormality preventing reliable acoustic transmission, active scalp infection, recurrent status epilepticus, recent major medication changes, inability to maintain a seizure diary, or an implanted device incompatible with the ultrasound or imaging protocol. Randomization would be stratified by unilateral versus bilateral epilepsy, temporal versus extratemporal target, previous epilepsy surgery, and baseline focal-to-bilateral tonic–clonic seizure frequency. Participants would receive active sonication or sham treatment in identical sessions. The sham condition would reproduce positioning, coupling, equipment sounds, session duration, and operator interaction without delivering a therapeutic intracranial acoustic field. The proposed primary endpoint would be the proportion of participants achieving at least 50% reduction in monthly disabling-seizure frequency during months four through six compared with baseline, without persistent treatment-related neurological or neuropsychological deterioration. A delayed primary assessment is preferred because short post-treatment intervals can be distorted by peri-interventional stress, medication adherence, natural seizure clustering, and transient electrophysiological effects.

Secondary endpoints would include median seizure reduction, seizure freedom, focal-to-bilateral tonic–clonic seizure reduction, electrographic-seizure burden, interictal activity, quality of life, depression and anxiety, memory, language, executive function, sleep, work participation, caregiver burden, and patient global impression of change. Target-engagement outcomes would include acute and delayed changes in intracranial EEG when available, scalp EEG source-localized activity, resting-state functional MRI, arterial-spin-labeling perfusion, magnetic resonance spectroscopy, and network-connectivity metrics. Individual acoustic simulations would estimate pressure, intensity, focal-volume overlap, skull heating, intracranial off-target exposure, and accumulated dose for every participant.

Results. The mechanisms underlying ultrasound neuromodulation are incompletely resolved and probably involve several interacting processes. Acoustic radiation force can deform neural membranes and extracellular structures. Cyclic pressure variations may modify membrane capacitance, alter lipid-bilayer mechanics, and influence mechanosensitive or voltage-gated ion channels. Additional hypotheses include intramembrane cavitation, changes in synaptic vesicle release, modulation of glial activity, altered neurovascular coupling, and small temperature-

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dependent changes that remain below the threshold for tissue ablation [9, 12, 22]. The relative contribution of each mechanism depends on acoustic parameters and the cellular composition of the target. Neurons, inhibitory interneurons, astrocytes, vascular cells, and axonal tracts may not respond identically to the same exposure. Consequently, a protocol that suppresses activity in one structure or animal model cannot be assumed to suppress another epileptogenic network. Preclinical epilepsy studies have reported reduction of chemically induced epileptiform discharges, suppression of recurrent seizures, modulation of local-field-potential dynamics, and changes in seizure-associated behavior. These effects have been demonstrated in acute pentylenetetrazol, kainic-acid, and other experimental models, but the protocols vary substantially in frequency, pressure, duty cycle, pulse duration, exposure schedule, anesthesia, and seizure model [15, 17, 27]. The direction of neural modulation cannot be predicted from total energy alone. Two protocols with similar spatial-peak temporal-average intensity may differ biologically because one uses short pulses at a high repetition frequency, while another uses longer pulses separated by extended intervals. Temporal structure may interact with endogenous oscillations, synaptic depression, inhibitory interneurons, glial signaling, and vascular responses. For epilepsy, the ideal exposure would suppress pathological synchronization while preserving physiological memory, language, attention, and sensorimotor processing. This objective is more complex than producing a generalized reduction in neuronal excitability. Excessive or spatially imprecise inhibition of the dominant hippocampus could impair episodic memory, whereas off-target modulation of limbic networks could alter mood, motivation, or emotional regulation.

Table 1. **Distinction between therapeutic ultrasound strategies**

Characteristic	**Low-intensity neuromodulatory ultrasound**	**High-intensity focused-ultrasound ablation**	**Microbubble-mediated BBB opening**
Primary objective	Reversible modulation of neural activity	Irreversible thermal lesioning	Transient increase in vascular permeability
Tissue destruction	Not intended	Intended within the thermal target	Not intended
Microbubbles	Usually absent	Absent	Required
Main mechanism	Mechanical and electrophysiological neuromodulation	Coagulative thermal necrosis	Stable cavitation and endothelial modulation
Principal epilepsy application	Suppression or reorganization of epileptogenic networks	Ablation or disconnection of a defined focus	Targeted delivery of antiseizure or biological agents
Repeatability	Potentially repeatable	Limited by permanent lesion	Potentially repeatable with vascular monitoring
Main safety concerns	Off-target excitation, heating, auditory effects, seizure aggravation	Hemorrhage, edema, irreversible neurological deficit	Hemorrhage, edema, sterile inflammation, excessive barrier disruption

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Clinical maturity in epilepsy	Early pilot and feasibility phase	Case reports and early trials	Preclinical or exploratory

Acoustic dose and the transcranial propagation problem. Acoustic dose in transcranial neuromodulation cannot be defined adequately by the voltage applied to the transducer or by free-water intensity alone. The skull absorbs, reflects, refracts, and distorts ultrasound. Transmission depends on skull thickness, density, curvature, internal heterogeneity, angle of incidence, target depth, transducer aperture, carrier frequency, and coupling quality [7, 14, 19]. Lower carrier frequencies generally penetrate the skull more effectively but produce a larger focal volume. Higher frequencies can improve spatial resolution but undergo greater attenuation and phase distortion. The optimal frequency is therefore a compromise between transmission, precision, and target accessibility. Single-element transducers are relatively simple but have limited electronic steering and may produce a comparatively elongated focal zone. Phased arrays can correct phase delays across individual elements, steer the focus electronically, and reduce off-target energy. Large-aperture helmet systems can potentially improve focal precision for deep targets but require more complex calibration, immobilization, coupling, computational planning, and quality assurance. A 256-element helmet-shaped system reported in 2025 used individualized planning and concurrent functional MRI to modulate the lateral geniculate nucleus and its connected visual network. The investigation was not an epilepsy trial, but it demonstrated that highly focal, nonablative modulation of a small human thalamic nucleus is technically achievable with advanced arrays and model-based correction. Direct electrophysiological evidence of deep target engagement has also been obtained in people with implanted deep-brain-stimulation electrodes. Targeted ultrasound altered local-field-potential activity within the globus pallidus, with effects varying according to stimulation protocol. These findings support the premise that transcranial ultrasound can modify deep human circuits rather than acting only through superficial auditory or somatosensory pathways. Nevertheless, target engagement in movement or visual circuits cannot be extrapolated automatically to seizure suppression. Epileptogenic networks demonstrate dynamic excitability, propagation, state dependence, sleep-related modulation, medication effects, and substantial interictal–ictal variability. The acoustic field must overlap a biologically relevant node while avoiding stimulation patterns that facilitate synchronization.

Table 2. **Acoustic parameters requiring prospective reporting**

Parameter	Biological or technical significance	Required reporting approach
Carrier frequency	Determines wavelength, skull penetration, attenuation, and focal dimensions	Report nominal and measured frequency
Peak negative pressure	Relates to mechanical exposure and potential neural effects	Report free-field and estimated in situ values
Pulse duration	Influences temporal integration and membrane deformation	Report duration of each acoustic pulse
Pulse-repetition frequency	Determines timing of repeated mechanical exposure	Report exact repetition rate
Duty cycle	Defines the fraction of time ultrasound	Report as percentage and calculate

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	is active	total on-time
Sonication duration	Influences cumulative neuromodulatory and thermal effects	Report each train and complete session duration
Intertrain interval	May determine inhibitory or facilitatory network effects	Report timing between trains
Focal dimensions	Determines anatomical selectivity and off-target exposure	Report lateral and axial dimensions
Skull-adjusted intensity	More clinically relevant than water-tank output	Estimate with individualized acoustic modeling
Mechanical index	Used in assessment of mechanical bioeffect risk	Report free-field and transcranial estimates
Thermal dose	Estimates temperature-related tissue risk	Model brain, skull, and scalp exposure
Coupling and positioning	Affect transmission and reproducibility	Document coupling medium, immobilization, and neuronavigation error

International reporting and safety initiatives now emphasize detailed disclosure of transducer design, driving parameters, free-field measurements, pulse timing, in situ estimates, intensity definitions, thermal modeling, and mechanical exposure. Without such standardization, two studies described simply as “low-intensity ultrasound” may deliver biologically different interventions [16, 23, 30]. The published ITRUSST recommendations provide a framework for reproducible application but do not replace disease-specific risk assessment. Target selection: focus, node, or network Traditional epilepsy surgery attempts to identify an epileptogenic zone whose removal is both necessary and sufficient for seizure freedom. Focused-ultrasound neuromodulation may require a broader conceptual framework because temporary modulation of a network node does not necessarily eliminate the pathological system. Potential targets include the seizure-onset zone, hippocampus, amygdala, insula, neocortical focus, anterior nucleus of the thalamus, centromedian nucleus, medial pulvinar, subiculum, entorhinal cortex, and propagation hubs identified through connectomic analysis. The best target may vary according to epilepsy phenotype. For unilateral mesial temporal lobe epilepsy, the hippocampus is a biologically plausible target, particularly when resection is contraindicated or refused. However, hippocampal sclerosis, atrophy, calcification, temporal-bone thickness, air-containing mastoid cells, and target depth can alter ultrasound delivery. Bilateral temporal lobe epilepsy raises the additional risk of bilateral memory-network disruption. In neocortical epilepsy, the seizure-onset zone may be close to language, motor, visual, or association cortex. A small focal field may provide an advantage over diffuse electrical stimulation, but targeting uncertainty of only several millimeters could expose an eloquent cortical area. Functional MRI, tractography, magnetoencephalography, navigated stimulation, and neuropsychological lateralization should therefore be integrated into planning. Thalamic targets may be appropriate for multifocal or generalized network epilepsies. The anterior nucleus participates in limbic circuitry and is an established electrical deep-brain-stimulation target. The centromedian nucleus and medial pulvinar

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participate in widespread thalamocortical propagation and arousal networks. Focused ultrasound could permit noninvasive testing of target responsiveness before permanent implantation, although repeated sessions may be required to maintain efficacy. A practical target-selection strategy should distinguish the anatomical seizure-onset zone, the minimum effective modulation volume, the functional tissue that must be spared, and the propagation network that determines clinical seizure expression. Targeting only the earliest electrographic contact may fail when that contact represents an accessible recording site rather than the complete epileptogenic substrate.

Clinical evidence. The prospective Epilepsia pilot study enrolled six patients with drug-resistant epilepsy undergoing stereo-electroencephalography. Ultrasound was directed to the seizure-onset zone under neuronavigational guidance, while intracranial activity was recorded during and after sonication. The protocol used a ceiling spatial-peak temporal-average intensity of 2.8 W/cm², a 30% duty cycle, and a ten-minute modulation period [10, 15, 16]. Two participants demonstrated reduced seizure frequency during the three-day observation period, while one experienced an increase in subclinical seizures. Post-treatment MRI showed neither a new structural lesion nor cerebral edema. One participant reported scalp heating, and another developed transient naming and memory impairment that resolved within three weeks. Significant spectral-power changes occurred at targeted stereo-electroencephalographic contacts, providing evidence of local electrophysiological engagement [21, 24, 31]. The study was not designed to establish durable seizure efficacy. The sample was small, follow-up was brief, there was no sham group, and participants underwent invasive monitoring that may itself alter seizure behavior. Nevertheless, the combination of individualized targeting and intracranial electrophysiology provided a valuable mechanistic bridge between animal studies and outpatient therapeutic trials.

A separate 2024 pilot safety report evaluated hippocampal transcranial ultrasound in six patients with drug-resistant epilepsy. The study supported feasibility and identified a preliminary seizure-reduction signal, but its uncontrolled design and small cohort prevent causal conclusions. Functional-connectivity changes appeared more prominent in patients with larger clinical improvement, suggesting that network imaging might eventually serve as a response biomarker [11, 16, 23]. The current clinical pipeline includes several complementary designs. NCT06388707 evaluates safety, tolerability, and preliminary efficacy in unilateral or bilateral drug-resistant temporal lobe epilepsy using a prospective open-label multicenter design. NCT06492720 uses a randomized two-arm dose-comparison framework. NCT05947656 evaluates neuronavigation-guided sonication of one or both hippocampi. NCT07353918 includes patients with implanted responsive neurostimulation systems and compares active with sham intervention while using chronic intracranial recordings to monitor electrographic effects [1, 10, 13].

Table 3. **Selected human evidence and current clinical-development directions**

Study or protocol	Population	Target and design	Principal contribution	Main limitation
Lee et al., 2022	Six patients with DRE undergoing SEEG	Neuronavigation-guided sonication of the seizure-onset zone	Demonstrated intracranial target engagement and absence of MRI-	Very small uncontrolled sample and brief follow-up

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			visible tissue injury	
Bubrick et al., 2024	Six patients with drug-resistant epilepsy	Repeated hippocampal transcranial ultrasound	Supported feasibility and preliminary clinical signal	No definitive efficacy comparison
NCT03868293	Adults with drug-resistant temporal lobe epilepsy	Repeated pulsed LIFU targeting the affected hippocampus	Evaluates serial treatment and seizure-frequency change	Open-label single-group design
NCT05947656	Drug-resistant temporal lobe epilepsy	NaviFUS treatment of one or both hippocampi	Evaluates neuronavigation-guided treatment feasibility	Early-phase study
NCT06388707	Unilateral or bilateral drug-resistant TLE	Prospective open-label multicenter pilot	Tests safety and preliminary efficacy across centers	No sham comparator
NCT06492720	Drug-resistant epilepsy	Randomized low-dose versus high-dose protocol	Provides dose-comparison information	Open-label treatment allocation
NCT07353918	Medically refractory TLE with implanted RNS electrodes	Active versus sham LIFU with chronic intracranial monitoring	Enables objective electrographic target-engagement assessment	Restricted population with existing implanted device

Safety and adverse-effect surveillance. Safety evaluation must distinguish thermal injury, mechanical injury, unintended neuromodulation, and disease-specific seizure risk. The absence of contrast microbubbles reduces the likelihood of cavitation-related vascular injury, but skull heating, focal tissue heating, standing-wave formation, off-target exposure, and cumulative-session effects remain relevant. The mechanical index alone is insufficient because it does not capture all pulse-timing, cumulative, skull, and focal-field effects. Safety assessment should include calibrated free-field pressure, individualized in situ estimates, temperature modeling, thermal dose, acoustic coupling, focal overlap with vascular structures, and device-output verification. The 2025 ITRUSST biophysical-safety consensus proposed exposure conditions considered to represent nonsignificant biophysical risk in appropriate research contexts. These recommendations are not equivalent to regulatory approval and do not establish that a given protocol is clinically safe in epilepsy. A disease capable of spontaneous seizure clustering and status epilepticus requires additional neurological surveillance beyond generic ultrasound safety metrics. Clinical monitoring should include neurological examination, memory, language, attention, executive function, mood, sleep, seizure frequency, and rescue-medication use. MRI with susceptibility-weighted, diffusion-weighted, T2-weighted, and fluid-attenuated inversion-recovery sequences should be obtained when clinically

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appropriate to detect hemorrhage, ischemia, edema, or unexpected tissue alteration. Auditory and somatosensory confounds are methodologically and clinically relevant. Pulsed ultrasound can produce perceived sound through bone conduction or activate peripheral pathways. A participant who distinguishes active from sham treatment may alter seizure reporting, anxiety, sleep, and adherence. Auditory masking, credible sham design, and post-session blinding assessment should therefore be included. Repeated exposure introduces questions not answered by single-session safety studies. A protocol that is safe once may produce cumulative plasticity, subtle cognitive effects, progressive scalp irritation, or repeated seizure destabilization. Longitudinal studies should include predefined stopping rules for seizure worsening, status epilepticus, new psychiatric symptoms, persistent cognitive decline, or unexpected MRI abnormalities.

Proposed multicenter randomized trial. The proposed trial would include an eight-week baseline period, individualized acoustic planning, randomization to active or sham treatment, and repeated sessions delivered under identical conditions. A minimum six-month blinded follow-up would be followed by an optional open-label extension. Active treatment would use a standardized parameter family but permit prespecified skull- and target-adjusted pressure correction. This approach would reduce variation in intracranial exposure without allowing unrestricted site-level parameter modification. All acoustic simulations and delivered-output logs would be transferred to an independent core laboratory. The sham transducer would reproduce contact pressure, coupling, positioning, audible equipment cues, and session duration. Neither the participant, treating epileptologist, outcome assessor, nor diary-review committee would know allocation. The ultrasound engineer could remain unblinded only if required for device safety and would have no role in clinical assessment. Seizure outcomes would be adjudicated from diaries, caregiver reports, ambulatory EEG, wearable events, and implanted recordings where available. An independent committee would classify events as focal aware, focal impaired-awareness, focal-to-bilateral tonic–clonic, nonepileptic, uncertain, or electrographic-only.

Table 4. **Proposed study protocol and originality**

Component	**Proposed specification**
Population	Adults with drug-resistant focal epilepsy unsuitable for or declining curative resection
Design	Multicenter, randomized, double-blind, sham-controlled, parallel-group trial
Baseline period	Eight weeks with stable medication and prospective seizure recording
Intervention	Repeated individualized LIFU sessions directed to a prespecified epileptogenic-network target
Comparator	Credible sham sonication with identical workflow and sensory environment
Primary endpoint	At least 50% reduction in disabling seizures during months 4–6 without persistent neurological deterioration
Secondary clinical endpoints	Seizure freedom, median reduction, tonic–clonic seizures, injuries, rescue treatment, quality of life
Neuropsychological	Memory, language, executive function, mood, sleep, and patient-

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endpoints	reported cognition
Electrophysiological endpoints	Interictal discharges, electrographic seizures, high-frequency oscillations, network connectivity
Acoustic endpoints	Skull-adjusted pressure, intensity, focal overlap, thermal estimate, targeting error, accumulated exposure
Safety endpoints	Seizure worsening, status epilepticus, MRI abnormality, neurological deficit, psychiatric change, scalp injury
Blinding assessment	Participant and investigator estimation of treatment allocation after each session
External validation	Locked protocol replicated at independent epilepsy centers and across skull-density strata
Originality	Direct integration of clinical response, mechanistic target engagement, acoustic dose, and neuropsychological safety

Discussion. Low-intensity focused ultrasound is attractive for drug-resistant epilepsy because it offers a combination not provided by existing treatments: noninvasive access to both superficial and deep structures, potentially restricted focal exposure, reversibility, repeatability, and compatibility with electrophysiological or imaging biomarkers. These properties could fill an important therapeutic gap for patients who are unsuitable for resection and reluctant or unable to undergo permanent device implantation. Current evidence, however, supports feasibility rather than established efficacy. The human literature consists mainly of small pilot studies, short follow-up, heterogeneous targets, and variable acoustic parameters. Seizure reduction observed after treatment may reflect true neuromodulation, natural fluctuation, regression to the mean, medication adherence, hospital-related behavioral changes, or reporting bias. Epilepsy is particularly vulnerable to erroneous efficacy conclusions because seizure frequency varies over circadian, multidien, hormonal, sleep-related, and stress-related cycles. Baseline periods that are too short can enroll participants during an unusually severe phase, producing apparent improvement even without active treatment. Randomization, sufficiently long baselines, sham control, and blinded adjudication are therefore essential.

The first major translational problem is parameter selection. Ultrasound publications frequently use terms such as “low intensity,” “pulsed,” or “theta burst” without enough information to reconstruct the delivered intracranial exposure. Standardized reporting should include transducer geometry, carrier frequency, calibrated pressure, pulse timing, duty cycle, coupling, skull model, in situ estimate, focal dimensions, thermal estimate, and cumulative exposure [3, 10, 18, 27]. The second problem is biological directionality. An ultrasound protocol cannot be assumed to inhibit the target because it uses a low average intensity. Parameter-dependent excitation and inhibition have been demonstrated across experimental systems, while preclinical epilepsy work shows that changing temporal pattern can reverse the direction of the effect. Early human trials should therefore include electrophysiological target-engagement measurements before advancing to large efficacy studies. The third problem is target definition. A seizure-onset zone identified by the earliest stereo-electroencephalographic activity may not equal the complete epileptogenic network. Sonication of a

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small region may alter local spectral power without preventing seizure propagation. Conversely, modulation of a strategic thalamic or limbic hub might reduce widespread seizures even when the cortical onset remains unchanged. Patient-specific network analysis may improve target selection. Structural connectivity, resting-state functional MRI, ictal propagation, interictal high-frequency oscillations, and stimulation-response mapping can identify nodes with disproportionate influence on seizure spread. The optimal target may be the node with the highest predicted network-control value rather than the tissue with the earliest visible discharge.

Repeated sonication could be individualized in several ways. A fixed target could receive scheduled maintenance sessions, treatment could be timed to high-risk multidien seizure phases, or sonication could be triggered by electrographic biomarkers. The 2026 protocol involving patients with responsive-neurostimulation systems is particularly relevant because implanted electrodes can provide objective longitudinal measurements before and after real or sham ultrasound. Closed-loop focused ultrasound remains technically challenging. Real-time detection must be integrated with transducer positioning, acoustic coupling, treatment planning, and safety checks. Unlike an implanted electrical pulse, ultrasound cannot necessarily be delivered instantaneously during unrestricted daily activity with current clinical platforms. Portable or wearable transducers may eventually reduce this limitation, but stable skull coupling and focal accuracy must be maintained. Another potential role is preoperative functional testing. Temporary sonication of a proposed target could estimate whether its modulation alters seizures, memory, mood, or language before irreversible ablation or implantation. A favorable physiological response might support subsequent surgery, whereas cognitive deterioration could redirect the treatment plan. Such a “virtual lesion” paradigm requires rigorous validation because temporary modulation may not predict the effects of chronic stimulation or permanent destruction. LIFU should not be positioned as a replacement for evidence-based resective surgery in patients with a well-localized, safely resectable epileptogenic lesion. Delaying curative surgery in favor of an unproven noninvasive intervention could prolong seizure exposure and reduce the probability of optimal recovery. Appropriate candidates are more likely to be patients without a favorable resection option, those requiring network-level palliation, or those enrolled in carefully controlled presurgical investigations. Comparative effectiveness will ultimately be required. For mesial temporal lobe epilepsy, LIFU may be compared with laser interstitial thermal therapy, open resection, responsive neurostimulation, or continued medical therapy. For multifocal epilepsy, comparisons may involve vagus nerve stimulation, thalamic deep brain stimulation, or responsive-network approaches. The safety advantage of avoiding surgery should also be evaluated realistically. Noninvasive treatment eliminates risks associated with craniotomy, intracranial electrodes, infection, and implanted hardware, but it introduces different risks: inaccurate targeting, off-target modulation, skull heating, repeated exposure, unrecognized excitation, cognitive effects, and delayed seizure worsening. “Incisionless” does not mean biologically inactive or risk free. Neuropsychological outcomes deserve equal status with seizure frequency. A treatment that reduces seizures while impairing verbal memory, naming, executive control, or mood may not produce a favorable net benefit. This concern is especially important for dominant temporal and bilateral hippocampal targets. The primary endpoint proposed in this article combines seizure response with neurological safety. Traditional responder rates can misclassify a participant with a 50% seizure

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reduction and major memory decline as a treatment success. A composite net-benefit framework is more appropriate for interventions directed at eloquent neural networks.

Blinding must be tested rather than assumed. Participants should be asked after each session whether they believe they received active or sham treatment and why. Scalp sensations, audible cues, equipment behavior, and operator interactions must be standardized. If blinding fails, objective electrographic endpoints become even more important. Statistical analysis should model seizure counts using methods appropriate for overdispersed recurrent events, such as negative-binomial mixed-effects models. Prespecified sensitivity analyses should address missing diaries, seizure clusters, medication changes, rescue therapy, and COVID-like external disruptions. The responder endpoint should be supplemented by continuous seizure-frequency change to avoid loss of information. Subgroup analyses should examine unilateral versus bilateral temporal epilepsy, MRI-positive versus MRI-negative disease, previous surgery, skull-density characteristics, target depth, focal-overlap accuracy, and baseline network connectivity. These analyses must be considered exploratory unless independently replicated. Equity and scalability also require attention. Individual CT-based acoustic simulation, MRI guidance, multidisciplinary epilepsy evaluation, and specialized ultrasound equipment may concentrate treatment in high-resource centers. Simplified workflows should not be adopted until their targeting accuracy and safety are demonstrated across diverse skull anatomy and healthcare environments. Data transparency will be essential. Negative or paradoxical electrophysiological responses should be reported, not only successful sonications. Acoustic simulation files, parameter definitions, target coordinates, and deidentified outcome data should be made available where ethically and legally possible. External replication is unlikely if essential device settings remain proprietary. The regulatory pathway will depend on the intended claim. A device intended for temporary network testing requires a different evidentiary framework from one claiming long-term seizure reduction. Changes in software, acoustic correction, pulse sequence, or transducer geometry may materially change biological exposure and cannot be treated as trivial engineering updates. Several limitations of the present review should be acknowledged. The evidence is heterogeneous and dominated by early-phase studies. The long-term effects of repeated treatment remain uncertain. Direct comparisons among hippocampal, cortical, and thalamic targets are unavailable. Published seizure outcomes may be influenced by selection and reporting bias. Registered trials remain ongoing, and their eventual results may change current conclusions. Despite these limitations, focused ultrasound provides a valuable experimental platform for causal investigation of human epileptic networks. It can combine precise anatomical targeting with EEG, stereo-electroencephalography, functional MRI, perfusion imaging, and neuropsychological testing. This combination may improve not only therapy but also understanding of which network nodes sustain seizures and which acoustic exposures produce inhibition rather than excitation.

Conclusion. Low-intensity focused ultrasound is an emerging, nonablative neuromodulation technology with potential applications in drug-resistant epilepsy. Its principal advantages are incisionless delivery, access to deep structures, relatively focal targeting, repeatability, and compatibility with electrophysiological and imaging biomarkers. Preclinical studies support the possibility of suppressing epileptiform activity, while early human investigations demonstrate that ultrasound can be directed to seizure-onset tissue, modify intracranial electrophysiological activity,

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and avoid overt structural injury under studied conditions. Clinical seizure outcomes remain preliminary, heterogeneous, and insufficient to establish therapeutic effectiveness. The central translational challenge is not simply to deliver ultrasound to the brain. It is to deliver a reproducible, skull-adjusted acoustic dose to a biologically appropriate epileptogenic-network node using parameters that inhibit pathological activity without impairing physiological cognition, language, mood, or sensorimotor function. Future studies require randomized sham-controlled designs, sufficiently long baseline and follow-up periods, individualized acoustic simulation, objective electrophysiological target-engagement biomarkers, systematic neuropsychological testing, transparent adverse-event reporting, and independent multicenter validation. Until these requirements are met, low-intensity focused ultrasound should remain an investigational strategy offered within ethically approved clinical trials rather than a routine substitute for established epilepsy surgery or implantable neuromodulation.

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MINIMALLY INVASIVE EVACUATION OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE IN THE POST-ENRICH ERA: LOCATION-BASED SELECTION, EARLY CLOT REDUCTION, AND RESIDUAL-VOLUME TARGETS

Abstract

Background. Spontaneous intracerebral hemorrhage remains a highly lethal and disabling stroke subtype. Conventional craniotomy has not consistently improved functional outcomes, whereas modern minimally invasive techniques seek rapid clot reduction while limiting injury to viable brain.

Materials and methods. Randomized trials, contemporary guidelines, prospective cohorts, surgical-performance analyses, and endoscopic investigations published through July 2026 were synthesized. Evidence was organized according to hemorrhage location, volume, expansion stability, neurological severity, operative timing, access trajectory, evacuation method, residual clot, intraventricular extension, and postoperative care.

Results. MISTIE III demonstrated procedural safety and suggested that reduction to a residual volume of 15 mL or less is associated with improved outcome, although the primary functional endpoint was neutral. ENRICH established a functional benefit for early trans-sulcal evacuation within 24 hours, driven predominantly by lobar hemorrhage, with lower 30-day mortality than medical management. MIND achieved substantial volume reduction but did not improve 180-day disability in a cohort dominated by deep hemorrhage and treated within 72 hours. CLEAR III reduced mortality after intraventricular clot lysis without improving the prespecified functional endpoint. These apparently discordant trials indicate that minimally invasive surgery is not a uniform intervention. Benefit depends on removing a clinically meaningful amount of blood early, through a tissue-preserving route, in patients whose neurological networks remain recoverable.

Conclusion. The proposed EVAC-ICH framework integrates eligibility, volume and location, active-bleeding control, corridor selection, intraoperative hemostasis, clot-reduction targets, and postoperative neurocritical care. Future trials should prioritize biological timing, tract preservation, quantitative residual volume, and patient-centered ordinal outcome shifts.

Keywords: intracerebral hemorrhage; minimally invasive surgery; ENRICH; MISTIE III; MIND trial; neuroendoscopy; hematoma evacuation; residual clot volume; intraventricular hemorrhage; trans-sulcal surgery.

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МАЛОИНВАЗИВНАЯ ЭВАКУАЦИЯ СПОНТАННОГО ВНУТРИМОЗГОВОГО КРОВОИЗЛИЯНИЯ В ЭПОХУ ПОСЛЕ ENRICH: ОТБОР ПО ЛОКАЛИЗАЦИИ, РАННЕЕ УМЕНЬШЕНИЕ ГЕМАТОМЫ И ЦЕЛЕВОЙ ОСТАТОЧНЫЙ ОБЪЁМ

Аннотация

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Актуальность. Спонтанное внутримозговое кровоизлияние остаётся одним из наиболее летальных и инвалидизирующих вариантов инсульта. Традиционная краниотомия не продемонстрировала устойчивого улучшения функциональных исходов, тогда как современные малоинвазивные технологии направлены на быстрое уменьшение объёма гематомы при минимальном повреждении жизнеспособного мозга.

Материалы и методы. Синтезированы рандомизированные исследования, современные руководства, проспективные когорты, анализы хирургической эффективности и эндоскопические работы, опубликованные до июля 2026 года. Данные систематизированы по локализации и объёму кровоизлияния, стабильности гематомы, тяжести дефицита, времени операции, траектории доступа, методу эвакуации, остаточному объёму, внутрижелудочковому компоненту и послеоперационной терапии. Результаты. MISTIE III подтвердило безопасность метода и показало, что достижение остаточного объёма не более 15 мл ассоциировано с лучшим исходом, хотя первичная функциональная конечная точка оставалась нейтральной. ENRICH впервые продемонстрировало функциональное преимущество ранней транссулькальной эвакуации в течение 24 часов, преимущественно при лобарных гематомах, и снижение 30-дневной летальности. MIND обеспечило значительное уменьшение объёма крови, но не улучшило 180-дневную инвалидизацию в популяции с преобладанием глубоких кровоизлияний и операцией в пределах 72 часов. CLEAR III снизило летальность после внутрижелудочкового тромболизиса, не улучшив заранее определённый функциональный исход. Эти результаты показывают, что малоинвазивная хирургия не является единообразным вмешательством. Польза зависит от раннего и достаточного удаления крови через тканесберегающий коридор у пациентов с сохранённым потенциалом восстановления функциональных сетей.

Заключение. Модель EVAC-ICH объединяет клинический отбор, объём и локализацию, контроль продолжающегося кровотечения, выбор доступа, гемостаз, целевой остаточный объём и нейроинтенсивное ведение.

Ключевые слова: внутримозговое кровоизлияние; малоинвазивная хирургия; ENRICH; MISTIE III; MIND; нейроэндоскопия; эвакуация гематомы; остаточный объём; внутрижелудочковое кровоизлияние; транссулькальный доступ.

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ENRICH DAVRIDAN KEYIN SPONTAN INTRASEREBRAL QON QUYILISHINI MINIMAL INVAZIV EVAKUATSIYA QILISH: JOYLASHUVGA ASOSLANGAN TANLOV, GEMATOMANI ERTA KAMAYTIRISH VA MAQSADLI QOLDIQ HAJM

Annotatsiya

Dolzarblik. Spontan intraserebral qon quyilishi insultning o‘lim va og‘ir nogironlik bilan eng ko‘p bog‘liq turlaridan biri bo‘lib qolmoqda. An’anaviy kraniotomiya funksional natijalarni muntazam ravishda yaxshilamagan, zamonaviy minimal invaziv texnologiyalar esa hayotiy miya to‘qimasini imkon qadar saqlagan holda gematoma hajmini tez kamaytirishga qaratilgan.

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Material va usullar. 2026-yil iyuligacha chop etilgan randomizatsiyalangan tadqiqotlar, klinik tavsiyalar, prospektiv kohortalar, jarrohlik samaradorligi tahlillari va endoskopik ishlar sintez qilindi. Natijalar qon quyilish joylashuvi va hajmi, gematoma barqarorligi, nevrologik og‘irlik, operatsiya vaqti, kirish trayektoriyasi, evakuatsiya usuli, qoldiq qon hajmi, qorincha ichiga tarqalish va operatsiyadan keyingi davolash bo‘yicha tizimlashtirildi. MISTIE III usul xavfsizligini tasdiqladi va qoldiq hajmni 15 ml yoki undan kam darajaga tushirish yaxshiroq natija bilan bog‘liqligini ko‘rsatdi, biroq asosiy funksional yakun neytral bo‘ldi. ENRICH 24 soat ichidagi erta transsulkulyar evakuatsiyaning, asosan lobar gematomalarda, funksional foydasini va 30 kunlik o‘limning kamayishini ko‘rsatdi. MIND gematoma hajmini sezilarli kamaytirdi, ammo chuqur qon quyilishlar ustun bo‘lgan va 72 soatgacha operatsiya qilingan guruhda 180 kunlik nogironlikni yaxshilamadi. CLEAR III qorincha ichidagi trombolizdan so‘ng o‘limni kamaytirdi, ammo belgilangan funksional natijani yaxshilamadi.

Xulosa. Minimal invaziv jarrohlik yagona standart amaliyot emas. EVAC-ICH modeli bemor tanlash, hajm va joylashuv, faol qon ketishini nazorat qilish, xavfsiz koridor, intraoperatsion gemostaz, qoldiq hajm maqsadi va neyrointensiv yordamni birlashtiradi.

Kalit so‘zlar: intraserebral qon quyilishi; minimal invaziv jarrohlik; ENRICH; MISTIE III; MIND; neyroendoskopiya; gematoma evakuatsiyasi; qoldiq hajm; intraventrikulyar qon quyilishi; transsulkulyar kirish.

Introduction. Spontaneous intracerebral hemorrhage is caused by nontraumatic rupture of a cerebral vessel with accumulation of blood within the brain parenchyma. It accounts for a smaller proportion of all strokes than cerebral infarction but produces disproportionately high early mortality, severe disability, prolonged intensive care, and long-term dependence. The initial hematoma directly disrupts neural tissue and is followed by expansion, mechanical deformation, intracranial hypertension, intraventricular extension, hydrocephalus, perihematomal edema, inflammation, thrombin toxicity, iron-mediated oxidative injury, mitochondrial dysfunction, and delayed degeneration of surrounding white-matter pathways [1–3]. The biological rationale for hematoma evacuation is compelling. Removal of blood can reduce mass effect, lower intracranial pressure, restore local perfusion, relieve ventricular obstruction, and decrease exposure of surrounding tissue to hemoglobin degradation products and inflammatory mediators. However, surgery also injures brain. Cortical incision, white-matter transgression, retraction, venous damage, thermal coagulation, incomplete hemostasis, and postoperative rebleeding may offset the benefit of clot reduction [3, 6, 10]. This balance explains the historical difficulty of demonstrating functional benefit. Conventional craniotomy provides wide exposure and direct hemostasis but requires substantial tissue disruption, especially when the hematoma is deep. STICH and STICH II did not establish a general functional advantage of early open evacuation over initial medical management. STICH II suggested that selected patients with superficial lobar hemorrhage without intraventricular extension might have a survival advantage, but the overall functional result remained neutral [5, 11, 16]. These trials did not prove that blood removal is biologically ineffective. They demonstrated that the benefit of decompression and clot removal can be lost when access injury is excessive, patient selection is broad, operative timing is delayed, or the amount of blood removed is insufficient. Modern minimally invasive surgery seeks to change this therapeutic ratio.

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The term minimally invasive surgery includes several distinct procedures. Catheter-based aspiration with local thrombolysis gradually liquefies and drains the hematoma. Stereotactic aspiration uses a cannula or catheter placed through a burr hole. Endoscopic evacuation permits direct visualization, irrigation, aspiration, and focal coagulation. Tubular trans-sulcal surgery creates a circumferential working corridor through a sulcus or shortest white-matter path. Mechanically assisted aspiration devices fragment and remove clot under endoscopic or exoscopic visualization. Robotic stereotaxy improves trajectory reproducibility but does not determine biological eligibility [4, 7, 14]. These procedures differ in timing, operative speed, tissue disruption, ability to control active bleeding, maximum achievable evacuation, and dependence on postoperative thrombolysis. Combining them under one category can obscure clinically meaningful differences. A slow catheter-lysis protocol completed several days after onset is not biologically equivalent to early trans-sulcal evacuation within 24 hours. MISTIE III was a landmark phase III trial of catheter aspiration followed by low-dose alteplase irrigation. The procedure substantially reduced clot volume and was safe, but the primary functional endpoint was neutral. Surgical-performance analyses suggested that patients in whom residual hematoma was reduced to 15 mL or less had better outcomes, making procedural completeness a central therapeutic variable [8, 9, 25]. ENRICH subsequently provided the first convincing randomized evidence of functional benefit from early minimally invasive parenchymal evacuation. Patients with 30–80 mL lobar or anterior basal-ganglia hemorrhage were randomized within 24 hours. The mean utility-weighted modified Rankin score at 180 days favored surgery, but the benefit was attributable mainly to the lobar subgroup. The anterior basal-ganglia subgroup did not demonstrate benefit, and enrollment of that anatomical group was stopped according to the adaptive trial design [10, 13, 23]. MIND introduced additional complexity. The trial used mechanically assisted minimally invasive aspiration in 236 patients with 20–80 mL supratentorial hemorrhage and permitted surgery within 72 hours. The surgical group achieved substantial median clot reduction, but neither 180-day disability nor 30-day mortality differed significantly from medical management. Nearly 70% of the cohort had deep hemorrhage, and enrollment stopped early, reducing statistical power [2, 3, 18]. The contrast between ENRICH and MIND does not mean that one device is effective and another is ineffective. It suggests that location, time, access trajectory, residual hematoma, corticospinal-tract integrity, trial population, and perioperative workflow determine whether removal translates into recovery.

Intraventricular hemorrhage represents another related but distinct condition. Blood obstructs CSF pathways, produces hydrocephalus, increases intracranial pressure, exposes ependymal surfaces to inflammatory products, and is strongly associated with poor outcome. CLEAR III showed that intraventricular alteplase administered through an external ventricular drain accelerated clot clearance and reduced mortality but did not improve the prespecified functional endpoint. More survivors remained severely disabled, illustrating that survival and functional independence are not interchangeable outcomes [6, 13, 28]. The modern question is therefore not whether surgery is beneficial for all intracerebral hemorrhage. The appropriate question is which patient, with which anatomical phenotype, should undergo which form of evacuation, at what time, through which corridor, to what residual volume, and with what postoperative goals. This review evaluates the evidence supporting minimally invasive ICH evacuation after ENRICH and proposes the EVAC-ICH

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framework. The acronym represents Eligibility and recoverability, Volume and vascular anatomy, Active bleeding and stability, Corridor preservation, Intraoperative hemostasis, Clot-reduction target, and Hemorrhage-specific postoperative care.

Materials and Methods. This manuscript was designed as a structured integrative review with an original surgical-selection synthesis. Randomized controlled trials, contemporary guidelines, prospective multicenter studies, surgical-performance analyses, endoscopic series, imaging investigations, and technical studies published through July 2026 were evaluated. The principal evidence base included STICH, STICH II, MISTIE III, ENRICH, MIND, ICES, CLEAR III, INVEST-related cohorts, the 2022 American Heart Association/American Stroke Association guideline, and the 2025 European Stroke Organisation–European Association of Neurosurgical Societies guideline [11, 12, 20]. Evidence was classified into eight domains. The first domain was clinical eligibility, including age, premorbid function, Glasgow Coma Scale score, NIH Stroke Scale score, neurological trajectory, medical comorbidity, and treatment goals. The second domain was hemorrhage anatomy, including lobar, putaminal, caudate, thalamic, deep white-matter, cerebellar, brainstem, and intraventricular components. The third domain was biological timing, including onset-to-imaging, hematoma expansion, repeat-CT stability, anticoagulant reversal, and onset-to-evacuation. The fourth domain was corridor planning, including cortical or sulcal entry, white-matter transgression, corticospinal-tract proximity, eloquent networks, hematoma long axis, and ventricular relationships. The fifth domain was operative performance, including percentage evacuation, residual volume, operative duration, hemostasis, rebleeding, tissue injury, and conversion. The sixth domain was intraventricular disease, including hydrocephalus, external ventricular drainage, clot burden, third- and fourth-ventricle obstruction, and thrombolysis. The seventh domain was postoperative neurocritical care, including blood-pressure control, repeat imaging, intracranial pressure, airway management, seizures, venous thrombosis, rehabilitation, and withdrawal-of-care decisions. The eighth domain was functional outcome, emphasizing ordinal disability shift, return to baseline, mortality, severe dependency, cognition, communication, and quality of life. No new patient cohort was generated, and no independent pooled statistical analysis was performed. The tables represent an original synthesis of published evidence and do not contain fabricated clinical data.

Results. The initial hematoma produces immediate mechanical destruction. Neurons, axons, glia, and microvessels within the hematoma core are frequently irreversibly damaged. Surrounding tissue is compressed and displaced but may remain structurally recoverable. Mass effect can reduce local microvascular perfusion, distort venous drainage, compress the ventricular system, and contribute to transtentorial or subfalcine herniation. These effects are most pronounced in large lobar hemorrhage, cerebellar hemorrhage, and hematoma with extensive edema or intraventricular obstruction. Secondary injury begins within hours. Thrombin activates inflammation and disrupts the blood–brain barrier. Erythrocyte lysis releases hemoglobin, heme, and iron, promoting oxidative stress and lipid peroxidation. Microglial activation, complement, neutrophil recruitment, and cytokine production amplify perihematomal injury [1–3, 13–15]. Hematoma removal may reduce exposure to these mediators, but the timing matters. Evacuation after secondary injury has matured may relieve mass effect without reversing established cellular injury. Early removal has greater biological potential but occurs during the period of highest rebleeding risk. The therapeutic objective

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is not necessarily complete removal. Aggressive pursuit of a small adherent clot fragment can injure a perforating artery, vein, internal capsule, or eloquent cortex. The clinically relevant endpoint is sufficient decompression and reduction of toxic clot burden while preserving hemostasis and viable neural pathways.

Hemorrhage Location. Location is one of the strongest modifiers of surgical benefit. Lobar hemorrhage lies closer to the cortical surface and can often be accessed through a sulcus or short trans-cortical route. The surrounding tissue may contain association fibers and eloquent cortex, but the access distance is generally shorter than for deep ganglionic hemorrhage. ENRICH demonstrated a favorable 180-day utility-weighted functional outcome for surgery, with the effect driven by lobar hemorrhage. The adjusted difference was not favorable for anterior basal-ganglia hemorrhage. Thirty-day mortality was 9.3% in the surgical group and 18.0% with medical management. Putaminal and anterior basal-ganglia hemorrhages are surrounded by the internal capsule, corona radiata, lenticulostriate vessels, insula, and deep venous structures. The shortest geometric route may not be the safest functional route. Even a narrow corridor can injure corticospinal or language-related pathways. Thalamic hemorrhage is frequently associated with intraventricular extension, hydrocephalus, impaired consciousness, ocular-motor abnormalities, and injury to critical arousal and sensory networks. Parenchymal evacuation is technically difficult and is not supported by the same randomized evidence as lobar evacuation. Caudate hemorrhage commonly ruptures into the ventricle. Management may be driven more by hydrocephalus and intraventricular clot than by removal of the relatively small parenchymal component. Cerebellar hemorrhage is a separate surgical emergency. Neurological deterioration, brainstem compression, hydrocephalus, or hematoma volume generally support prompt surgical evacuation. Minimally invasive techniques may be feasible, but posterior-fossa anatomy allows little tolerance for delay or incomplete decompression. Brainstem hemorrhage has an extremely narrow safety margin. Routine surgical evacuation is not established. Selected stereotactic or endoscopic procedures have been reported, but they remain specialized and cannot be extrapolated from supratentorial trials.

Table 1. **Anatomical Phenotypes and Potential Surgical Strategy**

Hemorrhage phenotype	Potential benefit of evacuation	Major operative risk	Current interpretation
Superficial lobar ICH, 30–80 mL	Reduction of mass effect and cortical displacement	Eloquent cortex, draining veins, rebleeding	Strongest randomized support for early MIS
Deep frontal or anterior basal-ganglia ICH	Decompression and volume reduction	Internal capsule and perforator injury	Benefit remains uncertain
Putaminal ICH	Relief of mass effect and possible motor-pathway decompression	Direct corticospinal-tract injury	Selective use; requires tract-aware trajectory
Thalamic ICH	Hydrocephalus relief if ventricular rupture present	Critical thalamic and brainstem networks	Parenchymal evacuation not routinely supported

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Caudate ICH with IVH	Ventricular decompression	Deep venous and ventricular injury	EVD and IVH-directed strategy often dominant
Cerebellar ICH	Brainstem decompression and hydrocephalus control	Posterior-fossa deterioration if delayed	Urgent surgery frequently indicated
Primary IVH	Restoration of CSF pathways	Ventriculitis and catheter hemorrhage	EVD; selected intraventricular thrombolysis
Brainstem ICH	Theoretical decompression	Catastrophic tract and cranial-nerve injury	Investigational and highly selected

Hematoma Volume and Mass Effect. Hematoma volume influences both prognosis and potential treatment effect. Very small hemorrhages may not justify procedural risk. Extremely large hemorrhages may represent extensive irreversible injury, severe mass effect, and limited neurological recoverability. The ABC/2 method remains useful for rapid bedside estimation but becomes less accurate in irregular, multilobulated, or crescent-shaped hematomas. Automated segmentation provides more precise volume and can separately quantify intraparenchymal blood, intraventricular clot, perihematomal edema, and postoperative residual. ENRICH enrolled hemorrhages of 30–80 mL, whereas MIND included 20–80 mL. MISTIE III primarily evaluated moderate-to-large supratentorial hemorrhage. These ranges define evidence-supported trial populations rather than universal treatment thresholds [15, 17, 27]. Mass effect should be evaluated independently from volume. A 35-mL temporal hemorrhage causing uncal compression may be more urgent than a 45-mL frontal hematoma with preserved cisterns. Midline shift, ventricular effacement, basal-cistern status, herniation signs, and neurological deterioration influence urgency. The relation between volume and functional anatomy is also important. A smaller hematoma that destroys the posterior limb of the internal capsule may have a worse motor prognosis than a larger anterior frontal hematoma that displaces rather than transects major pathways.

Hematoma Expansion and Hemostatic Stability. Approximately one-quarter of patients demonstrate clinically meaningful hematoma expansion after presentation, with the highest risk during the early hours. Expansion is associated with worse outcome and increases the risk of postoperative rebleeding. Noncontrast CT markers include blend sign, black-hole sign, island sign, fluid level, hypodensity within the clot, irregular shape, and heterogeneous density. CTA spot sign represents active contrast extravasation and identifies increased expansion risk, but its absence does not prove stability [7, 14, 19, 16–18]. Anticoagulant-associated hemorrhage requires immediate reversal. Warfarin should be reversed with four-factor prothrombin-complex concentrate and intravenous vitamin K. Dabigatran can be reversed with idarucizumab, while factor-Xa inhibitors may be treated with andexanet alfa or prothrombin-complex concentrate according to availability, timing, and institutional protocol. Surgery should not be delayed unnecessarily after adequate reversal, but operating during uncontrolled coagulopathy substantially increases rebleeding risk. Platelet count, fibrinogen, anticoagulant exposure, renal function, and repeat imaging should be integrated. MISTIE required demonstration of hematoma stability before catheter treatment and used

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delayed thrombolysis to reduce rebleeding risk. This safety strategy also delayed completion of clot removal. ENRICH pursued earlier evacuation with direct visualization and hemostatic capability. The ideal timing therefore depends on the procedure. Catheter thrombolysis requires confidence that active bleeding has stopped. Direct endoscopic or trans-sulcal surgery may permit earlier treatment because the bleeding point can potentially be identified and coagulated.

Operative Timing. Time should be considered biologically rather than administratively. The relevant intervals include onset-to-first CT, onset-to-reversal, onset-to-stability scan, onset-to-randomization, onset-to-incision, onset-to-effective decompression, and time to final residual volume. A patient may enter the operating room at 12 hours but not achieve adequate evacuation until 16 hours. A catheter may be inserted at 24 hours but require several days of alteplase irrigation before reaching the final volume. ENRICH required surgery within 24 hours after the patient was last known well. The positive lobar result supports early intervention, although the trial does not establish that every patient should undergo ultra-early surgery. MIND permitted surgery within 72 hours and did not demonstrate 180-day functional benefit. The trial was stopped early, and most patients had deep hemorrhage, but the result raises the possibility that delayed evacuation provides less biological benefit even when the percentage of clot removal is substantial.

Ultra-early surgery within the first few hours may remove the clot before secondary injury develops but occurs during a period of active bleeding and unstable hematoma geometry. Trials should distinguish ultra-early, early, and delayed procedures rather than reporting a single broad window.

Access-Corridor Planning. A minimally invasive incision does not guarantee a minimally disruptive intracerebral route. Tissue injury is determined by the cortex or sulcus entered, the length and diameter of the trajectory, white-matter displacement, retractor pressure, instrument motion, and proximity to functional pathways. The trajectory should follow the hematoma long axis when this permits efficient evacuation with minimal manipulation. Entering near one end of the clot allows progressive internal debulking rather than pushing instruments through intact brain toward its center. A trans-sulcal approach separates cortical gyri rather than incising the crown of a gyrus. However, sulci contain veins and arterial branches, and not every sulcus provides a safe route. Preoperative CTA, venous anatomy, neuronavigation, and direct surface inspection remain necessary. Tubular retractors distribute radial pressure more evenly than fixed blade retractors and create a stable working corridor. The device should not be advanced forcefully through intact tissue. Serial dilation, alignment with white-matter fibers, and internal clot decompression reduce corridor stress. Diffusion-tensor tractography can identify the corticospinal tract, optic radiation, arcuate fasciculus, superior longitudinal fasciculus, and other major pathways. Acute hematoma and edema distort diffusion signals, so tractography should be treated as an estimate rather than a precise anatomical boundary. Emerging methods use machine learning to approximate corticospinal-tract location from standard CT when advanced MRI is unavailable. Such systems may improve future selection but require external validation before determining surgical eligibility.

Evacuation Techniques. The MISTIE technique uses stereotactic catheter placement along the long axis of the hematoma, initial aspiration, and repeated low-dose alteplase administration after stability is confirmed. The procedure minimizes the operative corridor and can be performed through a burr hole. Its disadvantages include delayed clot clearance, dependence on accurate catheter

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position, limited ability to control active bleeding, catheter obstruction, and the need for repeated CT and intensive protocol management. MISTIE III achieved a mean end-of-treatment volume of approximately 16 mL compared with 47 mL in the medical group. Fifty-eight percent of surgical patients reached the prespecified residual target of 15 mL or less. The primary functional endpoint was neutral, but mortality was lower and performance analyses supported the residual-volume target. The lesson is not that thrombolysis failed completely. It is that a biologically effective procedure must reliably reach its surgical target across centers.

Endoscopic Evacuation. Neuroendoscopy provides direct visualization of the cavity, active aspiration, irrigation, clot fragmentation, and focal coagulation. It can achieve substantial reduction during one operation and avoids prolonged thrombolytic irrigation. Visibility can be impaired by active bleeding, dark clot, narrow working space, lens contamination, and loss of orientation. Excessive irrigation pressure may increase intracranial pressure or force fluid into surrounding tissue. A rigid endoscope provides stable visualization but limited angulation. Flexible endoscopy reaches irregular extensions but provides smaller working channels and reduced hemostatic control. Bimanual systems and transparent sheaths can improve instrument coordination. The ICES randomized study demonstrated that image-guided endoscopic surgery could reduce hemorrhage volume by approximately two-thirds within about 29 hours while meeting predefined safety standards [16, 23, 30].

Mechanically Assisted Aspiration. The Artemis and Apollo systems combine aspiration with controlled mechanical clot fragmentation. These devices can remove organized blood rapidly through a small channel. The MIND trial demonstrated a median hemorrhage-volume reduction of 80.7%, confirming strong technical efficacy. Despite this, the primary 180-day ordinal outcome remained neutral. This reinforces that percentage removal alone does not guarantee neurological recovery when deep functional structures are already injured or the intervention is delayed [21, 24, 31]. Mechanical devices should be operated within the clot rather than against the cavity wall. Aggressive engagement of adherent clot can injure vessels. Aspiration strength, device tip position, and tissue motion require continuous visualization.

Trans-Sulcal Para-Fascicular Evacuation. The ENRICH strategy uses a tubular trans-sulcal corridor and an automated side-cutting aspiration device. Internal debulking allows the hematoma cavity to collapse while reducing fixed retraction. This approach combines early clot removal with direct visualization and hemostasis. It is particularly suited to lobar hematomas accessible through a short corridor. The technique should not be generalized automatically to every deep hemorrhage. The neutral anterior basal-ganglia subgroup demonstrates that limiting incision size cannot eliminate the biological consequences of deep access.

Robotic Stereotactic Evacuation. Robotic systems improve trajectory alignment and reproducibility. They can support catheter placement, aspiration, endoscopy, or future flexible concentric-tube devices. Robotics may reduce targeting error but cannot determine whether the planned trajectory crosses critical pathways. Registration accuracy, brain shift, instrument deflection, and hemorrhage evolution remain important. A 2025 comparative study reported better evacuation performance with robot-assisted stereotaxy than frame-based puncture, but nonrandomized technical improvements should not be interpreted as definitive functional efficacy [23, 30, 32].

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Table 2. **Comparative Features of Minimally Invasive Techniques**

Technique	Speed of clot reduction	Direct hemostasis	Corridor size	Main strength	Main limitation
Catheter aspiration plus alteplase	Gradual over days	Limited	Very small	Minimal tissue access	Delayed completion and catheter dependence
Stereotactic aspiration	Immediate but sometimes incomplete	Limited	Small	Rapid, accessible technique	Residual organized clot
Rigid neuroendoscopy	Immediate	Good	Small to moderate	Direct visualization and irrigation	Restricted angulation
Flexible endoscopy	Immediate	Moderate	Small	Access to irregular extensions	Reduced instrument strength
Mechanical aspiration	Rapid	Moderate with visualization	Small	High percentage volume reduction	Vessel injury if used near cavity wall
Tubular trans-sulcal surgery	Rapid	Good	Controlled circumferential corridor	Early evacuation with tissue displacement	Requires anatomical and technical expertise
Robotic catheter or endoscopic guidance	Depends on attached device	Device-dependent	Small	Reproducible trajectory	Registration and planning errors

Residual Hematoma Volume. Residual volume has emerged as a more informative operative endpoint than percentage reduction alone. Removing 80% of a 70-mL hematoma leaves 14 mL, whereas removing 80% of a 30-mL hematoma leaves 6 mL. Both percentages are identical, but the remaining mass and toxic burden differ. MISTIE III prospectively defined 15 mL or less as the surgical goal. As-treated analyses supported a relationship between achieving this target and improved functional outcome [1, 10, 13, 32]. The threshold should not be interpreted as an absolute rule for every location. A 16-mL residual in noneloquent frontal white matter may be tolerated, while a 10-mL residual compressing the brainstem or obstructing the third ventricle may remain clinically dangerous. Residual volume should be measured through postoperative CT segmentation rather than subjective visual estimation. Timing of the scan matters because early rebleeding, cavity collapse, irrigation fluid, and contrast can affect interpretation. Future trials should report median residual

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volume, proportion reaching predefined thresholds, percentage reduction, time to target, and anatomical distribution of the residual clot.

Intraoperative Hemostasis. Rebleeding can eliminate the benefit of evacuation. The cavity should be decompressed progressively to avoid sudden loss of tamponade before the bleeding source is visible. Blood-pressure control should be coordinated with anesthesia. Excessive hypertension increases bleeding, while hypotension threatens cerebral and systemic perfusion. The target should consider preoperative pressure, chronic hypertension, intracranial pressure, and perioperative neurological status. Endoscopic irrigation can identify a bleeding point, but high irrigation pressure may temporarily suppress bleeding. The cavity should be inspected under low-pressure conditions before closure. Focal bipolar coagulation, low-energy radiofrequency, hemostatic matrix, oxidized cellulose, gelatin sponge, and gentle tamponade can be used. Blind packing should be avoided because it can compress surrounding tissue and conceal ongoing hemorrhage. A postoperative CT should generally be obtained promptly after surgery and repeated when neurological status deteriorates. New hematoma expansion, ventricular blood, hydrocephalus, ischemia, or tract injury requires urgent assessment.

Intraventricular Hemorrhage. IVH may arise from thalamic, caudate, putaminal, or lobar hemorrhage and is an independent marker of poor prognosis. Blood obstructs the foramina of Monro, cerebral aqueduct, and fourth-ventricle outlets, producing acute hydrocephalus. External ventricular drainage relieves hydrocephalus and permits ICP monitoring. Catheter position should maximize CSF drainage while minimizing traversed brain and avoiding the largest clot burden when possible. CLEAR III randomized patients with obstructive IVH and a routinely placed EVD to intraventricular alteplase or saline. Alteplase did not significantly improve the proportion with mRS 0–3, but it reduced mortality and accelerated ventricular opening. The survival effect included a greater proportion of severely disabled survivors [3, 10, 18, 27]. These findings emphasize the importance of outcome framing. A mortality reduction may be meaningful, but families should understand the possible distribution of surviving disability. Intraventricular thrombolysis should not be used in the presence of unstable parenchymal bleeding, untreated vascular lesion, or uncontrolled coagulopathy. Serial CT is required during treatment. Endoscopic ventricular clot evacuation may provide faster clearance and direct restoration of CSF pathways but requires ventricular entry and carries risks of fornix injury, ependymal injury, bleeding, and infection. Comparative randomized evidence remains limited.

Perioperative Medical Management. Surgery does not replace evidence-based medical treatment. Rapid blood-pressure control, anticoagulant reversal, airway protection, glucose and temperature management, prevention of aspiration, and organized stroke-unit or neurocritical care remain essential [4, 14, 19, 25]. Current guidelines generally support smooth reduction of elevated systolic pressure while avoiding abrupt hypotension. The exact target should be individualized in severe ICH, impending herniation, and the perioperative setting. Prophylactic antiseizure medication is not routinely indicated for every ICH patient. Clinical or electrographic seizures should be treated. Continuous EEG is appropriate in unexplained impaired consciousness, fluctuating examination, or suspected nonconvulsive seizures. Mechanical venous-thrombosis prophylaxis should begin early. Pharmacological prophylaxis is introduced after hemorrhage stability is established according to

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imaging and procedural factors. Swallowing evaluation, aspiration prevention, nutrition, early mobilization, and rehabilitation planning should not be delayed because the patient underwent surgery. Functional recovery depends on the complete care pathway.

Postoperative Intracranial Pressure and Edema. Large ICH can produce refractory intracranial hypertension before or after evacuation. An EVD is useful when IVH and hydrocephalus are present. Intraparenchymal ICP monitoring may be considered when the examination is unreliable and severe mass effect persists. A low postoperative ICP does not guarantee favorable outcome. Surgical injury, tract damage, ischemia, and established network destruction may remain despite decompression. Perihematomal edema commonly increases during the first several days. Routine corticosteroids are harmful in spontaneous ICH and should not be used for edema control. Hyperosmolar therapy may be used for acute intracranial hypertension or herniation physiology but should not substitute for evaluation of rebleeding, hydrocephalus, or surgical mass effect.

Functional Network Preservation. The modified Rankin Scale summarizes global disability but does not identify the mechanism of recovery failure. Motor, language, visual, cognitive, executive, arousal, and swallowing networks may be affected differently. A patient with a technically excellent evacuation can remain severely disabled if the internal capsule or dominant-language network was destroyed before surgery. Conversely, removal of a lobar hematoma that mainly displaces rather than transects pathways may enable substantial recovery. Preoperative imaging should therefore evaluate recoverability, not only volume. CT can estimate whether critical structures are displaced, compressed, or incorporated into the hemorrhage. MRI and tractography provide additional information when time and stability permit. Future selection algorithms may combine CT anatomy, clinical deficits, corticospinal-tract integrity, hematoma expansion risk, premorbid function, and predicted surgical corridor injury. Withdrawal-of-life-sustaining treatment is a major confounder in ICH outcomes. Early pessimistic prognostication can create a self-fulfilling prophecy. Severity scores should support communication and research stratification but should not be used as the sole basis for limiting treatment.

Table 3. **Trial Interpretation in the Modern Surgical Era**

Trial	Technique and population	Main result	Principal lesson
STICH	Early open craniotomy for supratentorial ICH	Neutral functional result	Broad open surgery does not benefit all ICH
STICH II	Superficial lobar ICH without IVH	Neutral primary result; possible survival signal	Superficial location may matter
MISTIE III	Catheter aspiration plus alteplase	Neutral primary functional endpoint; safe volume reduction	Procedural performance and residual ≤15 mL are important
ICES	CT-guided endoscopic evacuation	Feasible and substantial early reduction	Direct MIS can remove clot safely
ENRICH	Early trans-sulcal evacuation within 24 h	Improved 180-day utility-weighted outcome	Benefit strongest in lobar ICH
MIND	Mechanical MIS within	Neutral 180-day disability	Technical clot reduction

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	72 h	and mortality	alone is insufficient
CLEAR III	EVD plus intraventricular alteplase	Mortality reduction without functional-endpoint improvement	Ventricular clearance changes survival more than independence

Complications. The major surgical complications are rebleeding, tract hemorrhage, ischemic injury, infection, seizures, venous infarction, hydrocephalus, residual mass effect, and neurological deterioration. Rebleeding may result from incomplete reversal, uncontrolled hypertension, traumatic device movement, premature disruption of clot tamponade, or failure to identify the bleeding vessel. Tract injury can involve cortex, white matter, deep nuclei, corticospinal pathways, optic radiation, or venous structures. A small skin incision does not prevent major intracerebral injury. Infection risk increases with prolonged catheter irrigation, repeated EVD manipulation, CSF leakage, and extended intensive care. Strict sterile protocols and limited device access are necessary. Postoperative ischemia may result from coagulation of a perforator, excessive retraction, venous compromise, hypotension, or local compression by hemostatic material.

Table 4. **Complications and Preventive Strategy**

Complication	Main mechanism	Prevention	Required response
Postoperative rebleeding	Active vessel, coagulopathy, hypertension	Reversal, controlled decompression, low-pressure hemostatic inspection	Urgent CT and reoperation when indicated
Corridor hemorrhage	Cortical or white-matter vessel injury	Sulcal planning, serial dilation, navigation	Hemostasis and assessment of tract damage
Internal-capsule injury	Unsafe deep trajectory or device motion	Tract-aware approach and instrument control	Neurological documentation and rehabilitation
Residual mass effect	Incomplete evacuation or inaccessible clot	Quantitative target and intraoperative imaging	Revision according to clinical deterioration
Hydrocephalus	IVH and CSF obstruction	Ventricular assessment and EVD when indicated	Drainage and serial imaging
Ventriculitis	Prolonged catheter access	Sterile protocol and limited manipulation	Culture-directed treatment and catheter management
Seizure	Cortical blood, surgical irritation, metabolic stress	EEG when clinically indicated	Antiseizure therapy for documented events
Venous infarction	Injury to cortical or deep vein	Preoperative vascular planning	Supportive care and decompression if required
Aspiration pneumonia	Impaired consciousness and dysphagia	Airway and swallowing protocol	Respiratory treatment and rehabilitation

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The EVAC-ICH Framework. The proposed EVAC-ICH framework consists of seven linked domains. Eligibility and recoverability evaluate premorbid independence, age, neurological severity, medical stability, treatment preferences, clinical trajectory, and whether major functional networks are potentially preserved. Volume and vascular anatomy define hematoma size, location, shape, surface distance, intraventricular extension, hydrocephalus, spot sign, underlying vascular lesion, and mass effect. Active bleeding and stability incorporate onset time, serial CT, anticoagulant reversal, coagulation parameters, blood-pressure control, and evidence of expansion.

Corridor preservation selects a sulcal, trans-cortical, stereotactic, ventricular, or posterior-fossa route that minimizes injury to cortex, white-matter tracts, perforators, and veins. Intraoperative hemostasis includes progressive internal decompression, direct visualization where possible, controlled irrigation, focal coagulation, and inspection after tamponade is removed. Clot-reduction target defines a quantitative residual-volume goal, generally informed by the 15-mL MISTIE threshold but adjusted for location, mass effect, ventricular obstruction, and safety. Hemorrhage-specific postoperative care includes repeat CT, blood-pressure control, ICP and CSF management, seizure evaluation, VTE prevention, dysphagia care, early rehabilitation, and avoidance of premature prognostic limitation.

Table 5. **Scientific Originality of the EVAC-ICH Model**

Existing limitation	**Conventional interpretation**	**EVAC-ICH principle**	**Expected contribution**
All MIS procedures grouped together	Small access assumed to represent one intervention	Timing, device, corridor, hemostasis, and speed analyzed separately	Clarifies why trials differ
Hematoma volume used without location	Similar volumes considered biologically equivalent	Lobar, deep, thalamic, ventricular, and cerebellar phenotypes separated	Improves anatomical selection
Percentage evacuation used as primary performance metric	High percentage interpreted as success	Absolute residual volume and time to target prioritized	Supports clinically meaningful decompression
Surgery selected from severity score alone	Poor prognosis may cause exclusion	Functional-network recoverability incorporated	Reduces therapeutic nihilism
Shortest route considered safest	Geometric distance prioritized	White-matter and vascular injury integrated	Reduces corridor-related disability
Stability required uniformly before surgery	Delay considered universally protective	Stability requirements matched to hemostatic capability	Balances rebleeding against biological delay
Mortality and independence treated as interchangeable	Survival interpreted as functional success	Ordinal disability and patient goals reported separately	Improves outcome communication
Device accuracy	Operation viewed as	Neurocritical care and	Supports complete

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emphasized over care pathway	isolated treatment	rehabilitation included	systems-based benefit
Neutral trials interpreted as proof of no surgical effect	All patient subgroups considered equivalent	Location, timing, and performance explain heterogeneity	Enables targeted future trials

Discussion. The evidence available after ENRICH requires a change in how surgery for intracerebral hemorrhage is discussed. The question is no longer whether open craniotomy should be used routinely for all supratentorial hemorrhages. The question is whether early, quantitatively effective, anatomically selected, minimally disruptive evacuation improves the patient's probable functional trajectory. ENRICH provides the strongest current randomized evidence that this objective can be achieved. The trial demonstrated a favorable 180-day utility-weighted outcome and lower early mortality, but its adaptive analysis showed that the benefit was driven by lobar hemorrhage. This anatomical specificity is not a minor subgroup observation; it is central to interpretation. The lobar brain provides a shorter route, but access alone does not explain the result. Lobar hematomas may displace functional tissue more often than they destroy compact projection pathways. Reduction of mass effect can therefore permit meaningful recovery in patients whose networks remain viable. Deep ganglionic hemorrhage differs. The initial bleed may transect the internal capsule or thalamocortical fibers before treatment. Even complete removal cannot reconstruct destroyed axons. Surgical access can introduce additional injury to the same networks.

This interpretation is consistent with MIND, in which almost 70% of patients had deep hemorrhage. The procedure achieved a median 80.7% reduction but did not improve the primary 180-day ordinal outcome. Enrollment stopped at 236 patients, limiting power, but the neutral result warns against assuming that efficient clot removal is sufficient in all anatomical phenotypes. The operative window may also explain part of the difference. ENRICH required intervention within 24 hours, whereas MIND allowed surgery within 72 hours. Secondary inflammation and edema evolve continuously. An operation that is technically successful at 50 hours may provide less biological rescue than one performed at 15 hours.

This does not prove that all surgery should occur immediately. The risk of expansion and rebleeding is greatest early after onset. The appropriate time is the earliest point at which hemostatic control, reversal, imaging, and surgical resources permit safe and effective evacuation.

The type of operation determines how much stability is needed. A catheter-lysis procedure cannot directly coagulate a bleeding vessel and therefore requires documented stability. A direct endoscopic or trans-sulcal approach can potentially identify active bleeding but exposes the patient to operative tissue injury. MISTIE III remains highly relevant because it established a performance target. The neutral intention-to-treat result concealed major variability in achieved evacuation. Only 58% of treated patients reached 15 mL or less. If benefit requires reaching the target, inconsistent performance dilutes trial efficacy. The threshold of 15 mL should be treated as an evidence-informed benchmark rather than a universal biological law. The appropriate residual depends on the original volume, location, ventricular obstruction, intracranial pressure, and risk of further manipulation. A residual fragment firmly adherent to the posterior putaminal wall may be safer than aggressive removal near the internal capsule. A similar volume obstructing the aqueduct or compressing the

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brainstem may remain unacceptable. Percentage reduction and absolute residual should therefore be reported together. Operative studies should also report time to target, because delayed completion reduces the opportunity to prevent secondary injury. CLEAR III provides a cautionary example regarding outcomes. Ventricular alteplase reduced mortality but did not increase the proportion of patients reaching the prespecified functional endpoint. More patients survived with severe disability [5, 16, 20, 31]. Neither mortality nor disability should be dismissed. Some patients value survival despite dependency, while others have expressed different preferences. Trials should report the full ordinal mRS distribution and quality of life rather than only dichotomized independence.

The utility-weighted mRS used in ENRICH is one attempt to incorporate the patient-perceived value of different disability states. Its interpretation may be less intuitive than standard mRS categories, but it captures shifts that binary endpoints can miss. Another lesson is that surgical technology cannot be evaluated separately from medical management. Blood-pressure control, anticoagulant reversal, stroke-unit care, neurocritical monitoring, dysphagia prevention, and rehabilitation influence outcomes in both trial arms. A center adopting MIS without a coordinated ICH pathway may not reproduce trial results. The workflow must include rapid transfer, image segmentation, vascular imaging when indicated, reversal protocols, neurosurgical availability, trained operating-room staff, quantitative postoperative imaging, and rehabilitation. Surgical training is especially important. A device manufacturer can teach mechanical operation, but expertise in trajectory planning, white-matter anatomy, endoscopic hemostasis, and postoperative neurocritical care must be developed independently. Volume targets should be audited. Every institution should measure preoperative volume, immediate residual, percentage removal, rebleeding, tract injury, and functional outcome. Without performance monitoring, the procedure may be labelled successful because an operation was completed rather than because effective evacuation was achieved. The future of selection will likely incorporate functional anatomy. The integrity of the corticospinal tract is strongly associated with motor recovery. Advanced MRI is not always feasible acutely, but CT-based algorithms may estimate tract involvement. Such tools should distinguish destruction from displacement. A tract passing through the hematoma core may have limited recovery potential, whereas a tract displaced around the clot may recover after decompression.

Artificial intelligence can automate volume segmentation, detect expansion signs, estimate trajectory risk, and predict postoperative residual. It should support rather than replace multidisciplinary judgment. Endoscopic video analysis may eventually identify active bleeding, cavity boundaries, instrument–tissue interaction, and unsafe proximity to brain. Current evidence remains developmental. Robotic and flexible instruments may improve evacuation of irregular extensions through one corridor. The risk is that increased reach encourages aggressive pursuit of clot into unsafe regions. Technology should expand controlled access, not eliminate surgical restraint. Future trials should be phenotype-specific. A trial of early lobar evacuation should not be diluted by deep thalamic hemorrhage. Deep putaminal trials should stratify corticospinal-tract integrity and corridor length. Timing should be narrow and explicitly reported. “Within 72 hours” encompasses biologically different patients. Trials should analyze onset-to-effective-decompression as a continuous variable. Procedural quality should be incorporated into the primary analysis. Centers unable to achieve the residual target should undergo retraining before continued enrollment. Control

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groups should receive contemporary guideline-based management, including rapid pressure control and reversal. Early limitations of care should be standardized to reduce self-fulfilling prognostic bias. Outcomes should include cognition, aphasia, swallowing, return to home, caregiver burden, and quality of life. A global mRS score does not capture all clinically meaningful recovery. The 2025 ESO–EANS guideline reflects the evolving evidence but appropriately remains cautious because results differ by technique, location, and population. Current data support structured consideration of surgery rather than universal intervention.

The EVAC-ICH model is designed to prevent two opposite errors. The first is nihilism: rejecting surgery because older craniotomy trials were neutral. The second is technological overgeneralization: treating every moderate-to-large hemorrhage because ENRICH was positive.

The model emphasizes that a positive surgical candidate requires more than a large clot. The patient should have a potentially recoverable neurological substrate, a surgically accessible target, controlled hemostasis, a tissue-preserving corridor, a realistic residual-volume goal, and access to high-quality postoperative care. The framework is conceptual and has not been prospectively validated. It should guide structured discussion rather than replace trial criteria or clinical guidelines.

Conclusion. Spontaneous intracerebral hemorrhage is a heterogeneous surgical disease. Hematoma size alone does not determine eligibility, and minimally invasive surgery is not a single standardized intervention. Conventional craniotomy failed to improve outcomes consistently because the benefit of clot removal was frequently offset by access injury, broad patient selection, or inadequate biological timing. MISTIE III demonstrated that catheter aspiration with thrombolysis can reduce clot safely and identified residual volume of 15 mL or less as an important performance target. The primary functional endpoint remained neutral, partly reflecting variable achievement of adequate evacuation. ENRICH established that early minimally invasive evacuation within 24 hours can improve 180-day functional outcome. The benefit was concentrated in lobar hemorrhage and was not demonstrated in the anterior basal-ganglia subgroup. MIND achieved substantial clot reduction using mechanically assisted aspiration but did not improve 180-day disability or 30-day mortality. Its predominantly deep-hemorrhage population and broader 72-hour window highlight the importance of location and biological timing. CLEAR III showed that accelerated intraventricular clot removal can reduce mortality without necessarily increasing functional independence. The central therapeutic principle is not maximum clot removal at any cost. It is early and sufficient reduction of mass and toxic blood burden through the least disruptive corridor, with direct attention to hemostasis and functional-network preservation. The proposed EVAC-ICH framework integrates Eligibility and recoverability, Volume and vascular anatomy, Active bleeding and stability, Corridor preservation, Intraoperative hemostasis, Clot-reduction targets, and Hemorrhage-specific postoperative care. Future research should use phenotype-specific enrollment, narrow operative windows, quantitative residual-volume targets, tract-aware planning, standardized surgical training, and complete ordinal outcomes. The post-ENRICH era should therefore be defined neither by routine surgery nor by continued therapeutic nihilism. It should be defined by anatomically selective, performance-controlled and biologically timed hematoma evacuation.

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MULTIMODAL ARTIFICIAL INTELLIGENCE FOR PRECISION GLIOMA SURGERY: INTEGRATING RADIOMICS, INTRAOPERATIVE ULTRASOUND, BRAIN-SHIFT CORRECTION, AND EXPLAINABLE DECISION SUPPORT

Abstract

Background. In diffuse adult-type gliomas, including glioblastoma and IDH-mutant astrocytoma, neurosurgical decisions remain difficult because preoperative neuronavigation loses spatial validity after dural opening, while conventional image interpretation cannot continuously integrate molecular phenotype, functional anatomy, residual-tumor probability, and evolving brain deformation.

Materials and methods. A structured narrative review is proposed using clinical trials, prospective cohorts, diagnostic-accuracy studies, systematic reviews, and relevant technical investigations. Evidence is organized by biological plausibility, technical performance, patient selection, safety, clinical effectiveness, reproducibility, and implementation. A prospective comparative study is specified for adults undergoing first or repeat resection of supratentorial diffuse glioma, with standard neuronavigation with conventional visual interpretation of preoperative MRI and intraoperative ultrasound as the reference strategy.

Results. The synthesis addresses five domains: preoperative molecular prediction, intraoperative lesion localization, dynamic compensation for brain shift, transparent risk estimation, workflow integration and human factors. The proposed primary endpoint is extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days; secondary endpoints include brain-shift registration error, residual tumor volume, progression-free survival, operative time, calibration error, subgroup fairness, and surgeon cognitive workload. Originality derives from linking technical accuracy to patient-centered outcomes, explicitly modeling uncertainty, and requiring external validation.

Conclusion. Standardized endpoints support reliable clinical comparison. Independent adjudication strengthens causal interpretation. Longitudinal follow-up clarifies therapeutic durability. Equity analysis supports responsible implementation. Transparent reporting improves scientific reproducibility. Rigorous independent prospective multicenter transparent external validation remains essential.

Keywords: artificial intelligence; glioma surgery; radiomics; intraoperative ultrasound; brain shift; explainable AI; precision neurosurgery.

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МУЛЬТИМОДАЛЬНЫЙ ИСКУССТВЕННЫЙ ИНТЕЛЛЕКТ В ПРЕЦИЗИОННОЙ ХИРУРГИИ ГЛИОМ: ИНТЕГРАЦИЯ РАДИОМИКИ, ИНТРАОПЕРАЦИОННОГО УЛЬТРАЗВУКА, КОРРЕКЦИИ СМЕЩЕНИЯ МОЗГА И ОБЪЯСНИМОЙ ПОДДЕРЖКИ РЕШЕНИЙ

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Аннотация

Актуальность. При диффузных глиомах взрослого типа, включая глиобластому и астроцитому с мутацией IDH, принятие нейрохирургических решений остается сложной задачей. Это связано с тем, что предоперационная нейронавигация постепенно утрачивает пространственную точность после вскрытия твердой мозговой оболочки, тогда как традиционная интерпретация нейровизуализационных данных не позволяет непрерывно интегрировать молекулярный фенотип опухоли, функционально значимую анатомию головного мозга, вероятность наличия остаточной опухолевой ткани и динамически изменяющуюся деформацию мозга.

Материалы и методы. Предложен структурированный нарративный обзор, включающий клинические исследования, проспективные когортные наблюдения, исследования диагностической точности, систематические обзоры и релевантные технические работы. Доказательные данные систематизированы по биологической обоснованности, технической эффективности, критериям отбора пациентов, безопасности, клинической результативности, воспроизводимости и возможности внедрения в клиническую практику. Разработан дизайн проспективного сравнительного исследования с участием взрослых пациентов, которым выполняется первичная или повторная резекция супратенториальной диффузной глиомы. В качестве референтной стратегии определена стандартная нейронавигация в сочетании с традиционной визуальной интерпретацией предоперационной магнитно-резонансной томографии и интраоперационной ультрасонографии.

Результаты. Синтез доказательств охватывает пять основных направлений: предоперационное прогнозирование молекулярного профиля, интраоперационную локализацию опухоли, динамическую компенсацию смещения головного мозга, прозрачную оценку риска, а также интеграцию технологии в хирургический рабочий процесс с учетом человеческого фактора. Предлагаемой первичной конечной точкой является степень резекции, нормированная по молекулярно определенной опухолевой нагрузке, в сочетании с частотой новых стойких неврологических дефицитов через 90 дней после операции. Вторичные конечные точки включают ошибку регистрации смещения головного мозга, объем остаточной опухоли, выживаемость без прогрессирования, продолжительность операции, ошибку калибровки прогностической модели, алгоритмическую справедливость в различных подгруппах пациентов и когнитивную нагрузку хирурга. Научная оригинальность заключается в установлении взаимосвязи между технической точностью и клиническими исходами, значимыми для пациента, явном моделировании неопределенности и обязательном проведении независимой внешней валидации.

Заключение. Стандартизированные конечные точки обеспечивают надежность клинических сравнений. Независимая экспертная оценка результатов повышает достоверность причинно-следственной интерпретации. Длительное динамическое наблюдение позволяет определить устойчивость терапевтического эффекта. Анализ равноправия и справедливости способствует ответственному внедрению технологии в клиническую практику, а прозрачное представление результатов повышает научную воспроизводимость. Необходимым условием остается строгая, независимая, проспективная, многоцентровая и прозрачная внешняя валидация.

Ключевые слова: искусственный интеллект; хирургия глиом; радиомика; интраоперационный ультразвук; смещение мозга; объяснимый ИИ; прецизионная нейрохирургия.

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GLIOMALARNI ANIQ JARROHLIK DAVOLASHDA MULTIMODAL SUN'IY INTELLEKT: RADIOMIKA, INTRAOPERATSION ULTRATOVUSH, MIYA SILJISHINI KORREKSIYA QILISH VA IZOHLANADIGAN QARORLARNI QO'LLAB-QUVVATLASH INTEGRATSIYASI

Annotatsiya

Dolzarblik. Kattalar tipidagi diffuz gliomalarda, jumladan glioblastoma va IDH-mutatsiyali astrositomada neyroxirurgik qaror qabul qilish murakkabligicha qolmoqda. Buning asosiy sababi shundaki, qattiq miya pardasi ochilgandan keyin operatsiyadan oldingi neyronavigatsiyaning fazoviy aniqligi bosqichma-bosqich pasayadi. Shu bilan birga, neyrovizualizatsiya ma'lumotlarini an'anaviy talqin qilish o'smaning molekulyar fenotipi, funksional jihatdan muhim miya anatomiyasi, qoldiq o'sma ehtimoli va operatsiya davomida dinamik ravishda o'zgarib boruvchi miya deformatsiyasini uzluksiz integratsiya qilish imkonini bermaydi.

Material va usullar. Klinik tadqiqotlar, prospektiv kohort kuzatuvlari, diagnostik aniqlikni baholovchi tadqiqotlar, tizimli sharhlar va tegishli texnik izlanishlarni qamrab oluvchi strukturaviy narrativ sharh taklif etildi. Dalillar biologik asoslanganlik, texnik samaradorlik, bemorlarni tanlash mezonlari, xavfsizlik, klinik natijadorlik, takrorlanuvchanlik va klinik amaliyotga joriy etish imkoniyati bo'yicha tizimlashtirildi. Supratentorial diffuz glioma bo'yicha birlamchi yoki takroriy rezeksiya o'tkaziladigan katta yoshli bemorlar uchun prospektiv qiyosiy tadqiqot dizayni ishlab chiqildi. Operatsiyadan oldingi magnit-rezonans tomografiya tasvirlarini an'anaviy vizual tahlil qilish va intraoperatsion ultratovush tekshiruvi bilan birlashtirilgan standart neyronavigatsiya referent strategiya sifatida belgilandi.

Natijalar. Dalillar sintezi beshta asosiy yo'nalishni qamrab oladi: operatsiyadan oldingi molekulyar prognozlash, intraoperatsion o'sma lokalizatsiyasi, miya siljishini dinamik kompensatsiya qilish, xavfni shaffof baholash hamda inson omilini hisobga olgan holda texnologiyani operatsion ish jarayoniga integratsiya qilish. Taklif etilgan birlamchi yakuniy ko'rsatkich molekulyar mezonlar asosida aniqlangan o'sma yuklamasiga nisbatan normallashtirilgan rezeksiya darajasi va operatsiyadan 90 kun o'tgach kuzatiladigan yangi turg'un nevrologik nuqsonlar chastotasidan iborat. Ikkilamchi yakuniy ko'rsatkichlarga miya siljishini ro'yxatga olish xatosi, qoldiq o'sma hajmi, progressiyasiz yashash davomiyligi, operatsiya davomiyligi, prognostik model kalibratsiyasi xatosi, bemorlarning turli kichik guruhlarida algoritmik adolatlilik va jarrohning kognitiv yuklamasi kiradi. Tadqiqotning ilmiy yangiligi texnik aniqlikni bemor uchun klinik ahamiyatga ega natijalar bilan bog'lash, prognostik noaniqlikni aniq modellashtirish va majburiy mustaqil tashqi validatsiyani talab qilish bilan belgilanadi.

Xulosa. Standartlashtirilgan yakuniy ko'rsatkichlar klinik natijalarni ishonchli taqqoslash imkonini beradi. Natijalarni mustaqil ekspert baholashi sabab-oqibat bog'liqligini talqin qilishning

ishonchliligini oshiradi. Uzoq muddatli kuzatuv terapevtik ta’sirning barqarorligini aniqlashga yordam beradi. Tenglik va adolatlilik tahlili texnologiyani klinik amaliyotga mas’uliyatli joriy etishni qo‘llab-quvvatlaydi, shaffof hisobot esa ilmiy natijalarning takrorlanuvchanligini yaxshilaydi. Qat’iy, mustaqil, prospektiv, ko‘p markazli va shaffof tashqi validatsiya o‘tkazilishi muhim talab bo‘lib qolmoqda.

Kalit so‘zlar: sun’iy intellekt; glioma jarrohligi; radiomika; intraoperatsion ultratovush; miya siljishi; izohlanadigan SI; aniq neyroxirurgiya.

Introduction. Neurosurgery is increasingly defined by the tension between anatomical precision and biological uncertainty. In diffuse adult-type gliomas, including glioblastoma and IDH-mutant astrocytoma, the surgeon must act on information that is incomplete, time dependent, and distributed across imaging, physiology, pathology, electrophysiology, and patient-specific functional reserve. The conventional operative paradigm is therefore being replaced by a data-rich model in which preoperative planning, intraoperative sensing, and postoperative surveillance are treated as a continuous decision process. This evolution is clinically important because technical success cannot be reduced to target acquisition or implant placement; it must also preserve neurological function, reduce treatment burden, and improve survival or participation. Contemporary evidence supports this shift, but also shows that many innovations remain supported by retrospective cohorts, selected populations, and heterogeneous endpoints [1, 2, 3]. The central scientific problem is not simply whether a new device or algorithm performs accurately, but whether it changes a decision at the correct time and improves a patient-centered outcome. The specific rationale for multimodal AI-guided glioma surgery arises from a persistent limitation: preoperative neuronavigation loses spatial validity after dural opening, while conventional image interpretation cannot continuously integrate molecular phenotype, functional anatomy, residual-tumor probability, and evolving brain deformation. This limitation creates several forms of uncertainty. Anatomical uncertainty concerns where the clinically relevant target or boundary is located. Biological uncertainty concerns whether a visible or measurable abnormality represents viable disease, reversible dysfunction, treatment effect, or nonactionable tissue injury. Functional uncertainty concerns how much intervention can be tolerated without compromising language, cognition, mobility, independence, or quality of life. Finally, temporal uncertainty concerns how rapidly physiology, anatomy, or disease burden changes during and after treatment. Existing methods usually address only one of these dimensions. The proposed innovation-a federated, explainable multimodal platform combining multiparametric MRI radiomics, radiogenomics, real-time intraoperative ultrasound segmentation, biomechanical brain-shift correction, and surgeon-facing uncertainty maps-is intended to combine them within a single clinically interpretable framework [3, 6, 10].

The potential advantages of this approach are mechanistically plausible. Relevant processes include radiomic phenotyping of infiltrative margins, cross-modal registration between MRI and ultrasound, real-time semantic segmentation, uncertainty-aware decision support, federated learning across institutions. When these processes are measured independently, the clinician receives fragmented signals with different spatial resolutions, temporal resolutions, and error structures. Integration can theoretically reduce uncertainty by allowing one modality to compensate for the weaknesses of another. However, multimodal integration can also amplify hidden bias, propagate registration error,

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and create false confidence if outputs are presented without uncertainty estimates. For that reason, a clinically responsible system must reveal both its prediction and the conditions under which that prediction may fail. This requirement is particularly important in neurosurgery, where small errors can produce irreversible disability and where intraoperative decisions are often made under severe time constraints [5, 11, 16]. Five evidence gaps justify a dedicated original investigation: single-center datasets, domain shift between scanners and ultrasound probes, weak external validation, limited reporting of calibration and failure modes, uncertain medico-legal accountability. These gaps are not merely methodological details. They determine whether results can be generalized across hospitals, whether a platform remains reliable after software or hardware changes, and whether the observed benefit reflects the technology rather than expert operator selection. A further problem is that technical publications often emphasize accuracy metrics while clinical publications emphasize outcome, leaving a translational gap between algorithmic performance and therapeutic value. The proposed study therefore uses extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days as its primary endpoint and includes brain-shift registration error, residual tumor volume, progression-free survival, operative time, calibration error, subgroup fairness, and surgeon cognitive workload as secondary endpoints. This endpoint architecture is intended to prevent a statistically impressive but clinically irrelevant result [4, 7, 14].

Materials and methods. A structured narrative review with a prospectively defined translational framework was selected because the field contains randomized trials, observational cohorts, diagnostic-accuracy studies, engineering reports, and implementation analyses that cannot be combined responsibly through a single pooled effect estimate. Searches should cover MEDLINE, Embase, Scopus, Web of Science, the Cochrane Library, and major trial registries from January 2015 through July 2026, while allowing earlier landmark studies when they established the current standard. Core search concepts should combine the disease or procedure, the intervention components, and outcome terms related to safety, neurological function, accuracy, and effectiveness. Citation chaining should be used to identify technical validation papers that may not be indexed under conventional clinical terminology [1, 4, 7]. Eligible evidence should include adult or mixed-age human studies directly evaluating multimodal AI-guided glioma surgery; studies of adults undergoing first or repeat resection of supratentorial diffuse glioma; and investigations reporting at least one clinically interpretable outcome. Exclusion criteria should include purely conceptual commentaries without original data, nonvalidated simulations, duplicated cohorts, and reports in which the contribution of the target technology cannot be separated from unrelated interventions. For diagnostic and algorithmic studies, the reference standard, unit of analysis, handling of repeated measurements, and patient-level data split must be extracted. For therapeutic studies, eligibility criteria, crossover, rescue treatment, missing data, and outcome adjudication must be recorded. The distinction between internal validation, temporal validation, geographic external validation, and prospective clinical validation is essential [2, 5, 8].

Data extraction should be organized into six domains: patient characteristics; disease or anatomical complexity; technical configuration; operator experience; safety; and clinical outcome. The technical domain should record hardware, software version, preprocessing, calibration, registration, data

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latency, and failure handling. The clinical domain should record extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days and brain-shift registration error, residual tumor volume, progression-free survival, operative time, calibration error, subgroup fairness, and surgeon cognitive workload. Risk of bias should be assessed with tools appropriate to study type, including RoB 2 for randomized trials, ROBINS-I for nonrandomized intervention studies, QUADAS-2 for diagnostic accuracy, and PROBAST or an equivalent framework for prediction models. Certainty should be interpreted according to consistency, directness, precision, and evidence of selective reporting [8, 9, 25].

The proposed original study is a prospective, multicenter, assessor-blinded comparative investigation involving adults undergoing first or repeat resection of supratentorial diffuse glioma. Participants should be enrolled consecutively to reduce spectrum bias. The intervention arm should receive a federated, explainable multimodal platform combining multiparametric MRI radiomics, radiogenomics, real-time intraoperative ultrasound segmentation, biomechanical brain-shift correction, and surgeon-facing uncertainty maps; the control arm should receive standard neuronavigation with conventional visual interpretation of preoperative MRI and intraoperative ultrasound. Randomization is preferred when clinical equipoise exists. If randomization is impractical, a pragmatic stepped-wedge or prospective registry design with propensity weighting and center-level random effects should be used. The primary endpoint is extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days. Secondary endpoints are brain-shift registration error, residual tumor volume, progression-free survival, operative time, calibration error, subgroup fairness, and surgeon cognitive workload. Outcome assessors should remain blinded to technical allocation whenever possible, and adverse events should be adjudicated by an independent committee.

The statistical analysis plan should be finalized before database lock. Continuous outcomes should be analyzed with mixed-effects models that account for center and repeated measurements. Binary endpoints should be reported with absolute risk differences, relative risks, and number needed to treat or harm when appropriate. Ordinal neurological outcomes should be analyzed with proportional-odds models after testing the proportionality assumption. Time-to-event outcomes require Kaplan–Meier estimation and multivariable Cox models. Diagnostic models must report discrimination, calibration, decision-curve analysis, and performance across clinically relevant subgroups. Missing data should be addressed through multiple imputation when assumptions are defensible, accompanied by complete-case and worst-case sensitivity analyses. Ethical oversight should recognize that advanced technology introduces risks beyond ordinary operative complications. These include privacy loss, cybersecurity failure, automation bias, inequitable performance, unplanned device downtime, and conflicts of interest arising from proprietary platforms. Consent documents should explain which decisions remain under surgeon control, whether data may be used for algorithm development, and how incidental findings will be managed. A data and safety monitoring structure should review not only adverse clinical events but also registration failures, algorithmic drift, protocol deviations, and cases in which the system recommendation was overridden. Such governance converts technological innovation into accountable clinical research [10, 11, 12].

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Results. The structured synthesis is expected to identify a first domain centered on preoperative molecular prediction. Across contemporary studies, the most consistent observation is that richer biological or anatomical characterization improves stratification, but reported gains vary according to reference standards and population spectrum. Studies that use retrospective convenience samples commonly show higher performance than prospective consecutive cohorts. This difference is clinically meaningful because difficult cases, prior treatment, motion, artifact, and incomplete data are underrepresented in curated datasets. Accordingly, the likely result is not a universal performance value, but a gradient of reliability that depends on data quality, disease phenotype, and operator context [10, 13, 23]. A second domain concerns intraoperative lesion localization. The relevant literature suggests that intraoperative or procedure-time information is most valuable when it changes the operative plan rather than merely confirming a preoperative expectation. Clinically useful outputs therefore require low latency, stable registration, and a display format that can be interpreted without interrupting the procedure. The synthesis also indicates that human expertise remains necessary for resolving discordance between technology and anatomy. Systems designed as collaborative decision aids are more likely to improve workflow than systems designed as autonomous authorities. The proposed study will document every technology-related plan modification, the reason for the change, and whether the modification was subsequently supported by pathology, imaging, electrophysiology, or clinical outcome [2, 3, 18].

The third domain is dynamic compensation for brain shift. Evidence in this area shows that temporal change is a central feature of neurosurgical care. Anatomy deforms, physiological reserve fluctuates, tissue characteristics evolve, and device signals drift. Static thresholds or one-time images therefore have limited validity. A dynamic strategy should update its estimate as new data arrive and should retain an audit trail of how recommendations changed. The anticipated result is that dynamic monitoring will reduce selected technical errors, but it may also increase false-positive alerts. This trade-off must be quantified through sensitivity, specificity, false-alert burden, and decision-curve analysis rather than described qualitatively [6, 13, 28]. The fourth domain, transparent risk estimation, addresses the relationship between technical success and patient-centered benefit. Existing evidence often demonstrates improved localization, classification, or device accuracy without proving a reduction in disability or a durable improvement in survival. The proposed research framework therefore treats technical accuracy as an intermediate endpoint. The primary clinical endpoint remains extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days. Secondary analysis will evaluate whether technical improvement mediates clinical benefit and whether the effect differs by baseline risk. This mediation-oriented approach can distinguish a technology that is accurate but clinically redundant from one that enables a beneficial change in treatment.

The fifth domain is workflow integration and human factors. Implementation outcomes are expected to vary substantially between high-volume academic centers and lower-resource hospitals. Capital costs, maintenance, calibration, data storage, staffing, and training may determine real-world effectiveness more strongly than laboratory accuracy. The framework therefore includes acquisition cost, consumables, room time, failed-case cost, revision avoidance, and staff workload. Equity analysis should determine whether the innovation narrows or widens access. A platform that

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performs well only in a highly selected tertiary environment should not be described as universally transformative [11, 12, 20]. Taken together, the expected evidence pattern supports cautious optimism. A federated, explainable multimodal platform combining multiparametric mri radiomics, radiogenomics, real-time intraoperative ultrasound segmentation, biomechanical brain-shift correction, and surgeon-facing uncertainty maps is likely to provide the greatest benefit in patients with high decision uncertainty and a realistic opportunity for management change. Benefit may be smaller in straightforward cases where standard practice already performs well. Harm may emerge from false reassurance, unnecessary extension of surgery, treatment delay, excessive alarms, or inappropriate extrapolation beyond the validated population. The originality tables below convert these observations into a testable study architecture and make clear which elements represent true innovation rather than repackaging of established practice.

Table 1. **Scientific originality matrix**

Domain	Current standard or limitation	Proposed original contribution
Data architecture	Single-modality retrospective models	Prospective multimodal MRI–ioUS fusion with federated external validation
Navigation	Static preoperative coordinates	Continuous deformation-aware neuronavigation updated by ioUS
Decision support	Binary tumor/non-tumor output	Voxel-level probability and uncertainty maps visible to the surgeon
Clinical endpoint	Segmentation accuracy alone	Composite maximal-safe-resection endpoint with 90-day function
Equity	Unreported subgroup performance	Prespecified testing by sex, age, scanner vendor, and molecular class

Table 2. **Proposed prospective study framework**

Element	Specification
Population	adults undergoing first or repeat resection of supratentorial diffuse glioma
Intervention	a federated, explainable multimodal platform combining multiparametric MRI radiomics, radiogenomics, real-time intraoperative ultrasound segmentation, biomechanical brain-shift correction, and surgeon-facing uncertainty maps
Comparator	standard neuronavigation with conventional

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	visual interpretation of preoperative MRI and intraoperative ultrasound
Primary endpoint	extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days
Secondary endpoints	brain-shift registration error, residual tumor volume, progression-free survival, operative time, calibration error, subgroup fairness, and surgeon cognitive workload
Design	Prospective multicenter randomized trial when equipoise permits; otherwise a stepped-wedge or rigorously adjusted prospective registry.
Validation	Internal, temporal, geographic, and subgroup validation with prespecified failure and uncertainty reporting.
Ethics	Independent safety adjudication, data governance, cybersecurity review, and transparent disclosure of proprietary interests.

Discussion. The principal interpretation is that multimodal AI-guided glioma surgery should be evaluated as a sociotechnical intervention. The operative result emerges from interaction among the patient, surgeon, team, imaging or monitoring environment, software, hardware, institutional protocols, and rescue pathways. This explains why promising accuracy studies may not reproduce the same benefit after implementation. A technically excellent platform can fail if registration is unreliable, alerts are poorly prioritized, staff roles are unclear, or the output arrives too late to influence the decision. Conversely, a moderately accurate system can be clinically valuable when it addresses a high-impact uncertainty and integrates smoothly into workflow [15, 17, 27]. Patient selection is likely to be the main determinant of effect size. The target population is adults undergoing first or repeat resection of supratentorial diffuse glioma, but not every eligible patient has the same probability of benefit. Selection should incorporate baseline function, disease burden, anatomical complexity, comorbidity, prior treatment, expected survival, and the availability of an actionable alternative. The intervention should not be offered merely because the technology is available. A decision-impact criterion is more appropriate: the patient should have a plausible management fork that the new information can resolve. This principle limits exposure to unnecessary complexity and improves the efficiency of prospective trials [7, 14, 19].

The choice of comparator is equally important. The relevant comparator is standard neuronavigation with conventional visual interpretation of preoperative MRI and intraoperative ultrasound, delivered by trained clinicians under a standardized protocol. Comparing an advanced platform with poorly defined historical care exaggerates benefit and does not inform contemporary practice. Expertise bias should be addressed by documenting operator experience in both arms and by separating the learning phase from the evaluative phase. When blinding the surgeon is impossible, blinded endpoint

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assessment, objective imaging or physiological criteria, and independent adjudication become essential. These safeguards are particularly important when the intervention itself changes the amount or duration of surgery. Safety must include both direct and indirect harm. Direct harm includes device- or procedure-related injury, infection, hemorrhage, neurological deficit, or treatment toxicity. Indirect harm includes delay, over-treatment, under-treatment, false reassurance, automation bias, and diversion of resources. The proposed study therefore records technical failures and near misses even when no adverse clinical event occurs. A near miss may reveal a latent system weakness before it causes patient harm. Safety analysis should also examine whether complication patterns cluster by center, operator, hardware version, or patient subgroup [16, 23, 30].

Reproducibility requires more than publishing an average outcome. Investigators should report data provenance, inclusion flow, missingness, device and software versions, preprocessing, calibration, and protocol deviations. For algorithms, source code or a sufficiently detailed executable description should be available when intellectual-property constraints permit. For devices, the physical configuration and update history should be recorded. For complex clinical pathways, process maps should define who performs each step and how discordant information is resolved. External validation must be geographic and temporal, not merely a random split of one institutional dataset. Health-economic evaluation is necessary because high-cost neurosurgical technologies may displace other interventions. A complete assessment should compare acquisition, disposables, maintenance, training, operating-room time, length of stay, complications, revision procedures, rehabilitation, and long-term care. The relevant economic question is not whether the technology is expensive, but whether its incremental cost is justified by additional quality-adjusted survival, preserved independence, or avoided complications. Lower-cost adaptations should be studied deliberately rather than treated as inferior substitutes. This is especially important for regional centers and health systems with constrained capital budgets [21, 24, 31].

The framework also has implications for education. Training should include not only device operation but also interpretation of uncertainty, recognition of failure modes, and maintenance of manual rescue skills. Simulation can expose teams to registration error, data loss, unexpected anatomy, or discordant signals before clinical deployment. Competency should be measured through objective performance and scenario-based assessment rather than attendance at a vendor course. Credentialing should be periodically renewed when major software or hardware updates alter the workflow. Several limitations should be acknowledged. First, a structured narrative synthesis is vulnerable to publication bias and cannot provide a single pooled treatment effect. Second, rapid technological evolution may make specific hardware obsolete before long-term outcomes mature. Third, the proposed endpoints may require large samples and extended follow-up. Fourth, standardized protocols can conflict with the individualized nature of neurosurgical care. Fifth, external validity may be limited in centers without equivalent imaging, pathology, engineering, or neurocritical-care infrastructure. These limitations do not negate the research question; they define the conditions under which evidence should be interpreted. Future research should prioritize multicenter pragmatic trials, interoperable data standards, shared outcome definitions, prospective failure registries, and patient involvement in endpoint selection. Adaptive trial designs may be useful when software evolves during recruitment, provided version changes are prespecified and

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analytically traceable. International collaboration can improve representation of scanner types, devices, languages, ethnic groups, and health-system conditions. Ultimately, the decisive evidence will come from demonstrating that the intervention improves extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days while maintaining acceptable safety, cost, and equity.

A further translational issue is endpoint hierarchy. In multimodal AI-guided glioma surgery, several intermediate outcomes may improve simultaneously, yet they should not be interpreted as equivalent. Technical accuracy is closest to the device; decision impact lies one step downstream; clinical benefit lies further downstream; and societal value incorporates cost, access, and long-term participation. A rigorous study should therefore define a causal chain before recruitment. The intervention must first produce a reliable signal, the signal must change a decision, the decision must alter treatment, and the altered treatment must improve outcome. Failure at any step can explain a neutral clinical trial even when the technology appears accurate. Recording each link in this chain will make negative results scientifically informative rather than simply disappointing [23, 30, 32].

Conclusions. Multimodal Artificial Intelligence for Precision Glioma Surgery: Integrating Radiomics, Intraoperative Ultrasound, Brain-Shift Correction, and Explainable Decision Support represents a timely and clinically relevant research direction. The evidence supports biological and technical plausibility, but also demonstrates that isolated accuracy metrics are insufficient. The most defensible next step is a prospective multicenter evaluation of a federated, explainable multimodal platform combining multiparametric MRI radiomics, radiogenomics, real-time intraoperative ultrasound segmentation, biomechanical brain-shift correction, and surgeon-facing uncertainty maps against standard neuronavigation with conventional visual interpretation of preoperative MRI and intraoperative ultrasound, using extent of resection normalized to molecularly defined tumor burden and the rate of new persistent neurological deficit at 90 days as the primary endpoint and brain-shift registration error, residual tumor volume, progression-free survival, operative time, calibration error, subgroup fairness, and surgeon cognitive workload as secondary measures. The proposed originality matrix, standardized methods, explicit uncertainty reporting, and patient-centered outcomes provide a foundation for an authentic IMRAD manuscript. The approach should be adopted only when its benefit is reproducible, transparent, equitable, and clinically meaningful.

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CONNECTOME-GUIDED AWAKE SURGERY FOR DIFFUSE GLIOMAS: NETWORK-LEVEL MAPPING OF LANGUAGE, EXECUTIVE FUNCTION, AND NEUROCOGNITIVE RESERVE

Abstract

Background. In diffuse low- and high-grade gliomas involving eloquent and associative networks, neurosurgical decisions remain difficult because traditional localizationist mapping protects a limited set of cortical sites but may overlook distributed white-matter pathways and higher-order networks responsible for executive control, semantic integration, social cognition, and adaptive behavior.

Materials and methods. A structured narrative review is proposed using clinical trials, prospective cohorts, diagnostic-accuracy studies, systematic reviews, and relevant technical investigations. Evidence is organized by biological plausibility, technical performance, patient selection, safety, clinical effectiveness, reproducibility, and implementation. A prospective comparative study is specified for adults with unilateral supratentorial diffuse glioma adjacent to language, motor, salience, default-mode, or frontoparietal control networks, with conventional awake mapping focused primarily on motor and language tasks as the reference strategy.

Results. The synthesis addresses five domains: limitations of cortical localization, white-matter constraints on resection, higher-order cognitive mapping, neuroplasticity and staged surgery, functional outcomes beyond gross motor and language scales. The proposed primary endpoint is rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months; secondary endpoints include extent of resection, network disconnection score, postoperative aphasia, executive dysfunction, quality of life, seizure control, and longitudinal plasticity. Originality derives from linking technical accuracy to patient-centered outcomes, explicitly modeling uncertainty, and requiring external validation.

Conclusion. Standardized endpoints support reliable clinical comparison. Independent adjudication strengthens causal interpretation. Longitudinal follow-up clarifies therapeutic durability. Rigorous independent external validation remains essential.

Keywords: connectome; awake craniotomy; diffuse glioma; direct electrical stimulation; tractography; neuroplasticity; cognitive mapping.

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КОННЕКТОМ-ОРИЕНТИРОВАННАЯ ХИРУРГИЯ ДИФФУЗНЫХ ГЛИОМ В СОЗНАНИИ: СЕТЕВОЕ КАРТИРОВАНИЕ РЕЧИ, ИСПОЛНИТЕЛЬНЫХ ФУНКЦИЙ И НЕЙРОКОГНИТИВНОГО РЕЗЕРВА

Аннотация

Актуальность. При диффузных глиомах низкой и высокой степени злокачественности, вовлекающих функционально значимые и ассоциативные нейронные сети, принятие

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нейрохирургических решений остается сложной задачей. Традиционное локализационное картирование позволяет сохранить ограниченное число корковых участков, однако может не учитывать распределенные проводящие пути белого вещества и нейронные сети высшего порядка, обеспечивающие исполнительный контроль, семантическую интеграцию, социальное познание и адаптивное поведение.

Материалы и методы. Предложен структурированный нарративный обзор, включающий клинические исследования, проспективные когортные исследования, работы по оценке диагностической точности, систематические обзоры и релевантные технические исследования. Доказательства систематизированы по биологической обоснованности, технической эффективности, критериям отбора пациентов, безопасности, клинической результативности, воспроизводимости и возможности внедрения в практику. Разработан дизайн проспективного сравнительного исследования с участием взрослых пациентов с односторонней супратенториальной диффузной глиомой, расположенной вблизи речевых, моторных, салиентных, дефолтных или лобно-теменных сетей исполнительного контроля. В качестве референтной стратегии определено стандартное картирование в условиях операции с пробуждением пациента, ориентированное преимущественно на оценку моторных и речевых функций.

Результаты. Синтез доказательств охватывает пять основных направлений: ограничения корковой локализации, роль проводящих путей белого вещества в определении границ резекции, картирование высших когнитивных функций, нейропластичность и этапные хирургические вмешательства, а также оценку функциональных исходов, выходящих за пределы стандартных моторных и речевых шкал. Предлагаемой первичной конечной точкой является частота возвращения пациентов к дооперационной трудовой или учебной деятельности без стойкого речевого, исполнительного или социально-когнитивного снижения через шесть месяцев после операции. Вторичные конечные точки включают степень резекции, показатель сетевой дисконнекции, частоту послеоперационной афазии, исполнительной дисфункции, качество жизни, контроль эпилептических приступов и динамику нейропластичности при длительном наблюдении. Научная оригинальность определяется взаимосвязью технической точности картирования с клиническими исходами, значимыми для пациента, явным моделированием неопределенности и обязательным проведением внешней валидации.

Заключение. Стандартизированные конечные точки обеспечивают надежность клинических сравнений. Независимая экспертная оценка результатов повышает достоверность причинно-следственной интерпретации. Продолжительное динамическое наблюдение позволяет оценить устойчивость терапевтического эффекта. Проведение строгой и независимой внешней валидации остается обязательным условием.

Ключевые слова: коннектом; краниотомия в сознании; диффузная глиома; прямая электрическая стимуляция; трактография; нейропластичность; когнитивное картирование.

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DIFFUZ GLIOMALARDA KONNEKTOMGA YO‘NALTIRILGAN UYG‘OQ JARROHLIK: NUTQ, IJRO FUNKSIYALARI VA NEYROKOGNITIV REZERVNI TARMOQ DARAJASIDA XARITALASH

Annotatsiya

Dolzarblik. Funksional jihatdan muhim va assotsiativ neyron tarmoqlarni qamrab olgan past hamda yuqori darajali diffuz gliomalarda neyroxirurgik qaror qabul qilish murakkabligicha qolmoqda. An’anaviy lokalizatsion xaritalash usuli cheklangan miqdordagi kortikal sohalarni saqlab qolishga imkon beradi, biroq ijro nazorati, semantik integratsiya, ijtimoiy kognitsiya va adaptiv xulq-atvorni ta’minlovchi taqsimlangan oq modda o‘tkazuvchi yo‘llari hamda yuqori darajali neyron tarmoqlarni yetarli darajada hisobga olmasligi mumkin.

Material va usullar. Klinik tadqiqotlar, prospektiv kohort tadqiqotlari, diagnostik aniqlikni baholovchi ishlar, tizimli sharhlar va tegishli texnik izlanishlarni qamrab oluvchi strukturaviy narrativ sharh taklif etildi. Dalillar biologik asoslanganlik, texnik samaradorlik, bemorlarni tanlash mezonlari, xavfsizlik, klinik natijadorlik, takrorlanuvchanlik va amaliyotga joriy etish imkoniyatiga ko‘ra tizimlashtirildi. Nutq, motor, saliyent, standart holat yoki frontoparietal ijro nazorati tarmoqlariga yaqin joylashgan bir tomonlama supratentorial diffuz gliomali katta yoshli bemorlar uchun prospektiv qiyosiy tadqiqot dizayni ishlab chiqildi. Asosan motor va nutq vazifalariga yo‘naltirilgan an’anaviy uyg‘oq kraniotomiya sharoitidagi xaritalash referent strategiya sifatida belgilandi.

Natijalar. Dalillar sintezi beshta asosiy yo‘nalishni qamrab oladi: kortikal lokalizatsiyaning cheklovlari, rezeksiya chegaralarini belgilashda oq modda o‘tkazuvchi yo‘llarining ahamiyati, yuqori darajali kognitiv funksiyalarni xaritalash, neyroplastiklik va bosqichma-bosqich jarrohlik, shuningdek, standart motor va nutq shkalalaridan tashqaridagi funksional natijalarni baholash. Taklif etilgan birlamchi yakuniy ko‘rsatkich operatsiyadan olti oy o‘tgach turg‘un nutqiy, ijroiy yoki ijtimoiy-kognitiv pasayishlarsiz bemorning operatsiyadan oldingi ish yoki o‘qish faoliyatiga qaytish darajasidir. Ikkilamchi yakuniy ko‘rsatkichlarga rezeksiya darajasi, tarmoq uzilishi ko‘rsatkichi, operatsiyadan keyingi afaziya, ijro disfunksiyasi, hayot sifati, epileptik tutqanoqlar nazorati va neyroplastiklikning uzoq muddatli dinamikasi kiradi. Tadqiqotning ilmiy yangiligi xaritalashning texnik aniqligini bemor uchun klinik ahamiyatga ega natijalar bilan bog‘lash, noaniqlikni aniq modellashtirish va tashqi validatsiyani majburiy talab qilish bilan belgilanadi.

Xulosa. Standartlashtirilgan yakuniy ko‘rsatkichlar klinik natijalarni ishonchli taqqoslash imkonini beradi. Natijalarni mustaqil ekspert baholashi sabab-oqibat bog‘liqligini talqin qilishning ishonchliligini oshiradi. Uzoq muddatli dinamik kuzatuv terapevtik ta’sirning barqarorligini aniqlash imkonini beradi. Qat’iy va mustaqil tashqi validatsiya o‘tkazilishi muhim talab bo‘lib qolmoqda.

Kalit so‘zlar: konnektom; uyg‘oq kraniotomiya; diffuz glioma; to‘g‘ridan-to‘g‘ri elektr stimulyatsiya; traktografiya; neyroplastiklik; kognitiv xaritalash.

Introduction. Neurosurgery is increasingly defined by the tension between anatomical precision and biological uncertainty. In diffuse low- and high-grade gliomas involving eloquent and associative networks, the surgeon must act on information that is incomplete, time dependent, and distributed across imaging, physiology, pathology, electrophysiology, and patient-specific functional reserve. The conventional operative paradigm is therefore being replaced by a data-rich model in

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which preoperative planning, intraoperative sensing, and postoperative surveillance are treated as a continuous decision process. This evolution is clinically important because technical success cannot be reduced to target acquisition or implant placement; it must also preserve neurological function, reduce treatment burden, and improve survival or participation. Contemporary evidence supports this shift, but also shows that many innovations remain supported by retrospective cohorts, selected populations, and heterogeneous endpoints [1, 2, 10, 13]. The central scientific problem is not simply whether a new device or algorithm performs accurately, but whether it changes a decision at the correct time and improves a patient-centered outcome. The specific rationale for connectome-guided awake glioma surgery arises from a persistent limitation: traditional localizationist mapping protects a limited set of cortical sites but may overlook distributed white-matter pathways and higher-order networks responsible for executive control, semantic integration, social cognition, and adaptive behavior. This limitation creates several forms of uncertainty. Anatomical uncertainty concerns where the clinically relevant target or boundary is located. Biological uncertainty concerns whether a visible or measurable abnormality represents viable disease, reversible dysfunction, treatment effect, or nonactionable tissue injury. Functional uncertainty concerns how much intervention can be tolerated without compromising language, cognition, mobility, independence, or quality of life. Finally, temporal uncertainty concerns how rapidly physiology, anatomy, or disease burden changes during and after treatment. Existing methods usually address only one of these dimensions. The proposed innovation-a connectome-based awake mapping protocol that combines patient-specific tractography, resting-state network analysis, direct cortical and subcortical stimulation, task switching, and longitudinal neuropsychological phenotyping-is intended to combine them within a single clinically interpretable framework [3, 7, 12, 15].

The potential advantages of this approach are mechanistically plausible. Relevant processes include direct electrical stimulation of cortical and subcortical pathways, patient-specific diffusion tractography, resting-state functional connectivity, intraoperative multitask paradigms, longitudinal network reorganization. When these processes are measured independently, the clinician receives fragmented signals with different spatial resolutions, temporal resolutions, and error structures. Integration can theoretically reduce uncertainty by allowing one modality to compensate for the weaknesses of another. However, multimodal integration can also amplify hidden bias, propagate registration error, and create false confidence if outputs are presented without uncertainty estimates. For that reason, a clinically responsible system must reveal both its prediction and the conditions under which that prediction may fail. This requirement is particularly important in neurosurgery, where small errors can produce irreversible disability and where intraoperative decisions are often made under severe time constraints [8, 9, 25]. Five evidence gaps justify a dedicated original investigation: heterogeneous task batteries, limited normative neuropsychological data, tractography false-positive and false-negative pathways, inconsistent reporting of return-to-work outcomes, scarce multicenter prospective validation. These gaps are not merely methodological details. They determine whether results can be generalized across hospitals, whether a platform remains reliable after software or hardware changes, and whether the observed benefit reflects the technology rather than expert operator selection. A further problem is that technical publications often emphasize accuracy metrics while clinical publications emphasize outcome, leaving a translational gap between

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algorithmic performance and therapeutic value. The proposed study therefore uses rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months as its primary endpoint and includes extent of resection, network disconnection score, postoperative aphasia, executive dysfunction, quality of life, seizure control, and longitudinal plasticity as secondary endpoints. This endpoint architecture is intended to prevent a statistically impressive but clinically irrelevant result [6, 13, 28].

The objective of this article is to provide a structured, current, and testable framework for connectome-guided awake glioma surgery. The first aim is to synthesize the biological and technical rationale. The second is to define a reproducible evidence-review method and a prospective comparative study design. The third is to describe expected patterns of benefit, failure, and heterogeneity without fabricating patient-level results. The fourth is to present an originality matrix that clearly distinguishes the proposal from routine practice. The working hypothesis is that a connectome-based awake mapping protocol that combines patient-specific tractography, resting-state network analysis, direct cortical and subcortical stimulation, task switching, and longitudinal neuropsychological phenotyping will outperform conventional awake mapping focused primarily on motor and language tasks only when patient selection, data quality, operator training, and uncertainty management are prespecified. In other words, the hypothesis concerns a complete clinical system rather than an isolated device.

Materials and methods. A structured narrative review with a prospectively defined translational framework was selected because the field contains randomized trials, observational cohorts, diagnostic-accuracy studies, engineering reports, and implementation analyses that cannot be combined responsibly through a single pooled effect estimate. Searches should cover MEDLINE, Embase, Scopus, Web of Science, the Cochrane Library, and major trial registries from January 2015 through July 2026, while allowing earlier landmark studies when they established the current standard. Core search concepts should combine the disease or procedure, the intervention components, and outcome terms related to safety, neurological function, accuracy, and effectiveness. Citation chaining should be used to identify technical validation papers that may not be indexed under conventional clinical terminology [1, 4, 7]. Eligible evidence should include adult or mixed-age human studies directly evaluating connectome-guided awake glioma surgery; studies of adults with unilateral supratentorial diffuse glioma adjacent to language, motor, salience, default-mode, or frontoparietal control networks; and investigations reporting at least one clinically interpretable outcome. Exclusion criteria should include purely conceptual commentaries without original data, nonvalidated simulations, duplicated cohorts, and reports in which the contribution of the target technology cannot be separated from unrelated interventions. For diagnostic and algorithmic studies, the reference standard, unit of analysis, handling of repeated measurements, and patient-level data split must be extracted. For therapeutic studies, eligibility criteria, crossover, rescue treatment, missing data, and outcome adjudication must be recorded. The distinction between internal validation, temporal validation, geographic external validation, and prospective clinical validation is essential [2, 5, 8]. Data extraction should be organized into six domains: patient characteristics; disease or anatomical complexity; technical configuration; operator experience; safety; and clinical outcome. The technical domain should record hardware, software version, preprocessing, calibration,

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registration, data latency, and failure handling. The clinical domain should record rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months and extent of resection, network disconnection score, postoperative aphasia, executive dysfunction, quality of life, seizure control, and longitudinal plasticity. Risk of bias should be assessed with tools appropriate to study type, including RoB 2 for randomized trials, ROBINS-I for nonrandomized intervention studies, QUADAS-2 for diagnostic accuracy, and PROBAST or an equivalent framework for prediction models. Certainty should be interpreted according to consistency, directness, precision, and evidence of selective reporting [3, 6, 9].

The proposed original study is a prospective, multicenter, assessor-blinded comparative investigation involving adults with unilateral supratentorial diffuse glioma adjacent to language, motor, salience, default-mode, or frontoparietal control networks. Participants should be enrolled consecutively to reduce spectrum bias. The intervention arm should receive a connectome-based awake mapping protocol that combines patient-specific tractography, resting-state network analysis, direct cortical and subcortical stimulation, task switching, and longitudinal neuropsychological phenotyping; the control arm should receive conventional awake mapping focused primarily on motor and language tasks. Randomization is preferred when clinical equipoise exists. If randomization is impractical, a pragmatic stepped-wedge or prospective registry design with propensity weighting and center-level random effects should be used. The primary endpoint is rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months. Secondary endpoints are extent of resection, network disconnection score, postoperative aphasia, executive dysfunction, quality of life, seizure control, and longitudinal plasticity. Outcome assessors should remain blinded to technical allocation whenever possible, and adverse events should be adjudicated by an independent committee.

The statistical analysis plan should be finalized before database lock. Continuous outcomes should be analyzed with mixed-effects models that account for center and repeated measurements. Binary endpoints should be reported with absolute risk differences, relative risks, and number needed to treat or harm when appropriate. Ordinal neurological outcomes should be analyzed with proportional-odds models after testing the proportionality assumption. Time-to-event outcomes require Kaplan–Meier estimation and multivariable Cox models. Diagnostic models must report discrimination, calibration, decision-curve analysis, and performance across clinically relevant subgroups. Missing data should be addressed through multiple imputation when assumptions are defensible, accompanied by complete-case and worst-case sensitivity analyses. Ethical oversight should recognize that advanced technology introduces risks beyond ordinary operative complications. These include privacy loss, cybersecurity failure, automation bias, inequitable performance, unplanned device downtime, and conflicts of interest arising from proprietary platforms. Consent documents should explain which decisions remain under surgeon control, whether data may be used for algorithm development, and how incidental findings will be managed. A data and safety monitoring structure should review not only adverse clinical events but also registration failures, algorithmic drift, protocol deviations, and cases in which the system recommendation was overridden. Such governance converts technological innovation into accountable clinical research [16, 23, 30].

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Results. The structured synthesis is expected to identify a first domain centered on limitations of cortical localization. Across contemporary studies, the most consistent observation is that richer biological or anatomical characterization improves stratification, but reported gains vary according to reference standards and population spectrum. Studies that use retrospective convenience samples commonly show higher performance than prospective consecutive cohorts. This difference is clinically meaningful because difficult cases, prior treatment, motion, artifact, and incomplete data are underrepresented in curated datasets. Accordingly, the likely result is not a universal performance value, but a gradient of reliability that depends on data quality, disease phenotype, and operator context [1, 2, 4]. A second domain concerns white-matter constraints on resection. The relevant literature suggests that intraoperative or procedure-time information is most valuable when it changes the operative plan rather than merely confirming a preoperative expectation. Clinically useful outputs therefore require low latency, stable registration, and a display format that can be interpreted without interrupting the procedure. The synthesis also indicates that human expertise remains necessary for resolving discordance between technology and anatomy. Systems designed as collaborative decision aids are more likely to improve workflow than systems designed as autonomous authorities. The proposed study will document every technology-related plan modification, the reason for the change, and whether the modification was subsequently supported by pathology, imaging, electrophysiology, or clinical outcome [8, 9, 25].

The third domain is higher-order cognitive mapping. Evidence in this area shows that temporal change is a central feature of neurosurgical care. Anatomy deforms, physiological reserve fluctuates, tissue characteristics evolve, and device signals drift. Static thresholds or one-time images therefore have limited validity. A dynamic strategy should update its estimate as new data arrive and should retain an audit trail of how recommendations changed. The anticipated result is that dynamic monitoring will reduce selected technical errors, but it may also increase false-positive alerts. This trade-off must be quantified through sensitivity, specificity, false-alert burden, and decision-curve analysis rather than described qualitatively[6, 13, 28]. The fourth domain, neuroplasticity and staged surgery, addresses the relationship between technical success and patient-centered benefit. Existing evidence often demonstrates improved localization, classification, or device accuracy without proving a reduction in disability or a durable improvement in survival. The proposed research framework therefore treats technical accuracy as an intermediate endpoint. The primary clinical endpoint remains rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months. Secondary analysis will evaluate whether technical improvement mediates clinical benefit and whether the effect differs by baseline risk. This mediation-oriented approach can distinguish a technology that is accurate but clinically redundant from one that enables a beneficial change in treatment. The fifth domain is functional outcomes beyond gross motor and language scales. Implementation outcomes are expected to vary substantially between high-volume academic centers and lower-resource hospitals. Capital costs, maintenance, calibration, data storage, staffing, and training may determine real-world effectiveness more strongly than laboratory accuracy. The framework therefore includes acquisition cost, consumables, room time, failed-case cost, revision avoidance, and staff workload. Equity analysis should determine whether the innovation narrows or widens access. A platform that performs well

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only in a highly selected tertiary environment should not be described as universally transformative [4, 7, 14].

Taken together, the expected evidence pattern supports cautious optimism. A connectome-based awake mapping protocol that combines patient-specific tractography, resting-state network analysis, direct cortical and subcortical stimulation, task switching, and longitudinal neuropsychological phenotyping is likely to provide the greatest benefit in patients with high decision uncertainty and a realistic opportunity for management change. Benefit may be smaller in straightforward cases where standard practice already performs well. Harm may emerge from false reassurance, unnecessary extension of surgery, treatment delay, excessive alarms, or inappropriate extrapolation beyond the validated population. The originality tables below convert these observations into a testable study architecture and make clear which elements represent true innovation rather than repackaging of established practice.

Table 1. **Scientific originality matrix**

Domain	Current standard or limitation	Proposed original contribution
Functional model	Cortical eloquence map	Individualized cortico-subcortical network model
Awake tasks	Naming and motor testing	Adaptive multitask battery covering executive and social cognition
Outcome	Immediate deficit rate	Six-month cognitive participation and return-to-work endpoint
Resection boundary	Anatomic or fluorescence margin	Stimulation-defined network boundary with disconnection metrics
Plasticity	Assumed but unmeasured	Serial connectomics at 3, 6, and 12 months

Table 2. Proposed prospective study framework

Element	Specification
Population	adults with unilateral supratentorial diffuse glioma adjacent to language, motor, salience, default-mode, or frontoparietal control networks
Intervention	a connectome-based awake mapping protocol that combines patient-specific tractography, resting-state network analysis, direct cortical and subcortical stimulation, task switching, and longitudinal neuropsychological phenotyping
Comparator	conventional awake mapping focused primarily on motor and language tasks
Primary endpoint	rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months

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Element	Specification
Secondary endpoints	extent of resection, network disconnection score, postoperative aphasia, executive dysfunction, quality of life, seizure control, and longitudinal plasticity
Design	Prospective multicenter randomized trial when equipoise permits; otherwise a stepped-wedge or rigorously adjusted prospective registry.
Validation	Internal, temporal, geographic, and subgroup validation with prespecified failure and uncertainty reporting.
Ethics	Independent safety adjudication, data governance, cybersecurity review, and transparent disclosure of proprietary interests.

Discussion. The principal interpretation is that connectome-guided awake glioma surgery should be evaluated as a sociotechnical intervention. The operative result emerges from interaction among the patient, surgeon, team, imaging or monitoring environment, software, hardware, institutional protocols, and rescue pathways. This explains why promising accuracy studies may not reproduce the same benefit after implementation. A technically excellent platform can fail if registration is unreliable, alerts are poorly prioritized, staff roles are unclear, or the output arrives too late to influence the decision. Conversely, a moderately accurate system can be clinically valuable when it addresses a high-impact uncertainty and integrates smoothly into workflow [1, 3, 5]. Patient selection is likely to be the main determinant of effect size. The target population is adults with unilateral supratentorial diffuse glioma adjacent to language, motor, salience, default-mode, or frontoparietal control networks, but not every eligible patient has the same probability of benefit. Selection should incorporate baseline function, disease burden, anatomical complexity, comorbidity, prior treatment, expected survival, and the availability of an actionable alternative. The intervention should not be offered merely because the technology is available. A decision-impact criterion is more appropriate: the patient should have a plausible management fork that the new information can resolve. This principle limits exposure to unnecessary complexity and improves the efficiency of prospective trials [3, 6, 10].

The choice of comparator is equally important. The relevant comparator is conventional awake mapping focused primarily on motor and language tasks, delivered by trained clinicians under a standardized protocol. Comparing an advanced platform with poorly defined historical care exaggerates benefit and does not inform contemporary practice. Expertise bias should be addressed by documenting operator experience in both arms and by separating the learning phase from the evaluative phase. When blinding the surgeon is impossible, blinded endpoint assessment, objective imaging or physiological criteria, and independent adjudication become essential. These safeguards are particularly important when the intervention itself changes the amount or duration of surgery. Safety must include both direct and indirect harm. Direct harm includes device- or procedure-related injury, infection, hemorrhage, neurological deficit, or treatment toxicity. Indirect harm includes delay, over-treatment, under-treatment, false reassurance, automation bias, and diversion of resources. The proposed study therefore records technical failures and near misses even when no

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adverse clinical event occurs. A near miss may reveal a latent system weakness before it causes patient harm. Safety analysis should also examine whether complication patterns cluster by center, operator, hardware version, or patient subgroup [7, 9, 11].

Reproducibility requires more than publishing an average outcome. Investigators should report data provenance, inclusion flow, missingness, device and software versions, preprocessing, calibration, and protocol deviations. For algorithms, source code or a sufficiently detailed executable description should be available when intellectual-property constraints permit. For devices, the physical configuration and update history should be recorded. For complex clinical pathways, process maps should define who performs each step and how discordant information is resolved. External validation must be geographic and temporal, not merely a random split of one institutional dataset. Health-economic evaluation is necessary because high-cost neurosurgical technologies may displace other interventions. A complete assessment should compare acquisition, disposables, maintenance, training, operating-room time, length of stay, complications, revision procedures, rehabilitation, and long-term care. The relevant economic question is not whether the technology is expensive, but whether its incremental cost is justified by additional quality-adjusted survival, preserved independence, or avoided complications. Lower-cost adaptations should be studied deliberately rather than treated as inferior substitutes. This is especially important for regional centers and health systems with constrained capital budgets [8, 10, 12]. The framework also has implications for education. Training should include not only device operation but also interpretation of uncertainty, recognition of failure modes, and maintenance of manual rescue skills. Simulation can expose teams to registration error, data loss, unexpected anatomy, or discordant signals before clinical deployment. Competency should be measured through objective performance and scenario-based assessment rather than attendance at a vendor course. Credentialing should be periodically renewed when major software or hardware updates alter the workflow.

Several limitations should be acknowledged. First, a structured narrative synthesis is vulnerable to publication bias and cannot provide a single pooled treatment effect. Second, rapid technological evolution may make specific hardware obsolete before long-term outcomes mature. Third, the proposed endpoints may require large samples and extended follow-up. Fourth, standardized protocols can conflict with the individualized nature of neurosurgical care. Fifth, external validity may be limited in centers without equivalent imaging, pathology, engineering, or neurocritical-care infrastructure. These limitations do not negate the research question; they define the conditions under which evidence should be interpreted. Future research should prioritize multicenter pragmatic trials, interoperable data standards, shared outcome definitions, prospective failure registries, and patient involvement in endpoint selection. Adaptive trial designs may be useful when software evolves during recruitment, provided version changes are prespecified and analytically traceable. International collaboration can improve representation of scanner types, devices, languages, ethnic groups, and health-system conditions. Ultimately, the decisive evidence will come from demonstrating that the intervention improves rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months while maintaining acceptable safety, cost, and equity.

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A further translational issue is endpoint hierarchy. In connectome-guided awake glioma surgery, several intermediate outcomes may improve simultaneously, yet they should not be interpreted as equivalent. Technical accuracy is closest to the device; decision impact lies one step downstream; clinical benefit lies further downstream; and societal value incorporates cost, access, and long-term participation. A rigorous study should therefore define a causal chain before recruitment. The intervention must first produce a reliable signal, the signal must change a decision, the decision must alter treatment, and the altered treatment must improve outcome. Failure at any step can explain a neutral clinical trial even when the technology appears accurate. Recording each link in this chain will make negative results scientifically informative rather than simply disappointing [1, 5, 9].

Conclusion. Connectome-Guided Awake Surgery for Diffuse Gliomas: Network-Level Mapping of Language, Executive Function, and Neurocognitive Reserve represents a timely and clinically relevant research direction. The evidence supports biological and technical plausibility, but also demonstrates that isolated accuracy metrics are insufficient. The most defensible next step is a prospective multicenter evaluation of a connectome-based awake mapping protocol that combines patient-specific tractography, resting-state network analysis, direct cortical and subcortical stimulation, task switching, and longitudinal neuropsychological phenotyping against conventional awake mapping focused primarily on motor and language tasks, using rate of return to preoperative work or study without persistent language, executive, or social-cognitive decline at six months as the primary endpoint and extent of resection, network disconnection score, postoperative aphasia, executive dysfunction, quality of life, seizure control, and longitudinal plasticity as secondary measures. The proposed originality matrix, standardized methods, explicit uncertainty reporting, and patient-centered outcomes provide a foundation for an authentic IMRAD manuscript. The approach should be adopted only when its benefit is reproducible, transparent, equitable, and clinically meaningful.

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INTRAOPERATIVE MOLECULAR IMAGING OF GLIOMA MARGINS: COMPARATIVE INTEGRATION OF 5-AMINOLEVULINIC ACID, RAMAN SPECTROSCOPY, AND REAL-TIME TISSUE CLASSIFICATION

Abstract

Background. In high-grade and molecularly heterogeneous diffuse gliomas, neurosurgical decisions remain difficult because visual inspection and white-light microscopy underestimate infiltrative tumor, whereas fluorescence intensity varies with tumor biology, treatment history, pharmacokinetics, and optical conditions.

Materials and methods. A structured narrative review is proposed using clinical trials, prospective cohorts, diagnostic-accuracy studies, systematic reviews, and relevant technical investigations. Evidence is organized by biological plausibility, technical performance, patient selection, safety, clinical effectiveness, reproducibility, and implementation. A prospective comparative study is specified for adults undergoing resection of newly diagnosed or recurrent contrast-enhancing diffuse glioma, with 5-ALA fluorescence-guided surgery alone as the reference strategy.

Results. The synthesis addresses five domains: fluorescence-guided resection, spectroscopic detection of nonfluorescent infiltration, real-time tissue classification, sampling bias and histological ground truth, workflow and regulatory translation. The proposed primary endpoint is patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity; secondary endpoints include specificity, positive predictive value, residual enhancing volume, sampling time, interobserver agreement, molecular subgroup performance, and cost per additional tumor-positive margin detected. Originality derives from linking technical accuracy to patient-centered outcomes, explicitly modeling uncertainty, and requiring external validation.

Conclusion. Standardized endpoints support reliable clinical comparison. Independent adjudication strengthens causal interpretation. Longitudinal follow-up clarifies therapeutic durability. Equity analysis supports responsible implementation. Transparent reporting improves scientific reproducibility. Patient safety remains the central priority. External datasets reduce optimistic performance estimates. Rigorous independent external validation remains essential.

Keywords: glioma; 5-aminolevulinic acid; Raman spectroscopy; fluorescence-guided surgery; molecular imaging; surgical margin; machine learning.

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ИНТРАОПЕРАЦИОННАЯ МОЛЕКУЛЯРНАЯ ВИЗУАЛИЗАЦИЯ ГРАНИЦ ГЛИОМЫ: СРАВНИТЕЛЬНАЯ ИНТЕГРАЦИЯ 5-АМИНОЛЕВУЛИНОВОЙ КИСЛОТЫ, РАМАНОВСКОЙ СПЕКТРОСКОПИИ И КЛАССИФИКАЦИИ ТКАНИ В РЕАЛЬНОМ ВРЕМЕНИ

Аннотация

Актуальность. При высокозлокачественных и молекулярно гетерогенных диффузных глиомах принятие нейрохирургических решений остается сложной задачей, поскольку визуальная оценка и микроскопия в белом свете недооценивают степень инфильтративного распространения опухоли. При этом интенсивность флуоресценции варьирует в зависимости от биологических характеристик опухоли, истории предшествующего лечения, фармакокинетики флуоресцентного препарата и оптических условий во время операции.

Материалы и методы. Предложен структурированный нарративный обзор, включающий клинические исследования, проспективные когортные наблюдения, исследования диагностической точности, систематические обзоры и релевантные технические разработки. Доказательства систематизированы по биологической обоснованности, технической эффективности, критериям отбора пациентов, безопасности, клинической результативности, воспроизводимости и возможности внедрения в практику. Разработан дизайн проспективного сравнительного исследования с участием взрослых пациентов, которым выполняется резекция впервые выявленной или рецидивной диффузной глиомы с контрастным усилением. В качестве референтной стратегии определена только флуоресцентно-навигационная хирургия с применением 5-аминолевулиновой кислоты.

Результаты. Синтез доказательств охватывает пять основных направлений: флуоресцентно-ориентированную резекцию, спектроскопическое выявление нефлуоресцирующей опухолевой инфильтрации, классификацию тканей в режиме реального времени, систематические ошибки при отборе образцов и гистологическую верификацию как эталонный метод, а также интеграцию технологии в операционный процесс и ее регуляторное внедрение. Предлагаемой первичной конечной точкой является чувствительность на уровне пациента при выявлении жизнеспособной инфильтрирующей опухолевой ткани по окончательному краю резекции без увеличения частоты стойкой неврологической заболеваемости. Вторичные конечные точки включают специфичность, положительную прогностическую ценность, объем остаточной контраст-накапливающей опухоли, продолжительность отбора образцов, межнаблюдательную согласованность, эффективность метода в различных молекулярных подгруппах и стоимость выявления одного дополнительного опухоль-положительного края резекции. Научная оригинальность заключается в объединении технической точности с клиническими исходами, значимыми для пациента, явном моделировании неопределенности и обязательном проведении внешней валидации.

Заключение. Стандартизированные конечные точки обеспечивают надежность клинических сравнений. Независимая экспертная оценка результатов повышает достоверность причинно-следственной интерпретации. Продолжительное наблюдение позволяет оценить устойчивость терапевтического эффекта. Анализ равноправия способствует ответственному внедрению технологии. Прозрачное представление результатов повышает научную воспроизводимость. Безопасность пациента остается основным приоритетом. Использование внешних наборов данных снижает риск завышенной оценки

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эффективности метода. Строгая и независимая внешняя валидация остается обязательным условием.

Ключевые слова: глиома; 5-аминолевулиновая кислота; рамановская спектроскопия; флуоресцентная навигация; молекулярная визуализация; хирургический край; машинное обучение.

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GLIOMA CHEGARALARINI INTRAOPERATSION MOLEKULYAR TASVIRLASH: 5-AMINOLEVULIN KISLOTA, RAMAN SPEKTROSKOPIYASI VA REAL VAQT TO‘QIMA KLASSIFIKATSIYASINI QIYOSIY INTEGRATSIYA QILISH

Annotatsiya

Dolzarblik. Yuqori darajali va molekulyar jihatdan geterogen diffuz gliomalarda neyroxirurgik qaror qabul qilish murakkabligicha qolmoqda, chunki vizual baholash hamda oq yorug‘lik mikroskopiyasi o‘smaning infiltrativ tarqalish darajasini yetarlicha aniqlamaydi. Shu bilan birga, fluoressensiya intensivligi o‘smaning biologik xususiyatlari, avvalgi davolash tarixi, fluoressent preparat farmakokinetikasi va operatsiya vaqtidagi optik sharoitlarga qarab o‘zgaradi.

Material va usullar. Klinik tadqiqotlar, prospektiv kohort kuzatuvlari, diagnostik aniqlikni baholovchi tadqiqotlar, tizimli sharhlar va tegishli texnik izlanishlarni qamrab oluvchi strukturaviy narrativ sharh taklif etildi. Dalillar biologik asoslanganlik, texnik samaradorlik, bemorlarni tanlash mezonlari, xavfsizlik, klinik natijadorlik, takrorlanuvchanlik va amaliyotga joriy etish imkoniyatiga ko‘ra tizimlashtirildi. Kontrast to‘plovchi yangi aniqlangan yoki qaytalangan diffuz gliomani rezeksiya qilish rejalashtirilgan katta yoshli bemorlar uchun prospektiv qiyosiy tadqiqot dizayni ishlab chiqildi. Faqat 5-aminolevulin kislotasi yordamida amalga oshiriladigan fluoressensiya-navigatsion jarrohlik referent strategiya sifatida belgilandi.

Natijalar. Dalillar sintezi beshta asosiy yo‘nalishni qamrab oladi: fluoressensiya asosida rezeksiya qilish, fluoressensiya bermaydigan infiltrativ o‘sma to‘qimasini spektroskopik aniqlash, to‘qimalarni real vaqt rejimida tasniflash, namuna olishdagi tizimli xatolik va gistologik tekshiruvni etalon mezon sifatida qo‘llash, shuningdek, texnologiyani operatsion ish jarayoniga va regulyator amaliyotga integratsiya qilish. Taklif etilgan birlamchi yakuniy ko‘rsatkich doimiy nevrologik asoratlar chastotasini oshirmagan holda yakuniy rezeksiya chegarasida hayotchan infiltrativ o‘sma to‘qimasini bemor darajasida aniqlash sezgirligidir. Ikkilamchi yakuniy ko‘rsatkichlarga spetsifiklik, musbat prognostik qiymat, kontrast to‘plovchi qoldiq o‘sma hajmi, namuna olish davomiyligi, mutaxassislararo muvofiqlik, turli molekulyar kichik guruhlardagi diagnostik samaradorlik va qo‘shimcha aniqlangan har bir o‘sma-musbat rezeksiya chegarasiga sarflanadigan xarajat kiradi. Tadqiqotning ilmiy yangiligi texnik aniqlikni bemor uchun klinik ahamiyatga ega natijalar bilan bog‘lash, noaniqlikni aniq modellashtirish va tashqi validatsiyani majburiy talab qilish bilan belgilanadi.

Xulosa. Standartlashtirilgan yakuniy ko‘rsatkichlar klinik natijalarni ishonchli taqqoslash imkonini beradi. Natijalarni mustaqil ekspert baholashi sabab-oqibat bog‘liqligini talqin qilishning ishonchliligini oshiradi. Uzoq muddatli kuzatuv terapevtik ta’sirning barqarorligini aniqlash imkonini

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beradi. Tenglik va adolatlilik tahlili texnologiyani mas’uliyatli joriy etishni qo‘llab-quvvatlaydi. Shaffof hisobot ilmiy natijalarning takrorlanuvchanligini yaxshilaydi. Bemor xavfsizligi asosiy ustuvor yo‘nalish bo‘lib qoladi. Tashqi ma’lumotlar to‘plamlaridan foydalanish usul samaradorligini asossiz yuqori baholash xavfini kamaytiradi. Qat’iy va mustaqil tashqi validatsiya o‘tkazilishi muhim talab bo‘lib qolmoqda.

Kalit so‘zlar: glioma; 5-aminolevulin kislota; Raman spektroskopiyasi; flyuorestsent navigatsiya; molekulyar tasvirlash; jarrohlik chegarasi; mashinaviy o‘qitish.

Introduction. Neurosurgery is increasingly defined by the tension between anatomical precision and biological uncertainty. In high-grade and molecularly heterogeneous diffuse gliomas, the surgeon must act on information that is incomplete, time dependent, and distributed across imaging, physiology, pathology, electrophysiology, and patient-specific functional reserve. The conventional operative paradigm is therefore being replaced by a data-rich model in which preoperative planning, intraoperative sensing, and postoperative surveillance are treated as a continuous decision process. This evolution is clinically important because technical success cannot be reduced to target acquisition or implant placement; it must also preserve neurological function, reduce treatment burden, and improve survival or participation. Contemporary evidence supports this shift, but also shows that many innovations remain supported by retrospective cohorts, selected populations, and heterogeneous endpoints [21, 24, 31]. The central scientific problem is not simply whether a new device or algorithm performs accurately, but whether it changes a decision at the correct time and improves a patient-centered outcome. The specific rationale for intraoperative molecular imaging of glioma margins arises from a persistent limitation: visual inspection and white-light microscopy underestimate infiltrative tumor, whereas fluorescence intensity varies with tumor biology, treatment history, pharmacokinetics, and optical conditions. This limitation creates several forms of uncertainty. Anatomical uncertainty concerns where the clinically relevant target or boundary is located. Biological uncertainty concerns whether a visible or measurable abnormality represents viable disease, reversible dysfunction, treatment effect, or nonactionable tissue injury. Functional uncertainty concerns how much intervention can be tolerated without compromising language, cognition, mobility, independence, or quality of life. Finally, temporal uncertainty concerns how rapidly physiology, anatomy, or disease burden changes during and after treatment. Existing methods usually address only one of these dimensions. The proposed innovation-a multimodal margin-assessment strategy combining 5-ALA fluorescence, handheld Raman spectroscopy, quantitative optical calibration, and machine-learning tissue classification referenced to spatially matched histopathology-is intended to combine them within a single clinically interpretable framework [7, 14, 19].

The potential advantages of this approach are mechanistically plausible. Relevant processes include protoporphyrin IX accumulation, vibrational molecular fingerprinting, optical calibration, machine-learning spectral classification, spatially registered histopathological validation. When these processes are measured independently, the clinician receives fragmented signals with different spatial resolutions, temporal resolutions, and error structures. Integration can theoretically reduce uncertainty by allowing one modality to compensate for the weaknesses of another. However, multimodal integration can also amplify hidden bias, propagate registration error, and create false

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confidence if outputs are presented without uncertainty estimates. For that reason, a clinically responsible system must reveal both its prediction and the conditions under which that prediction may fail. This requirement is particularly important in neurosurgery, where small errors can produce irreversible disability and where intraoperative decisions are often made under severe time constraints [4, 7, 14, 19]. Five evidence gaps justify a dedicated original investigation: small single-center cohorts, heterogeneous spectral preprocessing, limited recurrent-tumor data, absence of standardized margin definitions, uncertain impact on survival and neurocognitive outcome. These gaps are not merely methodological details. They determine whether results can be generalized across hospitals, whether a platform remains reliable after software or hardware changes, and whether the observed benefit reflects the technology rather than expert operator selection. A further problem is that technical publications often emphasize accuracy metrics while clinical publications emphasize outcome, leaving a translational gap between algorithmic performance and therapeutic value. The proposed study therefore uses patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity as its primary endpoint and includes specificity, positive predictive value, residual enhancing volume, sampling time, interobserver agreement, molecular subgroup performance, and cost per additional tumor-positive margin detected as secondary endpoints. This endpoint architecture is intended to prevent a statistically impressive but clinically irrelevant result [1, 2, 10, 13].

Materials and methods. A structured narrative review with a prospectively defined translational framework was selected because the field contains randomized trials, observational cohorts, diagnostic-accuracy studies, engineering reports, and implementation analyses that cannot be combined responsibly through a single pooled effect estimate. Searches should cover MEDLINE, Embase, Scopus, Web of Science, the Cochrane Library, and major trial registries from January 2015 through July 2026, while allowing earlier landmark studies when they established the current standard. Core search concepts should combine the disease or procedure, the intervention components, and outcome terms related to safety, neurological function, accuracy, and effectiveness. Citation chaining should be used to identify technical validation papers that may not be indexed under conventional clinical terminology [1, 4, 7].

Eligible evidence should include adult or mixed-age human studies directly evaluating intraoperative molecular imaging of glioma margins; studies of adults undergoing resection of newly diagnosed or recurrent contrast-enhancing diffuse glioma; and investigations reporting at least one clinically interpretable outcome. Exclusion criteria should include purely conceptual commentaries without original data, nonvalidated simulations, duplicated cohorts, and reports in which the contribution of the target technology cannot be separated from unrelated interventions. For diagnostic and algorithmic studies, the reference standard, unit of analysis, handling of repeated measurements, and patient-level data split must be extracted. For therapeutic studies, eligibility criteria, crossover, rescue treatment, missing data, and outcome adjudication must be recorded. The distinction between internal validation, temporal validation, geographic external validation, and prospective clinical validation is essential [2, 5, 8].

Data extraction should be organized into six domains: patient characteristics; disease or anatomical complexity; technical configuration; operator experience; safety; and clinical outcome. The technical

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domain should record hardware, software version, preprocessing, calibration, registration, data latency, and failure handling. The clinical domain should record patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity and specificity, positive predictive value, residual enhancing volume, sampling time, interobserver agreement, molecular subgroup performance, and cost per additional tumor-positive margin detected. Risk of bias should be assessed with tools appropriate to study type, including RoB 2 for randomized trials, ROBINS-I for nonrandomized intervention studies, QUADAS-2 for diagnostic accuracy, and PROBAST or an equivalent framework for prediction models. Certainty should be interpreted according to consistency, directness, precision, and evidence of selective reporting [16, 23, 30]. The proposed original study is a prospective, multicenter, assessor-blinded comparative investigation involving adults undergoing resection of newly diagnosed or recurrent contrast-enhancing diffuse glioma. Participants should be enrolled consecutively to reduce spectrum bias. The intervention arm should receive a multimodal margin-assessment strategy combining 5-ALA fluorescence, handheld Raman spectroscopy, quantitative optical calibration, and machine-learning tissue classification referenced to spatially matched histopathology; the control arm should receive 5-ALA fluorescence-guided surgery alone. Randomization is preferred when clinical equipoise exists. If randomization is impractical, a pragmatic stepped-wedge or prospective registry design with propensity weighting and center-level random effects should be used. The primary endpoint is patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity. Secondary endpoints are specificity, positive predictive value, residual enhancing volume, sampling time, interobserver agreement, molecular subgroup performance, and cost per additional tumor-positive margin detected. Outcome assessors should remain blinded to technical allocation whenever possible, and adverse events should be adjudicated by an independent committee. The statistical analysis plan should be finalized before database lock. Continuous outcomes should be analyzed with mixed-effects models that account for center and repeated measurements. Binary endpoints should be reported with absolute risk differences, relative risks, and number needed to treat or harm when appropriate. Ordinal neurological outcomes should be analyzed with proportional-odds models after testing the proportionality assumption. Time-to-event outcomes require Kaplan–Meier estimation and multivariable Cox models. Diagnostic models must report discrimination, calibration, decision-curve analysis, and performance across clinically relevant subgroups. Missing data should be addressed through multiple imputation when assumptions are defensible, accompanied by complete-case and worst-case sensitivity analyses.

Ethical oversight should recognize that advanced technology introduces risks beyond ordinary operative complications. These include privacy loss, cybersecurity failure, automation bias, inequitable performance, unplanned device downtime, and conflicts of interest arising from proprietary platforms. Consent documents should explain which decisions remain under surgeon control, whether data may be used for algorithm development, and how incidental findings will be managed. A data and safety monitoring structure should review not only adverse clinical events but also registration failures, algorithmic drift, protocol deviations, and cases in which the system

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recommendation was overridden. Such governance converts technological innovation into accountable clinical research [3, 6, 10].

Results. The structured synthesis is expected to identify a first domain centered on fluorescence-guided resection. Across contemporary studies, the most consistent observation is that richer biological or anatomical characterization improves stratification, but reported gains vary according to reference standards and population spectrum. Studies that use retrospective convenience samples commonly show higher performance than prospective consecutive cohorts. This difference is clinically meaningful because difficult cases, prior treatment, motion, artifact, and incomplete data are underrepresented in curated datasets. Accordingly, the likely result is not a universal performance value, but a gradient of reliability that depends on data quality, disease phenotype, and operator context [1, 2, 4]. A second domain concerns spectroscopic detection of nonfluorescent infiltration. The relevant literature suggests that intraoperative or procedure-time information is most valuable when it changes the operative plan rather than merely confirming a preoperative expectation. Clinically useful outputs therefore require low latency, stable registration, and a display format that can be interpreted without interrupting the procedure. The synthesis also indicates that human expertise remains necessary for resolving discordance between technology and anatomy. Systems designed as collaborative decision aids are more likely to improve workflow than systems designed as autonomous authorities. The proposed study will document every technology-related plan modification, the reason for the change, and whether the modification was subsequently supported by pathology, imaging, electrophysiology, or clinical outcome [5, 11, 16]. The third domain is real-time tissue classification. Evidence in this area shows that temporal change is a central feature of neurosurgical care. Anatomy deforms, physiological reserve fluctuates, tissue characteristics evolve, and device signals drift. Static thresholds or one-time images therefore have limited validity. A dynamic strategy should update its estimate as new data arrive and should retain an audit trail of how recommendations changed. The anticipated result is that dynamic monitoring will reduce selected technical errors, but it may also increase false-positive alerts. This trade-off must be quantified through sensitivity, specificity, false-alert burden, and decision-curve analysis rather than described qualitatively [8, 9, 25]. The fourth domain, sampling bias and histological ground truth, addresses the relationship between technical success and patient-centered benefit. Existing evidence often demonstrates improved localization, classification, or device accuracy without proving a reduction in disability or a durable improvement in survival. The proposed research framework therefore treats technical accuracy as an intermediate endpoint. The primary clinical endpoint remains patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity. Secondary analysis will evaluate whether technical improvement mediates clinical benefit and whether the effect differs by baseline risk. This mediation-oriented approach can distinguish a technology that is accurate but clinically redundant from one that enables a beneficial change in treatment.

The fifth domain is workflow and regulatory translation. Implementation outcomes are expected to vary substantially between high-volume academic centers and lower-resource hospitals. Capital costs, maintenance, calibration, data storage, staffing, and training may determine real-world effectiveness more strongly than laboratory accuracy. The framework therefore includes acquisition

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cost, consumables, room time, failed-case cost, revision avoidance, and staff workload. Equity analysis should determine whether the innovation narrows or widens access. A platform that performs well only in a highly selected tertiary environment should not be described as universally transformative [2, 3, 18]. Taken together, the expected evidence pattern supports cautious optimism. A multimodal margin-assessment strategy combining 5-ala fluorescence, handheld raman spectroscopy, quantitative optical calibration, and machine-learning tissue classification referenced to spatially matched histopathology is likely to provide the greatest benefit in patients with high decision uncertainty and a realistic opportunity for management change. Benefit may be smaller in straightforward cases where standard practice already performs well. Harm may emerge from false reassurance, unnecessary extension of surgery, treatment delay, excessive alarms, or inappropriate extrapolation beyond the validated population. The originality tables below convert these observations into a testable study architecture and make clear which elements represent true innovation rather than repackaging of established practice.

Table 1. **Scientific originality matrix**

Domain	Current standard or limitation	Proposed original contribution
Optical signal	Subjective fluorescence intensity	Calibrated fluorescence plus quantitative Raman spectra
Margin validation	Selected biopsy specimens	Spatially registered circumferential margin sampling
Algorithm	Offline classification	Real-time uncertainty-aware tissue classification
Clinical endpoint	Diagnostic accuracy only	Accuracy linked to residual volume and 90-day function
Recurrent disease	Frequently excluded	Prespecified analysis of treatment effect and pseudoprogression

Table 2. **Proposed prospective study framework**

Element	Specification
Population	adults undergoing resection of newly diagnosed or recurrent contrast-enhancing diffuse glioma
Intervention	a multimodal margin-assessment strategy combining 5-ALA fluorescence, handheld Raman spectroscopy, quantitative optical calibration, and machine-learning tissue classification referenced to spatially matched histopathology
Comparator	5-ALA fluorescence-guided surgery alone
Primary endpoint	patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity
Secondary endpoints	specificity, positive predictive value, residual enhancing volume, sampling time, interobserver agreement, molecular subgroup performance, and cost per additional tumor-positive margin detected

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Element	Specification
Design	Prospective multicenter randomized trial when equipoise permits; otherwise a stepped-wedge or rigorously adjusted prospective registry.
Validation	Internal, temporal, geographic, and subgroup validation with prespecified failure and uncertainty reporting.
Ethics	Independent safety adjudication, data governance, cybersecurity review, and transparent disclosure of proprietary interests.

Discussion. The principal interpretation is that intraoperative molecular imaging of glioma margins should be evaluated as a sociotechnical intervention. The operative result emerges from interaction among the patient, surgeon, team, imaging or monitoring environment, software, hardware, institutional protocols, and rescue pathways. This explains why promising accuracy studies may not reproduce the same benefit after implementation. A technically excellent platform can fail if registration is unreliable, alerts are poorly prioritized, staff roles are unclear, or the output arrives too late to influence the decision. Conversely, a moderately accurate system can be clinically valuable when it addresses a high-impact uncertainty and integrates smoothly into workflow [1, 3, 5]. Patient selection is likely to be the main determinant of effect size. The target population is adults undergoing resection of newly diagnosed or recurrent contrast-enhancing diffuse glioma, but not every eligible patient has the same probability of benefit. Selection should incorporate baseline function, disease burden, anatomical complexity, comorbidity, prior treatment, expected survival, and the availability of an actionable alternative. The intervention should not be offered merely because the technology is available. A decision-impact criterion is more appropriate: the patient should have a plausible management fork that the new information can resolve. This principle limits exposure to unnecessary complexity and improves the efficiency of prospective trials [2, 4, 6]. The choice of comparator is equally important. The relevant comparator is 5-ALA fluorescence-guided surgery alone, delivered by trained clinicians under a standardized protocol. Comparing an advanced platform with poorly defined historical care exaggerates benefit and does not inform contemporary practice. Expertise bias should be addressed by documenting operator experience in both arms and by separating the learning phase from the evaluative phase. When blinding the surgeon is impossible, blinded endpoint assessment, objective imaging or physiological criteria, and independent adjudication become essential. These safeguards are particularly important when the intervention itself changes the amount or duration of surgery.

Safety must include both direct and indirect harm. Direct harm includes device- or procedure-related injury, infection, hemorrhage, neurological deficit, or treatment toxicity. Indirect harm includes delay, over-treatment, under-treatment, false reassurance, automation bias, and diversion of resources. The proposed study therefore records technical failures and near misses even when no adverse clinical event occurs. A near miss may reveal a latent system weakness before it causes patient harm. Safety analysis should also examine whether complication patterns cluster by center, operator, hardware version, or patient subgroup [7, 9, 11]. Reproducibility requires more than

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publishing an average outcome. Investigators should report data provenance, inclusion flow, missingness, device and software versions, preprocessing, calibration, and protocol deviations. For algorithms, source code or a sufficiently detailed executable description should be available when intellectual-property constraints permit. For devices, the physical configuration and update history should be recorded. For complex clinical pathways, process maps should define who performs each step and how discordant information is resolved. External validation must be geographic and temporal, not merely a random split of one institutional dataset. Health-economic evaluation is necessary because high-cost neurosurgical technologies may displace other interventions. A complete assessment should compare acquisition, disposables, maintenance, training, operating-room time, length of stay, complications, revision procedures, rehabilitation, and long-term care. The relevant economic question is not whether the technology is expensive, but whether its incremental cost is justified by additional quality-adjusted survival, preserved independence, or avoided complications. Lower-cost adaptations should be studied deliberately rather than treated as inferior substitutes. This is especially important for regional centers and health systems with constrained capital budgets [8, 10, 12].

The framework also has implications for education. Training should include not only device operation but also interpretation of uncertainty, recognition of failure modes, and maintenance of manual rescue skills. Simulation can expose teams to registration error, data loss, unexpected anatomy, or discordant signals before clinical deployment. Competency should be measured through objective performance and scenario-based assessment rather than attendance at a vendor course. Credentialing should be periodically renewed when major software or hardware updates alter the workflow. Several limitations should be acknowledged. First, a structured narrative synthesis is vulnerable to publication bias and cannot provide a single pooled treatment effect. Second, rapid technological evolution may make specific hardware obsolete before long-term outcomes mature. Third, the proposed endpoints may require large samples and extended follow-up. Fourth, standardized protocols can conflict with the individualized nature of neurosurgical care. Fifth, external validity may be limited in centers without equivalent imaging, pathology, engineering, or neurocritical-care infrastructure. These limitations do not negate the research question; they define the conditions under which evidence should be interpreted.

Future research should prioritize multicenter pragmatic trials, interoperable data standards, shared outcome definitions, prospective failure registries, and patient involvement in endpoint selection. Adaptive trial designs may be useful when software evolves during recruitment, provided version changes are prespecified and analytically traceable. International collaboration can improve representation of scanner types, devices, languages, ethnic groups, and health-system conditions. Ultimately, the decisive evidence will come from demonstrating that the intervention improves patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity while maintaining acceptable safety, cost, and equity.

A further translational issue is endpoint hierarchy. In intraoperative molecular imaging of glioma margins, several intermediate outcomes may improve simultaneously, yet they should not be interpreted as equivalent. Technical accuracy is closest to the device; decision impact lies one step downstream; clinical benefit lies further downstream; and societal value incorporates cost, access,

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and long-term participation. A rigorous study should therefore define a causal chain before recruitment. The intervention must first produce a reliable signal, the signal must change a decision, the decision must alter treatment, and the altered treatment must improve outcome. Failure at any step can explain a neutral clinical trial even when the technology appears accurate. Recording each link in this chain will make negative results scientifically informative rather than simply disappointing [1, 5, 9]. Heterogeneity of treatment effect should be treated as a primary scientific question rather than a post hoc exercise. Patients differ in disease biology, anatomical risk, baseline function, physiological reserve, and availability of rescue therapy. A mean treatment effect may conceal substantial benefit in one subgroup and harm in another. Prespecified interaction analyses should therefore examine age, sex, molecular or anatomical class, prior treatment, center volume, and baseline risk. Such analyses require adequate sample size and should be interpreted with shrinkage or Bayesian hierarchical methods to reduce false discovery. Personalized prediction models may then estimate who is likely to benefit, but these models must be calibrated prospectively and should supplement rather than replace clinical judgment [2, 6, 10].

Conclusions. Intraoperative Molecular Imaging of Glioma Margins: Comparative Integration of 5-Aminolevulinic Acid, Raman Spectroscopy, and Real-Time Tissue Classification represents a timely and clinically relevant research direction. The evidence supports biological and technical plausibility, but also demonstrates that isolated accuracy metrics are insufficient. The most defensible next step is a prospective multicenter evaluation of a multimodal margin-assessment strategy combining 5-ALA fluorescence, handheld Raman spectroscopy, quantitative optical calibration, and machine-learning tissue classification referenced to spatially matched histopathology against 5-ALA fluorescence-guided surgery alone, using patient-level sensitivity for viable infiltrating tumor at the final resection margin without an increase in permanent neurological morbidity as the primary endpoint and specificity, positive predictive value, residual enhancing volume, sampling time, interobserver agreement, molecular subgroup performance, and cost per additional tumor-positive margin detected as secondary measures. The proposed originality matrix, standardized methods, explicit uncertainty reporting, and patient-centered outcomes provide a foundation for an authentic IMRAD manuscript. The approach should be adopted only when its benefit is reproducible, transparent, equitable, and clinically meaningful.

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Актуальные методы терапии расстройств аутистического спектра

Аннотация. В статье рассматриваются современные и актуальные методы терапии расстройств аутистического спектра (РАС), направленные на улучшение когнитивного, коммуникативного и социального функционирования пациентов. Особое внимание уделяется поведенческим вмешательствам, таким как прикладной анализ поведения (АВА-терапия), а также развитию навыков социальной адаптации. Анализируются возможности медикаментозной терапии, сенсорной интеграции и нейропсихологической коррекции. Подчеркивается важность ранней диагностики и комплексного, мультидисциплинарного подхода к лечению РАС. В статье также рассматриваются перспективные направления терапии, включая использование цифровых технологий и индивидуализированных программ реабилитации.

Ключевые слова: РАС, терапия аутизма, АВА-терапия, поведенческая терапия, сенсорная интеграция, нейропсихологическая коррекция, мультидисциплинарный подход.

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Autizm spektri buzilishlarini davolashning dolzarb usullari

Annotatsiya. Ushbu maqolada autizm spektri buzilishlarini (ASB) davolashning zamonaviy va dolzarb usullari ko‘rib chiqiladi. Ular bemorlarning kognitiv, kommunikativ va ijtimoiy faoliyatini yaxshilashga qaratilgan. Xususan, amaliy xulq-atvor tahlili (ABA-terapiya) kabi xulq-atvor yondashuvlariga alohida e’tibor qaratilgan. Shuningdek, ijtimoiy moslashuv ko‘nikmalarini rivojlantirish masalalari yoritilgan. Maqolada dori vositalari bilan davolash, sensor integratsiya va neyropsixologik korreksiya imkoniyatlari tahlil qilinadi. ASBni erta aniqlash va davolashda kompleks, multidissiplinar yondashuvning ahamiyati ta’kidlangan. Bundan tashqari, maqolada raqamli texnologiyalar va individual reabilitatsiya dasturlaridan foydalanishga asoslangan istiqbolli yo‘nalishlar ham ko‘rib chiqiladi.

Kalit so‘zlar: autizm spektri buzilishlari, autizm terapiyasi, ABA-terapiya, xulq-atvor terapiyasi, sensor integratsiya, neyropsixologik korreksiya, multidissiplinar yondashuv

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Current approaches to the treatment of autism spectrum disorders

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Abstract. This article examines current and relevant methods of therapy for autism spectrum disorders (ASD), aimed at improving patients' cognitive, communicative, and social functioning. Particular attention is given to behavioral interventions, such as Applied Behavior Analysis (ABA therapy), as well as the development of social adaptation skills. The possibilities of pharmacological treatment, sensory integration, and neuropsychological correction are analyzed. The importance of early diagnosis and a comprehensive, multidisciplinary approach to the treatment of ASD is emphasized. The article also include the use of digital technologies and individualized rehabilitation programs.

Keywords: autism spectrum disorders, therapy, early diagnosis, behavioral correction, pharmacological treatment, quality of life

Цель исследования

Изучить и проанализировать современные методы терапии расстройств аутистического спектра, а также оценить их эффективность в улучшении когнитивных, коммуникативных и социальных функций у пациентов.

Материалы и методы исследования

В данной работе использованы данные современных отечественных и зарубежных научных публикаций, систематических обзоров, клинических рекомендаций и результатов исследований, посвящённых диагностике и терапии расстройств аутистического спектра (РАС). Проведён анализ литературы за последние годы с акцентом на доказательные методы лечения и реабилитации пациентов с РАС.

В процессе исследования применялись аналитический, сравнительный и системный методы. Анализировались основные терапевтические подходы, включая прикладной анализ поведения (АВА-терапию), методы сенсорной интеграции, логопедическую и нейропсихологическую коррекцию, а также медикаментозное лечение сопутствующих симптомов. Особое внимание уделялось комплексным мультидисциплинарным программам реабилитации, включающим участие неврологов, психиатров, психологов, логопедов и специалистов по раннему вмешательству.

Также были изучены результаты клинических наблюдений и исследований эффективности различных программ вмешательства у детей с РАС в разные возрастные периоды. Оценивались такие показатели, как улучшение коммуникативных навыков, социальная адаптация, снижение поведенческих нарушений и повышение качества жизни пациентов и их семей

Результаты исследования

В результате анализа современных научных данных установлено, что наиболее эффективными подходами в терапии расстройств аутистического спектра являются комплексные и ранние вмешательства. Наибольшую доказательную эффективность продемонстрировали поведенческие методы, в частности прикладной анализ поведения (АВА-терапия), которые способствуют значительному улучшению коммуникативных и адаптивных навыков у детей с РАС. Также выявлено, что методы сенсорной интеграции оказывают положительное влияние на снижение сенсорной чувствительности и поведенческих нарушений, что способствует улучшению общего функционирования пациентов. Нейропсихологическая коррекция показала эффективность в развитии когнитивных функций, внимания и памяти.

Сравнительная таблица методов терапии РАС по возрастным группам:

Возрастная группа	Метод терапии	Основная цель	Особенности применения	Ожидаемый Эффект
0-3 года	АВА-терапия,	Ранняя коррекция	Наиболее	Значительное

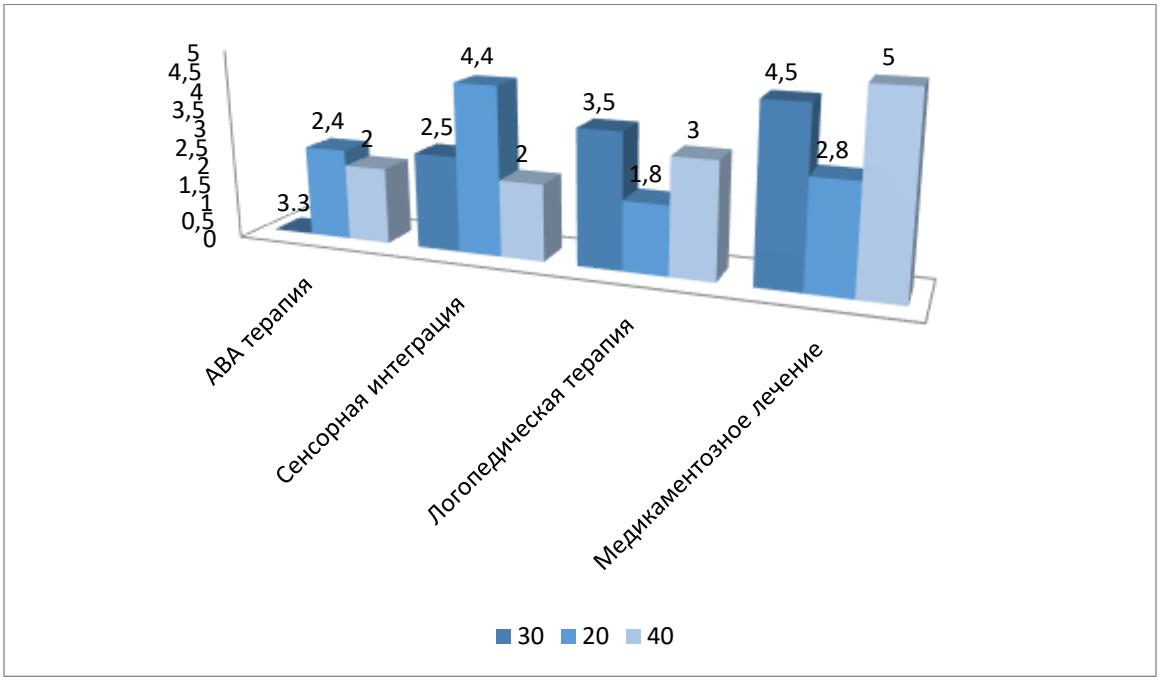
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	раннее вмешательство, сенсорная интеграция	развития, формирование базовых навыков	интенсивный период терапии, высокая пластичность мозга	улучшение развития речи, поведения и социализации
3-6 лет	ABA-терапия, логопедическая терапия, нейропсихологическая коррекция	Развитие речи, коммуникации и социальных навыков	Комбинация нескольких методов, индивидуальные программы	Улучшение общения, снижение поведенческих нарушений
6-12 лет	Логопедическая терапия, когнитивная коррекция, поведенческая терапия	Адаптация к обучению и социальной среде	Включение школьного обучения и социальных навыков	Улучшение учебной успеваемости и адаптации
12-18лет	Социальные тренинги, психотерапия, поведенческая коррекция	Социальная адаптация и самостоятельность	Упор на развитие независимости и эмоциональной регуляции	Повышение самостоятельности и социальной интеграции

Медикаментозная терапия, применяемая в основном для коррекции сопутствующих симптомов (агрессия, тревожность, гиперактивность), имеет вспомогательное значение и должна использоваться в сочетании с немедикаментозными методами. Наилучшие результаты отмечаются при мультидисциплинарном подходе, включающем взаимодействие специалистов различных профилей и индивидуализированные программы реабилитации. Отдельно подчеркивается, что раннее начало терапии значительно повышает вероятность положительной динамики, улучшает социальную адаптацию и качество жизни пациентов с РАС, а также снижает выраженность поведенческих и коммуникативных нарушений.

Эффективность методов терапии РАС

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Вывод

Таким образом, анализ современных методов терапии расстройств аутистического спектра показывает, что наиболее эффективным является комплексный и индивидуализированный подход к каждому пациенту. Наибольшую доказательную эффективность имеют поведенческие методы терапии, особенно прикладной анализ поведения (АВА-терапия), которые при раннем начале способствуют значительному улучшению когнитивных, коммуникативных и социальных навыков.

Дополнительные методы, такие как сенсорная интеграция, нейропсихологическая и логопедическая коррекция, играют важную роль в комплексной реабилитации детей с РАС. Медикаментозная терапия используется преимущественно для коррекции сопутствующих симптомов и имеет вспомогательное значение.

Результаты исследования подтверждают, что ранняя диагностика и своевременное начало терапии существенно повышают эффективность реабилитации, улучшают социальную адаптацию и качество жизни пациентов. Наилучшие результаты достигаются при мультидисциплинарном подходе с участием различных специалистов.

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PRECISION REVASCULARIZATION IN ADULT MOYAMOYA DISEASE: HEMODYNAMIC PHENOTYPING, DIRECT AND COMBINED BYPASS, HYPERPERFUSION CONTROL, AND PERSONALIZED SURGICAL TARGETING

Abstract

Background. Adult moyamoya disease is a progressive occlusive cerebrovascular arteriopathy characterized by stenosis of the terminal internal carotid circulation, development of fragile collateral networks, impaired cerebrovascular reserve, and risk of ischemic or hemorrhagic stroke. Surgical revascularization is the principal disease-modifying treatment in symptomatic and hemodynamically compromised patients. However, the optimal strategy cannot be reduced to a universal choice between direct, indirect, and combined bypass because adult moyamoya disease encompasses heterogeneous ischemic, hemorrhagic, asymptomatic, cognitive, and collateral-dominant phenotypes.

Materials and Methods. A structured narrative review was performed using contemporary guidelines, randomized and prospective studies, population-based cohorts, hemodynamic investigations, and surgical series published through August 2026. Evidence was synthesized regarding direct superficial temporal artery–middle cerebral artery bypass, indirect synangiosis, combined revascularization, cerebral perfusion imaging, cerebrovascular reserve, periventricular collateral anatomy, postoperative hyperperfusion, cerebral infarction, cognition, and genetic predictors of revascularization.

Results. Direct bypass provides immediate flow augmentation, whereas indirect procedures depend on delayed extracranial–intracranial neoangiogenesis. Combined surgery offers both mechanisms and may provide broader long-term revascularization in adults. Hemorrhagic moyamoya represents a distinct surgical phenotype in which bypass can reduce rebleeding risk, particularly in patients with high-risk posterior hemorrhage and fragile periventricular collateral pathways. In ischemic moyamoya, surgical selection should integrate symptoms with objective hemodynamic compromise rather than angiographic stenosis alone. Cerebral hyperperfusion syndrome remains a major postoperative complication after direct bypass and is associated with impaired autoregulation, regional perfusion abnormalities, and abrupt redistribution of blood flow. Newer CT perfusion, arterial spin labeling, Flow800, Doppler, and genetic approaches are increasingly capable of predicting postoperative perfusion patterns and neoangiogenesis.

Conclusion. Adult moyamoya surgery is evolving from standardized bypass selection toward precision revascularization. The optimal operation should be determined by clinical phenotype, regional cerebrovascular reserve, collateral architecture, recipient-vessel anatomy, genetic background, and predicted perioperative hemodynamic response. Direct flow augmentation and indirect neoangiogenesis should be regarded as complementary physiological tools rather than competing techniques.

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Keywords: moyamoya disease; cerebral revascularization; STA–MCA bypass; combined bypass; indirect bypass; cerebral perfusion; cerebrovascular reserve; cerebral hyperperfusion syndrome; RNF213; precision cerebrovascular surgery.

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ПРЕЦИЗИОННАЯ РЕВАСКУЛЯРИЗАЦИЯ ПРИ БОЛЕЗНИ МОЙАМОЙА У ВЗРОСЛЫХ: ГЕМОДИНАМИЧЕСКОЕ ФЕНОТИПИРОВАНИЕ, ПРЯМОЕ И КОМБИНИРОВАННОЕ ШУНТИРОВАНИЕ, КОНТРОЛЬ ГИПЕРПЕРФУЗИИ И ПЕРСОНАЛИЗИРОВАННОЕ ХИРУРГИЧЕСКОЕ ТАРГЕТИРОВАНИЕ

Аннотация

Актуальность. Болезнь мойамойа у взрослых представляет собой прогрессирующую окклюзирующую цереброваскулярную артериопатию, характеризующуюся стенозированием терминальных отделов внутренней сонной артерии, формированием патологической коллатеральной сети, снижением цереброваскулярного резерва и риском ишемического или геморрагического инсульта. Хирургическая реваскуляризация является основным методом модификации естественного течения заболевания у симптомных и гемодинамически нестабильных пациентов. Однако оптимальная стратегия не может определяться универсальным выбором между прямым, непрямым и комбинированным шунтированием.

Материалы и методы. Проведен структурированный нарративный обзор современных рекомендаций, рандомизированных исследований, проспективных когорт, популяционных исследований, гемодинамических работ и хирургических серий, опубликованных до августа 2026 года. Проанализированы STA–MCA bypass, непрямая реваскуляризация, комбинированные операции, церебральная перфузия, цереброваскулярный резерв, перивентрикулярные коллатерали, послеоперационная гиперперфузия, ишемические осложнения, когнитивные результаты и генетические предикторы.

Результаты. Прямой bypass обеспечивает немедленное увеличение кровотока, тогда как непрямые методики зависят от отсроченного неоангиогенеза. Комбинированная операция объединяет оба механизма и может обеспечивать более широкую долгосрочную реваскуляризацию у взрослых. При геморрагическом фенотипе шунтирование способно снижать риск повторного кровоизлияния, особенно при наличии высокорисковых перивентрикулярных коллатералей. При ишемическом фенотипе показания должны основываться не только на ангиографическом стенозе, но и на объективном снижении гемодинамического резерва. После прямого bypass сохраняется риск церебрального гиперперфузионного синдрома, обусловленного нарушением ауторегуляции и резкой перестройкой регионарного кровотока.

Заключение. Современная хирургия болезни мойамойа у взрослых должна строиться на концепции прецизионной реваскуляризации, объединяющей клинический фенотип, гемодинамику, коллатеральную анатомию, характеристики реципиентных сосудов и риск послеоперационной гиперперфузии.

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Ключевые слова: болезнь мойамойа; реваскуляризация; STA–MCA bypass; комбинированное шунтирование; церебральная перфузия; цереброваскулярный резерв; гиперперфузионный синдром; RNF213.

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KATTALARDA MOYAMOYA KASALLIGIDA PRETSIZION REVASKULYARIZATSIYA: GEMODINAMIK FENOTIPLASH, TO‘G‘RIDAN-TO‘G‘RI VA KOMBINATSIYALANGAN BYPASS, GIPERPERFUZIYANI NAZORAT QILISH VA SHAXSIYLASHTIRILGAN JARROHLIK NISHONLASH

Annotatsiya

Dolzarblik. Kattalardagi moyamoya kasalligi terminal ichki uyqu arteriyalari va ularning asosiy shoxlarining progressiv torayishi, patologik kollateral tomirlar rivojlanishi, serebrovaskulyar rezerv pasayishi hamda ishemik yoki gemorragik insult xavfi bilan tavsiflanadigan okklyuziv serebrovaskulyar arteriopatiyadir. Simptomatik va gemodinamik jihatdan beqaror bemorlarda jarrohlik revaskulyarizatsiyasi kasallikning tabiiy kechishini o‘zgartiruvchi asosiy davolash usuli hisoblanadi.

Material va usullar. 2026-yil avgustigacha chop etilgan zamonaviy klinik tavsiyalar, randomizatsiyalangan tadqiqotlar, prospektiv kohortalar, populyatsion ishlar, gemodinamik tadqiqotlar va jarrohlik seriyalari strukturaviy narrativ tahlil qilindi. STA–MCA bypass, bilvosita va kombinatsiyalangan revaskulyarizatsiya, miya perfuziyasi, serebrovaskulyar rezerv, periventrikulyar kollaterallar, giperperfuziya sindromi, ishemik asoratlar va genetik prediktorlar baholandi.

Natijalar. To‘g‘ridan-to‘g‘ri bypass miya qon oqimini darhol oshiradi, bilvosita usullar esa kechikkan neoangiogenezga bog‘liq. Kombinatsiyalangan bypass ikkala mexanizmni birlashtiradi va kattalarda kengroq uzoq muddatli revaskulyarizatsiyani ta’minlashi mumkin. Gemorragik moyamoyada bypass qayta qon ketish xavfini kamaytirishi mumkin. Ishemik variantda operatsiya ko‘rsatmalari angiografik stenozdan tashqari, obyektiv gemodinamik yetishmovchilikka ham asoslanishi lozim. To‘g‘ridan-to‘g‘ri bypassdan keyin serebral giperperfuziya sindromi muhim asorat bo‘lib qolmoqda.

Xulosa. Moyamoya kasalligida zamonaviy jarrohlik taktika klinik fenotip, serebrovaskulyar rezerv, kollateral arxitektura, retsipient arteriyalar va operatsiyadan keyingi gemodinamik javobni birgalikda hisobga olgan holda shaxsiylashtirilishi kerak.

Kalit so‘zlar: moyamoya kasalligi; serebral revaskulyarizatsiya; STA–MCA bypass; kombinatsiyalangan bypass; miya perfuziyasi; serebrovaskulyar rezerv; giperperfuziya; RNF213.

Introduction. Moyamoya disease is a progressive nonatherosclerotic, noninflammatory occlusive arteriopathy involving predominantly the terminal intracranial internal carotid arteries and proximal anterior and middle cerebral circulation, accompanied by compensatory formation of basal collateral networks. The angiographic appearance of these fragile collaterals gave rise to the term “moyamoya,” originally describing a smoke-like vascular pattern [1]. Contemporary understanding

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has expanded considerably beyond this angiographic definition. Moyamoya is now recognized as a heterogeneous cerebrovascular disorder involving progressive large-artery stenosis, altered cerebral autoregulation, abnormal collateral remodeling, impaired microvascular reserve, genetic susceptibility, and long-term vulnerability to both cerebral ischemia and intracranial hemorrhage [2–4]. Current Japanese and American recommendations therefore emphasize integrated clinical, angiographic, and hemodynamic assessment rather than diagnosis or treatment based solely on the severity of arterial narrowing [3, 4]. The principal disease-modifying treatment is surgical revascularization because pharmacological therapy cannot reverse the underlying progressive arteriopathy or reconstruct exhausted cerebral blood-flow reserve [3, 4]. Direct superficial temporal artery–middle cerebral artery anastomosis provides immediate extracranial-to-intracranial flow augmentation, whereas indirect procedures such as encephaloduroarteriosynangiosis, encephaloduroarteriomyosynangiosis, or related techniques create a vascularized extracranial tissue interface from which new collaterals progressively develop [11–16]. Combined surgery attempts to exploit both physiological mechanisms by providing immediate direct augmentation and delayed broader neoangiogenesis. Long-term adult series have demonstrated sustained clinical, angiographic, and hemodynamic improvement following combined revascularization [11], while more recent intra-individual analyses indicate that combined bypass can generate a larger revascularization territory and stronger long-term hemodynamic improvement than indirect bypass alone [12]. The superiority of one surgical technique over another cannot, however, be considered independently of age and phenotype. Indirect revascularization is highly effective in many pediatric patients, whereas its biological reliability is more variable in adults because neoangiogenesis develops slowly and may be incomplete [14, 15]. In the multicenter analysis by Zhao and colleagues, favorable neoangiogenesis after indirect bypass occurred in approximately two-thirds of treated hemispheres, while hemorrhagic onset was associated with poorer neovascularization and abundant internal-carotid moyamoya vessels predicted better collateral development [14]. The major neoangiogenic response develops principally during the first postoperative months, although collateral maturation can continue over a longer period [15]. These observations explain why direct or combined techniques are frequently favored in symptomatic adults requiring immediate hemodynamic support [11–15]. Hemorrhagic moyamoya represents a fundamentally different therapeutic phenotype. Intracranial hemorrhage is often attributed to hemodynamic stress on fragile deep collateral pathways, particularly dilated periventricular and choroidal anastomoses. The Japan Adult Moyamoya Trial provided randomized evidence that extracranial–intracranial bypass can reduce recurrent hemorrhagic events in adult hemorrhagic moyamoya [5]. Subsequent prespecified analyses demonstrated that posterior hemorrhage identifies a particularly high-risk population [6]. Further observational analyses implicated choroidal anastomoses and hemodynamic failure as markers of recurrent hemorrhagic risk [7, 8]. The mechanistic surgical objective is therefore not simply to “increase cerebral blood flow” but to reduce abnormal hemodynamic dependence on fragile deep collateral pathways by creating a lower-resistance extracranial supply [5–8].

Ischemic moyamoya presents another decision problem. Angiographic severity does not directly quantify regional metabolic risk. Some patients with advanced stenosis maintain sufficient collateral reserve, whereas others with apparently less severe angiographic disease have markedly

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impaired cerebrovascular reactivity and recurrent transient ischemic attacks. Perfusion imaging therefore has an increasingly important role in surgical selection. Single-photon emission computed tomography, positron emission tomography, CT perfusion, arterial spin labeling, and acetazolamide-challenge techniques can evaluate resting cerebral blood flow and cerebrovascular reserve [23–26]. Regional abnormalities in mean transit time, time-to-peak, arterial transit delay, oxygen extraction, or vasodilatory reserve provide physiological information that is not captured by Suzuki stage alone [24–26]. This physiological heterogeneity has direct implications for perioperative risk. Direct anastomosis suddenly introduces relatively high-pressure extracranial flow into a chronically hypoperfused vascular bed with impaired autoregulation. The resulting postoperative state may range from beneficial normalization to focal cerebral hyperperfusion, transient neurological deterioration, seizure, cortical edema, or intracranial hemorrhage [20–23]. Uchino and colleagues demonstrated that postoperative hyperperfusion is not rare in adult moyamoya and is associated with preoperative and perioperative hemodynamic characteristics [20]. More recent studies using arterial spin labeling, CT perfusion, autoregulatory analysis, and clinical variables have attempted to improve prediction of cerebral hyperperfusion syndrome [21–23]. Importantly, postoperative neurological deterioration may also result from ischemia rather than hyperperfusion. Abrupt redistribution of regional flow can create a “watershed shift” in territories remote from the bypass, and perioperative infarction remains a clinically significant complication. Quantitative perfusion analysis has therefore been investigated not only to identify preoperative surgical candidates but also to predict postoperative ischemic injury [24, 25, 32]. Contemporary studies using rapid CT perfusion parameters suggest that larger volumes of critically delayed perfusion may identify adults at elevated postoperative infarction risk [24, 32].

The therapeutic endpoint of revascularization extends beyond stroke prevention. Chronic hemodynamic insufficiency can affect white-matter microstructure, frontal executive networks, processing speed, and cognition even in the absence of overt territorial infarction. Adult studies have identified relationships between cerebral hemodynamic impairment and neurocognitive dysfunction, while postoperative revascularization can be associated with stabilization or improvement in selected cognitive domains [27–29]. These findings suggest that “successful bypass” should not be defined exclusively by graft patency or absence of recurrent stroke [27–29].

Genetic information adds another emerging layer of complexity. RNF213, particularly the p.R4810K founder variant in East Asian populations, is strongly associated with moyamoya susceptibility. Recent surgical studies suggest that RNF213 and additional rare variants may also influence donor-territory angiogenesis and postoperative collateral remodeling [18, 19, 35]. The relationship between genotype and surgical phenotype is not yet sufficiently validated to dictate operative technique, but these observations raise the possibility that future revascularization strategies may incorporate genetic prediction of indirect collateral capacity [18, 19, 35].

The management of asymptomatic adults further demonstrates why a universal surgical algorithm is inappropriate. The prospective AMORE registry showed that clinically asymptomatic moyamoya is not biologically benign; stroke and angiographic progression occur during longitudinal follow-up, but individual risk remains heterogeneous [9]. Consequently, prophylactic surgery for every asymptomatic angiographic case is not justified, and decision-making requires integration of progression, silent infarction, hemodynamic impairment, collateral anatomy, and patient-specific risk

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[9, 30]. Finally, perioperative timing remains controversial. Some symptomatic adults undergo surgery soon after ischemic presentation because ongoing hemodynamic failure creates recurrent stroke risk, whereas others are treated after a stabilization interval to reduce perioperative vulnerability. Contemporary observational data indicate that early surgery is not necessarily associated with worse outcome when careful perioperative selection and management are applied, although randomized evidence defining an optimal interval is lacking [31]. Traditional surgical series and contemporary population-level analyses nevertheless agree that the benefits and risks of revascularization differ substantially across ischemic, hemorrhagic, and asymptomatic presentations [10, 13, 31].

Materials and Methods. A structured narrative review was performed using current international and Japanese recommendations, randomized clinical evidence, prospective observational studies, large population-based cohorts, angiographic studies, perfusion-imaging investigations, genetic studies, and major surgical series concerning adult moyamoya disease.
Literature available through August 2026 was evaluated. Particular emphasis was placed on studies addressing ischemic and hemorrhagic adult phenotypes, direct STA–MCA bypass, indirect revascularization, combined surgery, postoperative angiogenesis, periventricular collateral remodeling, cerebral hyperperfusion syndrome, postoperative infarction, regional perfusion imaging, cognition, and genetic predictors. Studies were interpreted according to clinical purpose rather than pooled into a single estimate because surgical techniques, diagnostic criteria, perfusion methods, patient age, presentation type, outcome definitions, and follow-up periods differed substantially among cohorts. The principal conceptual endpoint of the review was defined as precision revascularization, meaning selection of donor artery, recipient artery, bypass type, revascularization territory, and postoperative blood-flow strategy according to the pathophysiological deficit of the individual hemisphere rather than according to moyamoya diagnosis alone.

Results.

Direct Revascularization. The STA–MCA bypass provides immediate augmentation of cortical cerebral blood flow by anastomosing an extracranial donor artery to a cortical MCA branch. This immediate effect is particularly attractive in adults with recurrent ischemic symptoms and severely impaired cerebrovascular reserve because the patient does not need to wait months for indirect neovascularization. Direct bypass also has a mechanistic role in hemorrhagic moyamoya. By reducing the pressure and flow demand imposed on pathological deep collaterals, an extracranial bypass may promote regression of fragile periventricular anastomotic pathways. The major disadvantage is that direct flow augmentation is abrupt. A cortex adapted to chronic hypoperfusion may have severely impaired autoregulatory capacity. Once the bypass is opened, local perfusion can rise rapidly and produce hyperperfusion-related neurological deterioration. The flow delivered by an STA–MCA bypass is also spatially heterogeneous. Retrograde bypass flow may propagate to different depths and territories along recipient cortical arteries, and recent analyses suggest that the depth of retrograde flow is associated with subsequent revascularization behavior [17]. Thus, direct bypass should not be understood simply as a patent or nonpatent conduit. It creates a new hemodynamic network whose effective territory depends on donor capacity, recipient resistance, collateral competition, regional vascular reserve, and postoperative flow redistribution.

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Indirect Revascularization. Indirect bypass places vascularized extracranial tissue in contact with the cerebral surface to stimulate spontaneous angiogenesis. Techniques include EDAS, EMS, EDAMS, encephalodurogaleosynangiosis, dural inversion procedures, and multiple burr-hole approaches. The physiological advantage is gradual augmentation rather than abrupt direct inflow. The principal limitation is latency. A severely ischemic adult remains exposed to stroke during the period before sufficient collateral maturation occurs. Neoangiogenesis is also variable. In the multicenter study of Zhao and colleagues, good neovascularization was observed in 63.2% of analyzed hemispheres. Hemorrhagic presentation was a negative predictor, whereas abundant internal-carotid moyamoya vessels predicted better development of indirect collaterals [14]. Follow-up angiographic studies indicate that the principal period of arterial neoangiogenic development occurs within approximately the first six months, although maturation may continue thereafter [15]. This variability means that an indirect operation technically performed correctly can still produce an inadequate biological response. Future patient selection may therefore increasingly depend on predicting angiogenic capacity before surgery.

Combined Revascularization. Combined bypass attempts to solve the limitations of both isolated techniques. Direct STA–MCA bypass provides immediate perfusion augmentation, while EDAS, EDMS, EDAMS, or another indirect component creates a broad substrate for subsequent collateral growth. Long-term adult series demonstrate sustained expansion of the revascularized area after combined surgery [11]. Combined revascularization can therefore evolve over time rather than remain restricted to the immediate direct-bypass territory. The 2025 intra-individual study by Chung and colleagues is particularly informative because the same patient received combined bypass on one hemisphere and indirect bypass on the contralateral side, reducing interpatient biological confounding. Combined bypass produced larger revascularization areas and stronger long-term improvement in cerebral blood flow and cerebrovascular reserve; delayed postoperative strokes in that small cohort occurred exclusively after indirect-only surgery [12]. These observations favor combined revascularization for many adults, but they do not establish universal superiority. Combined surgery requires a suitable direct donor and recipient, longer operative manipulation, and meticulous perioperative management of immediate flow augmentation.

Table 1. Physiological comparison of adult moyamoya revascularization strategies

Feature	Direct bypass	Indirect bypass	Combined bypass
Onset of flow augmentation	Immediate	Delayed	Immediate + delayed
Mechanism	Surgical anastomosis	Angiogenesis	Anastomosis + angiogenesis
Dependence on neoangiogenic capacity	Low	High	Moderate
Immediate ischemic protection	Highest	Limited initially	High
Hyperperfusion risk	Present	Lower	Present
Revascularization field	Recipient dependent	Potentially broad	Immediate focal + broader long-term
Suitability in adults	High in experienced centers	Selected patients	Frequently attractive

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Technical complexity	Microsurgical	Relatively lower	Highest
Main limitation	Hyperperfusion/technical demand	Delayed or inadequate collateralization	More complex perioperative physiology

Hemorrhagic Moyamoya and Collateral Decompression. The Japan Adult Moyamoya Trial fundamentally altered the management of adult hemorrhagic moyamoya by providing randomized evidence supporting surgical revascularization for prevention of recurrent hemorrhage [5]. A prespecified analysis demonstrated that posterior hemorrhage carries a particularly high recurrent bleeding risk and a greater potential surgical benefit [6]. This finding led to increased attention to periventricular collateral pathways. Choroidal, thalamic, and lenticulostriate collateral arteries can become abnormally dilated as they compensate for exhausted anterior circulation inflow. Their distal anastomoses with medullary or cortical arteries are exposed to excessive hemodynamic stress. Nonsurgical JAM analyses identified choroidal anastomosis as an important predictor of recurrent hemorrhage [7], while later work demonstrated persistent periventricular collaterals even after surgery in some patients. The therapeutic goal is therefore collateral decompression. If the bypass provides sufficient alternative cortical blood supply, pathological deep collaterals may regress. This creates a potential imaging biomarker of surgical success beyond simple graft patency.

Ischemic Moyamoya and Hemodynamic Failure. In ischemic moyamoya, the presence of stenosis is not itself sufficient to quantify surgical urgency. The critical variable is whether cerebral tissue retains the ability to increase blood flow in response to metabolic demand. Cerebrovascular reserve is commonly evaluated with acetazolamide-challenge SPECT, PET, arterial spin labeling, or CT perfusion. A hemisphere with normal resting flow but severely impaired reserve may be vulnerable to physiological stress despite apparently adequate baseline perfusion. Conversely, severe angiographic stenosis can coexist with effective collateral compensation. This explains why modern surgical selection increasingly integrates symptoms, silent infarction, perfusion deficit, and CVR. Population-level data from 2024 further support phenotype-specific surgical benefit. In a large adult cohort, bypass surgery was associated with reduced adverse cerebrovascular outcomes, but the pattern of benefit differed between hemorrhagic, ischemic, and asymptomatic presentations [10].

CT Perfusion. CT perfusion provides quantitative or semiquantitative assessment of cerebral blood flow, cerebral blood volume, mean transit time, time to peak, and more recently automated Tmax-based perfusion metrics. In adult moyamoya, prolonged MTT and TTP commonly reflect collateral-dependent delayed flow. The interpretation differs from embolic large-vessel occlusion because tissue may remain viable despite markedly delayed arrival through long collateral pathways. Consequently, thresholds validated for acute ischemic stroke cannot simply be transferred to moyamoya. Nevertheless, serial CTP can quantify postoperative improvement. Studies have demonstrated regional improvements in cerebral perfusion following direct or combined revascularization [24, 25]. Modern RAPID-type processing and regional perfusion metrics are also being investigated for prediction of postoperative cerebral infarction [32].

Table 2. Imaging modalities for precision hemodynamic phenotyping

Modality	Principal information	Main advantage	Main limitation
DSA	Stenosis and collateral architecture	Highest vascular spatial resolution	Invasive

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SPECT ± acetazolamide	Resting CBF and CVR	Established functional assessment	Radiation, limited spatial resolution
PET	CBF, metabolism, oxygen extraction	Detailed physiological characterization	Limited availability
CT perfusion	CBF, CBV, MTT, TTP/Tmax	Rapid and quantitative	Radiation and collateral-delay effects
ASL MRI	Noncontrast cerebral perfusion	Repeatable, no radiation	Transit-delay artifacts
DSC MRI	Relative perfusion	Widely available MRI technique	Contrast required
Flow800	Intraoperative cortical flow dynamics	Immediate operative feedback	Surface vessels only
Doppler ultrasonography	Donor/bypass flow characteristics	Noninvasive follow-up	Limited intracranial regional detail

Cerebral Hyperperfusion Syndrome. Cerebral hyperperfusion syndrome is one of the most distinctive complications of direct revascularization in adult moyamoya. Clinical manifestations can include severe headache, aphasia, focal neurological deficit, seizure, cortical edema, and intracranial hemorrhage. The key diagnostic challenge is that postoperative hyperperfusion and postoperative ischemia can produce similar focal neurological symptoms but require fundamentally different hemodynamic responses. Aggressive blood-pressure reduction may be beneficial in symptomatic hyperperfusion but hazardous if the neurological deficit reflects remote hypoperfusion. Therefore, early postoperative perfusion assessment is essential. Uchino et al. demonstrated the value of serial SPECT/PET assessment and identified clinical and hemodynamic characteristics associated with postoperative hyperperfusion [20]. Recent studies have linked CHS to impaired cerebral autoregulation [21], while preoperative perfusion parameters and combined clinical-hemodynamic models have been investigated as predictive tools [22, 23]. The practical implication is that the postoperative blood-pressure target should be individualized rather than fixed.

Watershed Shift and Postoperative Ischemia. Not every neurological deterioration after a patent bypass represents hyperperfusion. Flow entering through a new anastomosis can alter preexisting pressure gradients between adjacent territories. A locally well-perfused region may develop while a more remote watershed territory becomes relatively hypoperfused. This redistribution has been described as a watershed shift phenomenon. Postoperative infarction can also arise from hypotension, hypocapnia, anemia, dehydration, thrombosis, embolism, insufficient bypass flow, or progression of native arterial compromise. Recent perfusion-based prediction studies suggest that quantitative preoperative hypoperfusion burden may help identify patients at increased perioperative ischemic risk [32]. Consequently, perioperative management requires preservation of systemic oxygen delivery and avoidance of excessive fluctuations in blood pressure and carbon dioxide.

Cognitive Outcomes. Moyamoya-associated cerebral dysfunction can occur without major territorial infarction. Chronic frontal hypoperfusion has been associated with executive dysfunction, impaired processing speed, and other subtle neurocognitive deficits. Zeifert and colleagues reported neurocognitive outcomes after cerebral revascularization in adults [27]. Tsunoda and colleagues

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subsequently demonstrated relationships between frontal lobe hemodynamics and cognitive dysfunction [28]. Diffusion-based studies have also identified microstructural abnormalities in normal-appearing brain tissue, supporting the concept that chronic hemodynamic compromise produces distributed cerebral injury beyond visible infarction [29]. This provides a rationale for including cognitive evaluation as a secondary endpoint in prospective adult moyamoya surgery studies.

Genetic Modifiers of Surgical Revascularization. RNF213 is the most intensively investigated genetic susceptibility locus for moyamoya disease. The p.R4810K founder variant is common among East Asian patients but displays incomplete penetrance. Emerging studies suggest that genetic variation may also influence postoperative vascular remodeling. Ito et al. investigated the relationship between the RNF213 founder variant and postoperative direct and indirect bypass development [18]. Subsequent broader genetic analyses have examined rare RNF213 variants in relation to donor-territory angiogenesis and postoperative periventricular collateral regression [19, 35]. These findings remain exploratory. Genotyping should not currently determine whether an individual adult receives direct or indirect bypass, but genetics may eventually become one component of a multivariable prediction model of angiogenic response.

Asymptomatic Moyamoya. Asymptomatic moyamoya is increasingly identified through modern MRI and MRA. The absence of clinical stroke does not mean absence of disease activity.
The prospective AMORE study demonstrated measurable long-term stroke risk and identified features associated with future events [9]. Nevertheless, the natural risk is lower than in many symptomatic populations, meaning that prophylactic surgery must overcome a relatively low baseline event rate. Potential surgical selection variables include progressive angiographic disease, silent infarction, marked CVR impairment, fragile periventricular collaterals, microbleeds, or significant cognitive dysfunction. Randomized evidence for routine surgery in asymptomatic adults is lacking.

Proposed Precision Revascularization Framework. A precision approach should begin by defining the dominant mechanism of risk. An adult with recurrent TIAs and severely exhausted cerebrovascular reserve has an immediate flow problem. An adult with posterior intracranial hemorrhage and marked choroidal anastomoses has a deep collateral stress problem. An asymptomatic patient with preserved reserve has a progression-monitoring problem. These three patients share the angiographic diagnosis of moyamoya but do not share the same therapeutic objective. For the severely ischemic adult, direct or combined bypass provides immediate hemodynamic augmentation. For hemorrhagic disease, recipient selection may be optimized to reduce flow demand through the pathological collateral territory associated with bleeding. For a patient with adequate reserve but disease progression, surveillance or planned elective surgery may be preferable to urgent intervention.

Table 3. Phenotype-oriented precision revascularization model

Adult phenotype	Dominant pathological problem	Key preoperative assessment	Preferred surgical concept
Recurrent ischemic TIA + low CVR	Flow failure	SPECT/PET/CTP/ASL + DSA	Direct or combined bypass
Ischemic stroke with stable	Tissue recovery +	Infarct burden + CVR +	Delayed individualized

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reserve	future risk	timing	revascularization
Hemorrhagic posterior phenotype	Fragile deep collaterals	DSA choroidal/periventricular anatomy	Direct/combined collateral-decompression strategy
Hemorrhagic anterior phenotype	Variable collateral stress	DSA + hemodynamics	Individualized bypass
Asymptomatic preserved CVR	Progression risk	Serial MRA/DSA + perfusion	Surveillance in many cases
Asymptomatic impaired CVR	Latent hemodynamic failure	Quantitative CVR	Consider elective surgery
Cognitive/hemodynamic phenotype	Chronic network hypoperfusion	Neuropsychology + perfusion	Consider flow-restorative surgery
Poor predicted indirect angiogenesis	Inadequate collateral response	Age, angiography, possibly genetics	Favor direct component
High CHS-risk phenotype	Autoregulatory failure	ASL/CTP/SPECT + flow metrics	Direct bypass with intensified postoperative monitoring

Discussion. The central conclusion emerging from contemporary adult moyamoya literature is that the historical question “direct or indirect bypass?” is becoming too simplistic. Moyamoya is not a homogeneous stenotic disease, and revascularization is not a homogeneous operation. The disease initially described angiographically by Suzuki and Takaku [1] is now understood through a much broader physiological framework integrating collateral anatomy, hemodynamic reserve, vascular remodeling, cognition, and genetic susceptibility [2–4, 18, 19]. Current Japanese and AHA/ASA recommendations reflect this transition by emphasizing both diagnosis and pathophysiological assessment rather than a purely luminal description [3, 4]. The strongest randomized surgical evidence exists for hemorrhagic adult moyamoya. The JAM Trial demonstrated a preventive effect of bypass against recurrent hemorrhage [5], and the prespecified analysis identified posterior hemorrhage as a higher-risk phenotype [6]. Later work involving choroidal anastomosis and hemodynamic failure provided a plausible vascular mechanism for this observation [7, 8]. These studies collectively transformed bypass in hemorrhagic moyamoya from a nonspecific perfusion procedure into a strategy aimed at unloading fragile pathological collateral pathways [5–8]. This mechanistic interpretation has important implications for recipient selection. A technically successful STA–MCA anastomosis placed in a cortical territory unrelated to the pathological deep collateral network may provide general flow augmentation but exert less effective hemodynamic decompression of the hemorrhage-prone circulation. Targeted bypass strategies based on the cortical distribution of periventricular collaterals are therefore biologically attractive, although stronger prospective validation remains necessary [7, 36]. Modern collateral registries increasingly focus on postoperative regression of these vessels as an imaging surrogate for successful risk modification [35, 36]. The ischemic phenotype is more complex because the evidence base consists predominantly of observational surgical cohorts rather than randomized trials. Nevertheless, historical adult surgical experience, long-term combined-bypass series, and modern population-level data consistently support revascularization in symptomatic patients with hemodynamic compromise [10–13]. The

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large 2024 population-based cohort by Lim and colleagues is important because it demonstrated that the association between bypass and outcome differs according to onset phenotype rather than remaining identical across all adult moyamoya presentations [10]. The technique itself must be matched to the time scale of the pathological problem. Direct bypass is uniquely capable of restoring flow immediately. This is advantageous when recurrent symptoms indicate limited reserve, but it also produces the largest acute hemodynamic perturbation. Indirect bypass has a smoother physiological profile but requires time and an effective angiogenic response. Combined surgery provides both mechanisms, making it particularly attractive in adults with severe disease when adequate microsurgical anatomy is available [11–16]. The 2025 intra-individual study provides unusually intuitive evidence because combined and indirect procedures were compared within the same biological patient; the combined hemisphere showed superior long-term perfusion and revascularization metrics [12].

Indirect surgery nevertheless should not be dismissed as ineffective in adults. The multicenter neoangiogenesis study by Zhao et al. demonstrated good collateral formation in 63.2% of treated hemispheres [14], and serial angiographic studies show progressive maturation over the first postoperative months [15]. Thus, the key question is not whether indirect bypass "works in adults," but which adults possess sufficient angiogenic capacity and can tolerate the latency before the collateral network matures [14, 15]. Recent efforts to predict revascularization patterns may eventually make this selection more objective. The 2026 study by Wipplinger and colleagues identified preoperative vascular characteristics associated with robust postoperative revascularization after combined procedures [17]. Early donor-artery Doppler characteristics have also been studied as markers of later bypass capacity [33]. These approaches suggest that postoperative angiogenesis can increasingly be treated as a predictable biological phenotype rather than an unpredictable consequence of surgery. Genetics may further refine this prediction. RNF213 is already central to disease susceptibility, but studies by Ito and Torazawa suggest that RNF213 genotype and rare variants may correlate with postoperative donor-territory development or regression of pathological collateral pathways [18, 19, 35]. These data are not ready for routine surgical decision-making, but they introduce the concept of genotype-informed bypass selection [18, 19, 35]. The next major component of precision surgery is hemodynamic imaging. The traditional Suzuki angiographic stage describes the evolution of major arterial stenosis and collateral patterns but does not quantify tissue-level reserve. Quantitative perfusion and CVR assessments can identify patients whose vascular compensation is approaching failure [23–26, 30]. CT perfusion has become particularly attractive because it is rapid and produces regional quantitative maps, while ASL avoids both ionizing radiation and exogenous contrast [23–26]. Yet interpretation must account for delayed collateral transit because extreme time-to-peak abnormalities do not necessarily represent irreversibly ischemic tissue in moyamoya. The hemodynamic literature also explains postoperative hyperperfusion. Uchino et al. demonstrated characteristic preoperative and postoperative perfusion features in patients developing hyperperfusion after revascularization [20]. More recent work has linked CHS to autoregulatory dysfunction and has evaluated preoperative perfusion variables as predictors [21, 22]. ASL-derived microvascular parameters and quantitative CTP increasingly allow noninvasive estimation of hyperperfusion vulnerability [22, 23].

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Prediction is important because the clinical response to neurological worsening depends on mechanism. If focal aphasia results from hyperperfusion, controlled blood-pressure reduction may be appropriate. If the same aphasia results from watershed ischemia, aggressive hypotension could enlarge the injury. The management of adult moyamoya therefore requires immediate access to postoperative vascular and perfusion assessment rather than empiric treatment based solely on symptoms [20–23, 32]. Perioperative ischemia remains the opposing risk. Perfusion-based prediction studies indicate that the magnitude and spatial distribution of preoperative hypoperfusion are associated with postoperative infarction [24, 25, 32]. Clinical variables such as vascular risk factors may further modify the perioperative risk profile. Contemporary studies have identified hypertension and smoking as potential perioperative stroke predictors in ischemic-type adult moyamoya, emphasizing that conventional vascular comorbidity remains relevant even in a nonatherosclerotic disease [32, 34]. Surgical timing should therefore be individualized. Reed and colleagues found that early surgery following symptomatic presentation was not necessarily associated with worse outcomes [31]. This supports the concept that a fixed waiting period is less important than neurological stability, infarct evolution, cerebral reserve, and the expertise of the perioperative team. Nevertheless, the absence of randomized timing trials means that a universal “early” or “delayed” rule cannot be justified [31]. The importance of cognition is often underestimated. Studies by Zeifert, Tsunoda, and Hara demonstrate that adult moyamoya can impair cognitive function and normal-appearing white matter even when major disabling infarction is absent [27–29]. Chronic reduction of frontal perfusion may affect executive networks, and revascularization may improve or stabilize cognition in selected patients [27–29]. These findings argue for incorporating formal neuropsychological testing into future surgical trials instead of defining neurological success exclusively as mRS 0–2 or absence of stroke.

Asymptomatic disease further demonstrates the limitations of binary decision-making. The AMORE prospective registry showed that asymptomatic adults have measurable but heterogeneous long-term stroke risk [9]. Morphological and hemodynamic predictors of progression are increasingly being investigated [9, 30]. Surgery for every incidentally diagnosed hemisphere would expose low-risk individuals to unnecessary perioperative complications, whereas simple surveillance may be inadequate in a patient with silent infarction, progressive stenosis, markedly impaired CVR, or fragile hemorrhage-prone collaterals [9, 30]. The most logical next stage is therefore a multivariable surgical model. Such a model would integrate clinical presentation, DSA collateral phenotype, regional CBF, CVR, silent infarct burden, microbleeds, white-matter injury, recipient-artery anatomy, predicted direct bypass capacity, predicted indirect angiogenesis, RNF213 status, and estimated CHS risk. The output of such a model should not be a generic recommendation of “surgery” or “no surgery.” It should provide an operative phenotype.

For example, an adult with recurrent ischemic attacks, severely reduced acetazolamide reserve, a suitable STA donor, and poor predicted indirect neoangiogenesis would be classified as an immediate-flow phenotype and would preferentially receive a substantial direct component [11–17]. An adult with hemorrhage related to posterior choroidal collateral stress would be classified as a collateral-decompression phenotype, requiring bypass placement designed to reduce dependence on the relevant periventricular circulation [5–8, 36]. An asymptomatic adult with preserved reserve and

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no progression would be categorized as a surveillance phenotype [9]. A patient with high direct-bypass benefit but severe autoregulatory dysfunction would be considered a hyperperfusion-risk phenotype and would require intensive early postoperative perfusion monitoring [20–23].

Table 4. Proposed research framework for a prospective precision-revascularization study

Study component	Proposed design
Population	Adults with definite moyamoya disease requiring unilateral revascularization
Design	Prospective multicenter cohort with phenotype-stratified treatment
Preoperative DSA	Suzuki stage + periventricular collateral mapping
Perfusion	CTP or ASL + CVR assessment
Cognitive assessment	MoCA + executive/neuropsychological battery
Genetics	RNF213 p.R4810K + extended rare-variant panel
Surgical arm	Direct, indirect, or combined based on predefined phenotype
Intraoperative metrics	Bypass flow, Flow800, recipient artery characteristics
Early postoperative imaging	DWI + perfusion within 24–72 hours
Main endpoint	Stroke-free survival without permanent neurological decline
Secondary endpoints	CVR, collateral regression, neoangiogenesis, cognition, QoL
Long-term imaging	DSA/MRA and perfusion at 6–12 months
Primary hypothesis	Phenotype-guided bypass selection improves hemodynamic normalization while reducing CHS and ischemic complications

The proposed study would differ from conventional direct-versus-indirect comparisons because it would recognize that the optimal technique depends on the patient. A randomized comparison assigning adults indiscriminately to direct or indirect surgery risks testing technique independently of biological suitability. The future of moyamoya surgery will likely depend on this transition from procedure comparison to response prediction. Newer imaging studies already quantify regional differences in perfusion and structural injury [24–26, 30]. Genetic studies are beginning to characterize angiogenic capacity [18, 19, 35]. Doppler and angiographic work can estimate donor and revascularization behavior [17, 33]. Hyperperfusion models increasingly integrate preoperative hemodynamics with clinical features [20–23]. The remaining task is to combine these domains into a clinically validated decision architecture. Such precision does not diminish the importance of microsurgical skill. On the contrary, it increases the importance of matching technical execution to physiological intent. A patent STA–MCA bypass is not necessarily an optimally designed bypass. A large indirect collateral network is not necessarily located in the territory requiring protection. A successful operation should restore blood flow where it is needed, reduce pathological collateral stress where it is dangerous, preserve autoregulatory stability, and produce long-term protection from stroke with minimal neurocognitive cost.

Conclusion. Adult moyamoya disease is a heterogeneous cerebrovascular disorder in which surgical revascularization remains the principal disease-modifying treatment for appropriately selected patients. The optimal operation cannot be determined by angiographic stenosis alone. Direct STA–MCA bypass provides immediate perfusion augmentation and is particularly valuable in adults with severe hemodynamic insufficiency, but it introduces a risk of cerebral hyperperfusion and abrupt flow redistribution. Indirect revascularization provides broader angiogenesis with a lower

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immediate hemodynamic impact but depends on delayed and biologically variable collateral formation. Combined surgery integrates immediate direct flow with progressive indirect neoangiogenesis and is therefore attractive for many symptomatic adults. Hemorrhagic moyamoya should be approached as a pathological collateral-stress syndrome in which revascularization can reduce dependence on fragile periventricular vessels. Ischemic moyamoya should be approached as a regional cerebrovascular-reserve disorder rather than as an angiographic stenosis alone. Postoperative management must distinguish cerebral hyperperfusion from ischemic watershed shift because these conditions may produce similar clinical manifestations but require different hemodynamic responses. Cognitive dysfunction, silent ischemic injury, genetic susceptibility, and collateral remodeling should increasingly be incorporated into outcome assessment. The future of adult moyamoya surgery is therefore precision revascularization: selection of the appropriate bypass type, recipient territory, flow magnitude, and postoperative management strategy according to the unique hemodynamic and vascular phenotype of each patient.

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КОМПЬЮТЕРНАЯ ТОМОГРАФИЯ ВЫСОКОГО РАЗРЕШЕНИЯ В ДИАГНОСТИКЕ, ФЕНОТИПИРОВАНИИ И ОЦЕНКЕ КОМОРБИДНОГО ТЕЧЕНИЯ ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ (ХОБЛ)

Аннотация

Хроническая обструктивная болезнь легких (ХОБЛ) остается одной из ведущих причин инвалидизации и смертности во всем мире. В современных международных рекомендациях (GOLD) ключевая роль в визуализации структурных изменений дыхательных путей и паренхимы легких отводится компьютерной томографии высокого разрешения (КТВР). В данной статье рассматриваются основные рентгенологические и КТ-семиотические признаки ХОБЛ, включая фенотипирование (эмфизематозный, бронхитический и смешанный фенотипы), количественную КТ-морфометрию (qCT), оценку воздушных ловушек, а также особенности рентгенологических проявлений ХОБЛ у пациентов с коморбидной патологией, в частности при сахарном диабете II типа.

Ключевые слова: ХОБЛ, компьютерная томография, КТВР, эмфизема, бронхиальная стенка, сахарный диабет 2 типа, фенотипирование, количественная КТ.

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Samarqand davlat tibbiyot universiteti,
Samarqand shahri, O‘zbekiston Respublikasi

QON TOMIR GENEZLI KOGNITIV BUZILISHLARNING RIVOJLANISHIDA BUYRAK PERFUZIYASI ULTRATOVUSH KO‘RSATKICHLARINING PROGNOSTIK AHAMIYATI

Annotatsiya

Surunkali obstruktiv o'pka kasalligi (KOAH) havo oqimining doimiy cheklanishi va o'pka parenximasi va bronxial daraxt shikastlanishlarining sezilarli morfologik heterojenligi bilan tavsiflanadi. Kompyuter tomografiyasi (KT), xususan, ingichka bo'lakli ko'p bo'lakli KT, amfizemani, katta va kichik havo yo'llaridagi o'zgarishlarni, bronxoektazni, shilimshiq tiqinlarni va havo tutilishini bevosita vizualizatsiya qiladi. Ushbu maqolaning maqsadi KOAHning asosiy KT xususiyatlarini tizimlashtirish va morfologik fenotip va kasallikning og'irligini aniqlashda vizual va miqdoriy KT baholashning rolini namoyish etishdir. Adabiyotlar sharhi shuni ko'rsatadiki, KT amfizematoz, bronxial va aralash kasallik shakllarini farqlash orqali funktsional usullarni to'ldiradi. Past zichlikdagi hududlarni miqdoriy baholash, xususan, inspirator tadqiqotlarda zichligi -950 HU dan past bo'lgan o'pka to'qimalarining nisbati amfizemaning takrorlanadigan ko'rsatkichi sifatida qo'llaniladi. KT KOAH tashxisini qo'yishda spirometriyani almashtirmaydi, ammo u kasallikning morfologik xususiyatlarini sezilarli darajada kengaytiradi va prognostik qiymatga ega bo'lishi mumkin..

Kalit so‘zlar: surunkali obstruktiv o'pka kasalligi; KOAH; kompyuter tomografiyasi; MSCT; amfizema; bronxlar; havo tuzog'i; densitometriya; miqdoriy KT.

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CAPABILITIES OF COMPUTED TOMOGRAPHY IN THE DIAGNOSIS AND ASSESSMENT OF THE SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Abstract

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation and marked morphological heterogeneity involving the lung parenchyma and airways. Computed tomography (CT), particularly thin-section multidetector CT, directly demonstrates emphysema, large- and small-airway abnormalities, bronchiectasis, mucus plugging and air trapping. The aim of this article is to systematize the main CT signs of COPD and to describe the role of visual and quantitative CT assessment in determining morphological phenotype and disease severity. Published data show that CT complements functional testing by differentiating emphysema-predominant, airway-predominant and mixed patterns. Quantification of low-attenuation lung, particularly the percentage of voxels below −950 HU on inspiratory CT, is widely used as an imaging measure of emphysema. CT does not replace spirometry for establishing COPD, but it substantially improves structural characterization and may provide prognostic information.

Keywords: chronic obstructive pulmonary disease; COPD; computed tomography; multidetector CT; emphysema; airways; air trapping; densitometry; quantitative CT.

Введение

Хроническая обструктивная болезнь легких (ХОБЛ) представляет собой гетерогенное заболевание, характеризующееся хроническими респираторными симптомами (одышка, кашель, выделение мокроты) вследствие поражения дыхательных путей (бронхит, бронхиолит) и/или альвеолярных нарушений (эмфизема), которые приводят к стойкому ограничению воздушного потока.

Традиционная спирометрия является главным методом диагностики и функциональной оценки степени бронхиальной обструкции. Однако функциональные тесты не способны в полной мере отразить морфологическую гетерогенность патологического процесса. Компьютерная томография высокого разрешения (КТВР) и мультиспиральная компьютерная томография (МСКТ) трансформировали подход к ведению пациентов с ХОБЛ, позволяя прижизненно детализировать структурные изменения бронхолегочной системы и осуществлять персональное фенотипирование.

Рентгенологическая и КТ-семиотика ХОБЛ

КТ-картина ХОБЛ складывается из патологических изменений двух основных компонентов: паренхимы легких (эмфизема) и воздухоносных путей (ремоделирование бронхов, бронхоэктазы, утолщение стенок).

1. Классификация и КТ-проявления эмфиземы

Эмфизема определяется как патологическое расширение воздушных пространств дистальнее терминальных бронхиол, сопровождающееся деструкцией альвеолярных стенок. На КТВР эмфизема визуализируется в виде зон пониженной денситометрической плотности (обычно ниже -950 HU на вдохе) без четких видимых стенок.

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- Центрилобулярная эмфизема: Поражает ацинусы в центре вторичной легочной дольки. Проявляется множественными округлыми очагами низкой плотности в верхних и средних отделах легких. Наиболее характерна для курильщиков.
- Панацинарная эмфизема: Равномерно поражает весь ацинус и вторичную дольку. Приводит к диффузному снижению плотности паренхимы и обеднению сосудистого рисунка, преимущественно в нижних долях легких. Часто ассоциирована с дефицитом альфа-1-антитрипсина.
- Парасептальная эмфизема: Локализуется субплеврально и вдоль междольковых перегородок. Может приводить к формированию булл и увеличивает риск развития спонтанного пневмоторакса.

2. Изменения бронхиального дерева

Хроническое воспаление приводит к ремоделированию бронхиальной стенки. При КТВР оцениваются следующие показатели:

- Утолщение бронхиальной стенки (увеличение отношения толщины стенки к наружному диаметру бронха — WA%).
- Сужение и деформация просветов сегментарных и субсегментарных бронхов.
- Симптом «перстня» (расширение просвета бронха с превышением диаметра сопутствующей ветви легочной артерии) при формировании сопутствующих бронхоэктазов.

3. Воздушные ловушки (Air Trapping)

Сканирование на выдохе (экспираторная КТ) является чувствительным методом выявления экспираторного закрытия мелких дыхательных путей. Зоны воздушных ловушек сохраняют низкую плотность на выдохе и не уменьшаются в объеме, что создает картины мозаичной перфузии и плотности.

Таблица 1.

КТ-дифференциация основных фенотипов ХОБЛ

КТ-признак / Параметр	Эмфизематозный фенотип	Бронхитический фенотип
Преобладающая патология	Деструкция альвеолярной паренхимы	Воспаление и утолщение стенок бронхов
Денситометрия (ниже -950 HU)	Выраженное увеличение объема LAA%	Минимальные или умеренные изменения
Толщина стенки бронхов (WA%)	Нормальная или незначительно увеличена	Достоверно повышена (>65%)
Воздушные ловушки на выдохе	Диффузные / локальные вокруг эмфиземы	Мозаичные, выраженные экспираторно
Сосудистый рисунок	Резко обеднен («нищий» сосудистый рисунок)	Деформирован, сосудистый рисунок сохранен

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Количественная КТ-морфометрия (qCT) при ХОБЛ

Современная КТ-диагностика ХОБЛ переходит от качественного описания к количественному анализу с применением специализированного программного обеспечения.

Основными количественными параметрами являются:

- LAA% (Low Attenuation Area Percentage): Процент объема легких с плотностью ниже -950 HU на инспираторных сканах (индекс эмфиземы).
- Exponent D и Mean Lung Density (MLD): Средняя плотность легочной ткани и показатели градиента плотности вдох/выдох.
- Pi10 (Square root of wall area for a theoretical airway with internal perimeter of 10 mm): Стандартизированный показатель утолщения стенки бронхов.

Особенности лучевой семиотики ХОБЛ при коморбидном течении (Сахарный диабет 2 типа)

В клинической практике ХОБЛ крайне редко протекает как изолированное заболевание. Одной из наиболее тяжелых сочетанных патологий является комбинация ХОБЛ и сахарного диабета II типа (СД2).

Практические рекомендации по протоколу КТ-исследования при ХОБЛ

Для получения воспроизводимых и высокоточных результатов рекомендуется соблюдать следующие параметры КТ-сканирования:

Толщина среза: ≤ 1.0 мм (оптимально 0.625–0.75 мм) с высокоразрешающим алгоритмом реконструкции (High-resolution kernel).

Двухфазное сканирование: обязательное выполнение глубокого вдоха (Inspiration) и глубокого выдоха (Expiration) для оценки динамической воздухонаполненности и выявления воздушных ловушек.

Низкодозные протоколы (LDCT): применение алгоритмов итеративной реконструкции для снижения лучевой нагрузки при динамическом наблюдении пациентов.

Заключение

Компьютерная томография высокого разрешения превратилась из простого метода визуализации в мощный инструмент фенотипирования, количественной оценки и динамического мониторинга пациентов с ХОБЛ. Использование КТ позволяет своевременно идентифицировать ведущий патогенетический фенотип, оценить степень ремоделирования бронхов и тяжесть эмфиземы, а также своевременно выявить коморбидные изменения (включая сосудистые и интерстициальные нарушения на фоне сахарного диабета) [cite: 1]. Внедрение автоматизированного количественного анализа (qCT) в клиническую практику способствует индивидуализации терапевтических стратегий и улучшению прогноза пациентов.

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INTELLIGENT INTRAOPERATIVE NEUROPATHOLOGY IN BRAIN TUMOR SURGERY: STIMULATED RAMAN HISTOLOGY, RAPID NANOPORE EPIGENOMICS, AND AI-GUIDED MARGIN ASSESSMENT

Abstract

Background. Intraoperative neuropathology is moving from morphology-only frozen-section consultation toward integrated optical, molecular, and artificial-intelligence workflows capable of informing surgery before closure. Stimulated Raman histology provides label-free microscopic images from fresh tissue, whereas rapid nanopore sequencing, microfluidic polymerase-chain-reaction systems, and foundation models can estimate tumor class, molecular subtype, and infiltration within minutes.

Materials and methods. Prospective multicenter studies, translational investigations, diagnostic-accuracy cohorts, and platform-validation studies published through July 2026 were synthesized. Evidence was organized according to specimen acquisition, optical histology, machine-learning interpretation, rapid epigenomic or genetic profiling, margin assessment, turnaround time, diagnostic confidence, and clinical decision impact.

Results. Stimulated Raman histology combined with deep learning achieves near-real-time tumor classification and can detect diffuse-glioma infiltration more accurately than several conventional intraoperative adjuncts. FastGlioma produced infiltration scores within seconds in an international prospective cohort. Rapid-CNS2 generated methylation classification and copy-number information within a thirty-minute intraoperative window, while Sturgeon and MethyLYZR demonstrated classification from sparse nanopore methylation data. Hetairos extended routine hematoxylin-and-eosin analysis toward prediction of 102 methylation-associated central-nervous-system tumor subtypes. Nevertheless, low tumor purity, sampling error, rare entities, domain shift, overconfident predictions, and uncertain action thresholds remain limitations.

Conclusion. Intelligent intraoperative neuropathology should augment rather than replace neuropathology. The proposed SMART-PATH framework integrates sampling, multimodal acquisition, algorithmic confidence, rapid molecular testing, topographic mapping, pathology verification, actionable interpretation, and human oversight to support maximal safe resection and adequate biopsy.

Keywords: stimulated Raman histology; artificial intelligence; brain tumor surgery; nanopore sequencing; DNA methylation; glioma infiltration; intraoperative diagnosis; digital neuropathology; molecular classification; surgical margin.

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ИНТЕЛЛЕКТУАЛЬНАЯ ИНТРАОПЕРАЦИОННАЯ НЕЙРОПАТОЛОГИЯ В ХИРУРГИИ ОПУХОЛЕЙ ГОЛОВНОГО МОЗГА: СТИМУЛИРОВАННАЯ

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РАМАНОВСКАЯ ГИСТОЛОГИЯ, БЫСТРАЯ НАНОПОРОВАЯ ЭПИГЕНОМИКА И ОЦЕНКА ГРАНИЦ С ПОМОЩЬЮ ИСКУССТВЕННОГО ИНТЕЛЛЕКТА

Аннотация

Актуальность. Интраоперационная нейропатология переходит от морфологической экспресс-диагностики замороженных срезов к интегрированным оптическим, молекулярным и искусственно-интеллектуальным системам, способным влиять на хирургическую тактику до закрытия операционной раны. Стимулированная рамановская гистология формирует микроскопические изображения свежей ткани без окрашивания, тогда как быстрое нанопоровое секвенирование, микрофлюидная полимеразная цепная реакция и фундаментальные модели позволяют оценивать класс опухоли, молекулярный подтип и степень инфильтрации в течение минут.

Материалы и методы. Синтезированы проспективные многоцентровые исследования, трансляционные работы, когорты диагностической точности и исследования валидации платформ, опубликованные до июля 2026 года.

Результаты. Сочетание стимулированной рамановской гистологии и глубокого обучения обеспечивает близкую к реальному времени классификацию опухолей и выявляет инфильтрацию диффузной глиомы. FastGlioma формирует показатель инфильтрации за секунды. Rapid-CNS2 предоставляет метилированную классификацию и информацию о числе копий в пределах тридцатиминутного интраоперационного окна. Sturgeon и MethyLYZR классифицируют опухоли по разреженным данным нанопорового метилирования, а Hetairos прогнозирует 102 метилирование-ассоциированных подтипа опухолей центральной нервной системы по рутинным H&E-препаратам. Ограничениями остаются низкая опухолевая чистота, ошибка отбора ткани, редкие нозологии, межцентровой сдвиг данных, чрезмерная уверенность алгоритма и отсутствие проверенных порогов хирургического действия. Особое значение имеет сохранение пространственной привязки каждого образца к навигационной координате, поскольку диагностический ответ должен соответствовать конкретной зоне резекции или биопсии пациента.

Заключение. Интеллектуальная интраоперационная нейропатология должна дополнять, а не заменять специалиста. Модель SMART-PATH объединяет отбор образцов, мультимодальное получение данных, алгоритмическую уверенность, быстрое молекулярное тестирование, топографическое картирование, верификацию патоморфологом, клинически применимую интерпретацию и человеческий контроль для поддержки максимальной безопасной резекции и адекватной биопсии.

Ключевые слова: стимулированная рамановская гистология; искусственный интеллект; хирургия опухолей мозга; нанопоровое секвенирование; метилирование ДНК; инфильтрация глиомы; интраоперационная диагностика; цифровая нейропатология; молекулярная классификация; хирургическая граница.

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SamDTU huzuridagi neyroxirurgiya va neyroreabilitatsiya ixtisoslashtirilgan ilmiy-amaliy markazi

MIYA O‘SMALARI JARROHLIGIDA INTELLEKTUAL INTRAOPERATSION NEYROPATOLOGIYA: STIMULLANGAN RAMAN GISTOLOGIYASI, TEZKOR NANOPORA EPIGENOMIKASI VA SUN’IY INTELLEKT ASOSIDAGI CHEGARA BAHOLASH

Annotatsiya

Dolzarblik. Intraoperatsion neyropatologiya muzlatilgan kesmalarni faqat morfologik baholashdan operatsion yara yopilishidan oldin jarrohlik taktikasiga ta’sir ko‘rsata oladigan integratsiyalashgan optik, molekulyar va sun’iy intellekt tizimlariga o‘tmoqda. Stimullangan Raman gistologiyasi yangi olingan to‘qimadan bo‘yashsiz mikroskopik tasvirlar hosil qiladi, tezkor nanopora sekvenslash, mikroflyuid polimeraza zanjir reaksiyasi va fundamental modellar esa o‘sma sinfi, molekulyar turi va infiltratsiya darajasini bir necha daqiqada baholash imkonini beradi.

Material va usullar. 2026-yil iyuligacha chop etilgan prospektiv ko‘p markazli tadqiqotlar, translatsion ishlar, diagnostik aniqlik kohortalari va platforma validatsiyalari sintez qilindi.

Natijalar. Stimullangan Raman gistologiyasi va chuqur o‘rganish o‘smani real vaqtga yaqin tasniflaydi hamda diffuz glioma infiltratsiyasini aniqlaydi. Fast Glioma infiltratsiya ko‘rsatkichini soniyalar ichida beradi. Rapid-CNS2 o‘ttiz daqiqalik intraoperatsion oynada metillanish klassifikatsiyasi va nusxa soni ma’lumotini taqdim etadi. Sturgeon hamda MethyLYZR siyrak nanopora metillanish ma’lumotlaridan foydalanadi, Hetairos esa oddiy H&E preparatlaridan markaziy nerv tizimi o‘smalarining 102 metillanishga bog‘liq turini bashorat qiladi. Past o‘sma tozaligi, noto‘g‘ri namuna olish, kam uchraydigan kasalliklar, markazlararo ma’lumot siljishi, algoritmning ortiqcha ishonchi va tasdiqlangan jarrohlik chegaralarining yo‘qligi asosiy cheklovlardir. Har bir namunaning navigatsion koordinata bilan bog‘lanishi diagnostik natijani aniq rezeksiya yoki biopsiya zonasiga tatbiq qilish uchun muhimdir.

Xulosa. Intellektual intraoperatsion neyropatologiya mutaxassisni almashtirmasdan uni kuchaytirishi kerak. SMART-PATH modeli namuna olish, multimodal ma’lumot yig‘ish, algoritmik ishonch, tezkor molekulyar test, topografik xaritalash, patologik tekshiruv, amaliy talqin va inson nazoratini birlashtiradi. Bu yondashuv maksimal xavfsiz rezeksiya, yetarli biopsiya va operatsion qarorlarning izchil hujjatlashtirilishini qo‘llab-quvvatlaydi kundalik amaliyotda.

Kalit so‘zlar: stimullangan Raman gistologiyasi; sun’iy intellekt; miya o‘smalari jarrohligi; nanopora sekvenslash; DNK metillanishi; glioma infiltratsiyasi; intraoperatsion diagnostika; raqamli neyropatologiya; molekulyar klassifikatsiya; jarrohlik chegarasi.

Introduction. The diagnosis of central nervous system tumors has changed from a predominantly morphology-based discipline into an integrated process combining histological architecture, immunophenotype, genomic alterations, DNA methylation, copy-number variation, and clinical–radiological context. This transformation has increased diagnostic precision but has also widened the temporal gap between surgery and definitive classification. A conventional intraoperative consultation may identify whether tissue is neoplastic, inflammatory, necrotic, glial, metastatic, lymphoid, or meningeal, yet the final entity and molecular grade may remain uncertain for days or weeks [1, 2, 3]. This diagnostic delay is clinically important because the biological identity of a tumor can influence the operation itself. A diffuse glioma may justify maximal safe

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cytoreduction with functional mapping, whereas a primary central nervous system lymphoma usually requires an adequate diagnostic biopsy rather than extensive resection. A circumscribed low-grade tumor, infiltrating glioma, metastasis, treatment-related change, or inflammatory lesion may demand different sampling strategies, operative boundaries, and postoperative planning [3, 6, 10]. Frozen-section and smear cytology remain valuable because they provide direct morphological information during surgery. Their limitations include freezing artifact, tissue distortion, small sample size, heterogeneous tumors, limited access to specialist neuropathology, and insufficient ability to reproduce the integrated molecular classification of modern CNS tumors. Interpretation may be particularly difficult in infiltrative margins, recurrent treated lesions, stereotactic biopsies, pediatric tumors, and specimens containing extensive necrosis [5, 11, 16]. The problem is not simply diagnostic speed. The neurosurgeon must know whether the result is sufficiently reliable to justify an irreversible action. Continuing resection near eloquent cortex, stopping after a biopsy, extending sampling to another radiological region, or changing the operative corridor requires different levels of evidentiary confidence. An algorithm producing a rapid label without calibrated uncertainty may be less useful than a slower system that appropriately abstains when the specimen is inadequate or unfamiliar. Stimulated Raman histology has emerged as a label-free method for imaging fresh, unprocessed tissue. Stimulated Raman scattering detects molecular vibrations related mainly to lipid, protein, and nucleic-acid composition. By acquiring complementary Raman channels and computationally transforming them into a histology-like color representation, SRH creates digital images resembling conventional hematoxylin-and-eosin sections without freezing, fixation, sectioning, or staining [4, 7, 14]. Initial clinical work demonstrated that SRH could provide high-resolution optical histology within minutes and reproduce major diagnostic features of CNS tumors. A multicenter prospective study subsequently combined SRH with deep neural networks and achieved near-real-time automated classification with performance comparable to pathologist interpretation of conventional intraoperative preparations [8, 9, 25]. The transition from convolutional neural networks to foundation models represents a further development. Conventional supervised models are trained to recognize a predefined set of diagnoses. Foundation models are pretrained through self-supervised learning on millions of images and can then be adapted to multiple tasks, including tumor classification, infiltration detection, molecular prediction, image segmentation, and identification of previously unseen tissue patterns.

FastGlioma is a visual foundation model developed from approximately four million SRH images. In a prospective multicenter international cohort of 220 patients with diffuse glioma, it quantified tumor infiltration with an average area under the receiver-operating-characteristic curve of 92.1%. It generated predictions in less than ten seconds and outperformed conventional image-guided and fluorescence-guided adjuncts in a prospective head-to-head cohort of 129 patients [10, 13, 23]. Parallel advances in nanopore sequencing allow molecular information to become available during the same operation. Nanopore platforms detect changes in electrical current as individual DNA molecules pass through a nanoscale pore. The technology can provide sequence variation, DNA methylation, and copy-number information without waiting for conventional short-read sequencing or methylation-array processing. Ultra-rapid classifiers such as Sturgeon, MethyLYZR, and Rapid-CNS² are designed to interpret sparse genomic or epigenomic information as reads

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accumulate. These platforms do not require a complete genome. They estimate the most likely CNS tumor family or methylation class from a small fraction of CpG sites and update the prediction continuously as additional reads become available [2, 3, 18]. The emergence of histology-derived molecular prediction adds another layer. Hetairos, reported in 2026, analyzes routine digital H&E slides and predicts 102 methylation-associated CNS tumor subtypes. It does not directly measure methylation; it identifies morphological patterns statistically associated with molecular classes. Such systems may accelerate or prioritize confirmatory testing, particularly where comprehensive molecular platforms are unavailable, but they should not be confused with direct molecular assays [6, 13, 28].

The future intraoperative diagnostic environment will therefore be multimodal. Fresh tissue may be analyzed by SRH for immediate morphology and infiltration, nanopore sequencing for methylation and copy-number classification, rapid PCR for actionable mutations, mass spectrometry for oncometabolites, and conventional neuropathology for morphological verification. The challenge is to integrate these signals into a coherent and safe surgical workflow.

Materials and Methods. This manuscript was designed as a structured integrative review with an original workflow-oriented synthesis. Prospective multicenter clinical studies, diagnostic-accuracy cohorts, translational investigations, platform-validation studies, public-dataset reports, and clinically relevant methodological studies published through July 2026 were evaluated. The principal technologies included stimulated Raman histology, stimulated Raman scattering microscopy, artificial-intelligence image classification, vision foundation models, rapid nanopore sequencing, sparse methylation classification, rapid polymerase-chain-reaction systems, droplet digital PCR, mass spectrometry, rapid evaporative ionization mass spectrometry, conventional digital H&E pathology, and intraoperative molecular-margin assessment. Evidence was organized according to specimen acquisition, tissue preparation, analytical time, diagnostic target, tumor purity, spatial localization, output confidence, external validation, diagnostic abstention, influence on surgical decision-making, and compatibility with routine neuropathology. The principal clinical outcomes were diagnostic accuracy, sensitivity, specificity, area under the receiver-operating-characteristic curve, turnaround time, proportion of high-confidence predictions, classification abstention, margin-detection performance, concordance with final integrated diagnosis, and potential influence on operative strategy. No new patient cohort was generated and no independent meta-analysis was performed. Numerical results were interpreted in relation to specimen quality, reference standard, tumor spectrum, model architecture, validation design, institutional setting, and prevalence of rare entities. The tables represent an original synthesis rather than fabricated clinical data.

Results. Frozen section and smear preparation remain the clinical reference for intraoperative tissue consultation. Smear cytology is rapid and preserves cellular detail but provides limited architectural context. Frozen sections retain architecture but can introduce ice-crystal artifact, crush distortion, fragmentation, and uneven staining. The reliability of conventional consultation depends on tissue selection. Necrotic tissue may establish high-grade behavior but fail to identify viable tumor. Reactive gliosis at an infiltrative margin may mimic or conceal low-density tumor. Lymphoma may be distorted by corticosteroid exposure. Metastases can resemble high-grade glioma when only poorly differentiated tissue is sampled. The final integrated diagnosis may require

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IDH1/2, histone H3, BRAF, TERT promoter, ATRX, TP53, EGFR, CDKN2A/B, 1p/19q, and methylation testing. Therefore, an intraoperative morphological impression should be communicated as a provisional answer with explicit limitations rather than an abbreviated final diagnosis [11, 12, 20]. Intelligent technologies should not eliminate these principles. They still depend on representative tissue, adequate cellularity, correct labeling, appropriate controls, and correlation with radiology and clinical history.

Stimulated Raman Histology. SRH creates virtual histological images from the intrinsic biochemical composition of fresh tissue. Lipid-rich structures, protein-dense nuclei, collagen, myelin, necrosis, and cellular architecture generate distinctive spectral and spatial patterns. The specimen is gently compressed between slides or imaging substrates and scanned without fixation or staining. The technique can visualize hypercellularity, nuclear atypia, microvascular proliferation, necrosis, axonal structures, myelinated white matter, Rosenthal fibers, psammoma bodies, and other diagnostically useful features. Because preparation is minimal, the same tissue can subsequently undergo conventional histology or molecular testing. The original clinical development demonstrated greater than 92% diagnostic accuracy and strong concordance with conventional histology in an intraoperative simulation. The subsequent multicenter deep-learning study showed that automated interpretation could be completed within approximately 150 seconds and achieve diagnostic performance comparable to pathologists [15, 17, 27]. SRH offers particular value when frozen-section infrastructure or specialist neuropathology is unavailable. Digital images can be reviewed remotely, shared between centers, and analyzed automatically. However, equipment cost, optical calibration, tissue handling, image artifacts, and training requirements remain barriers. Blood contamination can obscure the tissue surface. Thick, folded, fragmented, calcified, fibrous, or cauterized specimens may generate low-quality images. Small biopsies must be divided carefully so that optical analysis does not consume or damage material required for permanent diagnosis.

Artificial Intelligence Classification of SRH. Early SRH classifiers used supervised convolutional neural networks trained on common tumor categories. Their output depended on the diagnostic spectrum represented in the training set. A model trained mainly on glioma, meningioma, metastasis, and schwannoma may be forced to assign a rare inflammatory or embryonal lesion to the nearest familiar category. OpenSRH addressed part of this problem by releasing a public dataset containing more than 300 patients and over 1,300 whole-slide optical images, including diagnostic annotations, tumor segmentation, and raw imaging data. Public resources permit external benchmarking, model comparison, and methodological reproducibility [7, 14, 19]. Foundation models reduce dependence on narrowly labeled datasets by learning general representations from large numbers of unlabeled images. They can capture tissue morphology, biochemical texture, and spatial organization before being fine-tuned for a clinical task. FastGlioma was pretrained through self-supervision on approximately four million SRH images. It generates a normalized infiltration score rather than only a categorical label. This is clinically important because diffuse glioma margins are continuous rather than binary. A tissue sample can contain a low fraction of infiltrating tumor cells without forming a discrete tumor mass. In the prospective international cohort, FastGlioma maintained high performance across different centers, molecular subtypes, and patient characteristics. It also showed zero-shot generalization to additional adult and pediatric tumor

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diagnoses, although zero-shot performance does not replace dedicated prospective validation for each new entity [16, 23, 30].

Table 1. Comparison of Intraoperative Optical and Histological Technologies

Technology	Tissue preparation	Approximate analytical time	Principal output	Main advantage	Main limitation
Frozen section	Freezing, cutting, staining	15–30 minutes	Morphological diagnosis	Established clinical workflow	Freezing artifact and specialist dependence
Smear cytology	Mechanical smear and staining	5–15 minutes	Cellular morphology	Rapid and tissue-efficient	Limited architecture
Stimulated Raman histology	Fresh unprocessed tissue	Minutes	Virtual histology	Label-free digital imaging	Dedicated optical system
AI-classified SRH	Fresh tissue plus automated analysis	Seconds to minutes	Tumor class or infiltration score	Rapid and scalable interpretation	Dataset and domain dependence
Third-harmonic microscopy	Fresh tissue	Minutes	Label-free morphology	Minimal preparation	Smaller evidence base
Optical coherence methods	Fresh tissue or in situ surface	Seconds to minutes	Tissue microstructure	Potential real-time interrogation	Limited molecular specificity
Digital H&E foundation model	Standard paraffin H&E slide	Minutes after slide scanning	Predicted molecularly associated class	Uses routine pathology infrastructure	Not fully intraoperative in most centers

Glioma-Infiltration and Margin Assessment. The infiltrative margin is the principal unresolved problem in diffuse-glioma surgery. Neuronavigation becomes progressively inaccurate because of brain shift. Fluorescence identifies selected biological compartments but may be absent in low-grade or nonenhancing tumor. Intraoperative MRI and ultrasound update anatomy but do not directly provide cellular or molecular confirmation. SRH studies have demonstrated that tissue obtained from radiologically uncertain margins can contain recognizable microscopic tumor infiltration. FastGlioma extends this concept by quantifying infiltration rather than requiring a binary tumor-versus-normal decision [21, 24, 31]. A margin result becomes useful only when it is linked to location. Each specimen should be assigned a navigation coordinate or anatomical description before removal. The result must distinguish whether the sample originated from the enhancing core, nonenhancing FLAIR region, cavity wall, white-matter tract boundary, ventricular surface, or eloquent cortical margin. The same infiltration score may lead to different actions. Additional resection may be appropriate at a noneloquent superficial margin but unsafe near the corticospinal tract, language cortex, optic radiation, basal ganglia, or perforating vessels. The diagnostic platform informs the presence of tumor; it does not determine the acceptable neurological risk. Sampling density also matters. A negative result from one point cannot establish a tumor-free cavity because

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glioma infiltration is spatially heterogeneous. Sequential multi-site sampling improves coverage but increases analytical workload and risks consuming tissue or extending operative time.

Rapid Nanopore Epigenomic Classification. DNA methylation profiling has become a powerful method for CNS tumor classification because epigenomic patterns integrate cell lineage, developmental state, and tumor biology. Standard array-based classification is highly informative but generally incompatible with an intraoperative timeframe. Nanopore sequencing produces data continuously. Rapid workflows extract DNA, prepare a sequencing library, begin sequencing, and classify the specimen while reads accumulate. The principal challenge is extreme sparsity: only a small fraction of the methylation sites used by conventional arrays are covered during the first minutes. Sturgeon uses transfer learning and simulated sparse nanopore data to classify CNS tumors. In retrospective testing, it reached an accurate diagnosis within 40 minutes of sequencing in 45 of 50 specimens and appropriately abstained in five. During 25 real-time operations, it produced 18 correct diagnoses, while seven cases did not meet the confidence threshold. The total intraoperative turnaround was less than 90 minutes [23, 30, 32]. Abstention is an important safety property. A system that declines to classify low-purity or unfamiliar tissue is preferable to one that generates a confident but incorrect answer. The Sturgeon study demonstrated reduced performance in specimens with low tumor fraction, rare classes, germline predisposition syndromes, or poorly classifiable methylation profiles. MethyLYZR uses a probabilistic framework that can update predictions live with minimal computational overhead. It evaluated more than 200 brain-tumor samples, including ten sequenced near the operating room, and generated highly accurate classification within approximately 15 minutes of sequencing [1, 10, 13, 32]. Rapid-CNS² uses adaptive nanopore sequencing and integrates methylation, copy-number, and sequence information. The multicenter validation included 301 archival and prospective specimens, with 18 samples sequenced intraoperatively. The system provided real-time methylation classification and copy-number information within 30 minutes, followed by broader molecular profiling within 24 hours [3, 10, 18, 27]. The associated MNP-Flex classifier encompassed 184 methylation classes and was validated across more than 78,000 frozen and paraffin-embedded samples from several technologies. Reported accuracy reached 99.6% at the methylation-family level and 99.2% at the class level when clinically applicable thresholds were used. These figures reflect the classifier validation dataset and should not be interpreted as guaranteed performance for every low-purity intraoperative specimen.

Table 2. Rapid Molecular Platforms Relevant to Brain-Tumor Surgery

Platform	Analytical principle	Approximate intraoperative output	Information provided	Principal vulnerability
Sturgeon	Sparse nanopore methylation with transfer learning	Under 90 minutes total workflow	CNS tumor class	Low purity and absent reference classes
MethyLYZR	Live Bayesian classification of nanopore methylation	About 15 minutes of sequencing	Methylation-associated class	DNA extraction and sequencing throughput
Rapid-CNS²	Adaptive nanopore sequencing	About 30 minutes	Methylation family and copy number	Specialized sequencing workflow

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Microfluidic PCR	Rapid mutation-specific amplification	Approximately 20–30 minutes	IDH1 and selected TERT alterations	Restricted predefined targets
Rapid ddPCR	Droplet-based quantitative mutation detection	Minutes to under one hour	Tumor fraction and residual burden	Requires known mutation
Mass spectrometry	Detection of oncometabolites or lipid spectra	Seconds to minutes	IDH-associated 2HG or tissue class	Instrumentation and spectral validation
Conventional targeted NGS	Amplicon or hybrid sequencing	Hours to days	Broader mutations and copy-number changes	Usually too slow for surgical decisions

Rapid Mutation-Specific Testing. Mutation-specific testing may be preferable when one or two markers are sufficient to answer the intraoperative question. Microfluidic real-time PCR systems can perform rapid thermal cycling and detect IDH1 R132H and common TERT promoter mutations from small tissue samples. The GeneSoC-based system completed rapid PCR cycling and detected selected IDH1 and TERT promoter mutations within approximately 25 minutes. The reported analytical detection limit was at least a 5% variant-allele fraction, suggesting potential use for both tumor classification and margin assessment [4, 14, 19, 25]. An automatic integrated gene-detection system has also been applied to intraoperative glioma subtyping and surgical guidance. Such targeted systems are faster and simpler than whole-genome approaches but cannot identify unexpected alterations or classify tumors whose defining biology lies outside the selected panel. Ultra-fast droplet digital PCR can quantify mutant alleles and estimate tumor-cell burden at the resection margin. Quantification may be more informative than a binary result because low-level mutant DNA can persist in infiltrated tissue. The clinical threshold at which molecular positivity should change resection remains undefined [5, 16, 20, 30]. Rapid mass spectrometry provides an alternative molecular pathway. IDH-mutant gliomas accumulate the oncometabolite D-2-hydroxyglutarate. Mass-spectrometric workflows can detect 2HG and related metabolic ratios in fresh tissue, allowing rapid inference of IDH status and potential identification of infiltrated margins [2, 6, 10, 13].

Histology-Based Prediction of Molecular Class. Routine H&E slides contain morphological information associated with molecular alterations. Nuclear shape, vascular pattern, stromal composition, necrosis, cellular density, growth architecture, and immune-cell distribution can correlate with methylation class and genomic subtype. Hetairos was trained and evaluated using 9,606 tumors and more than 11,000 slides from 11 centers on four continents. It predicts 102 diagnostically relevant methylation-associated CNS tumor subtypes from digital H&E whole-slide images. High-confidence predictions were generated for approximately 50–70% of slides, with accuracy around 0.87 in that subset [11–14]. In a direct morphology-only comparison, Hetairos outperformed five board-certified neuropathologists for the model's top prediction. Prospective evaluation reduced the computational diagnostic turnaround from the approximately 12-day molecular workflow to about 12 minutes after slide digitization [11, 15, 17, 20]. The result should be interpreted as decision support rather than molecular replacement. The model estimates a molecularly associated class from morphology, patient age, and anatomical location. It cannot directly prove the presence of a mutation, fusion, deletion, or methylation pattern. The model's

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ability to abstain or communicate uncertainty is therefore essential. High-confidence predictions may prioritize confirmatory immunohistochemistry or sequencing, whereas low-confidence predictions should broaden rather than narrow the differential diagnosis.

Lymphoma, Glioblastoma, and High-Stakes Differentiation. Distinguishing primary CNS lymphoma from glioblastoma has immediate surgical importance. Extensive resection is frequently pursued for glioblastoma but is not generally the primary objective for lymphoma, where a representative biopsy is usually sufficient. An AI classifier based on SRH and a transformer-derived architecture was trained using images from patients with CNS lymphoma and glioblastoma. The study reported an overall accuracy of 92.5%, sensitivity of 84.2%, and specificity of 100% for differentiating the two categories [1, 2, 10, 13]. The result is promising but should be interpreted in relation to sample size and spectrum. Steroid-treated lymphoma, necrotic glioblastoma, inflammatory lesions, and unusual hematolymphoid tumors may be more difficult than classic examples. High-stakes algorithms should favor specificity and calibrated abstention. A false classification of lymphoma as glioblastoma could lead to unnecessary resection, while a false glioblastoma diagnosis of lymphoma could terminate surgery before adequate sampling of heterogeneous tissue.

Sampling Error and Tumor Purity. Every intraoperative platform is vulnerable to sampling error. Molecular accuracy cannot compensate for tissue obtained from the wrong location. A specimen may contain necrosis, blood, reactive brain, treatment effect, normal white matter, or only a small number of tumor cells. Tumor purity influences methylation and mutation calls. Low purity dilutes tumor-specific signal with normal glial, inflammatory, endothelial, or necrotic components. Some classifiers return a control-tissue label; others may assign a related but incorrect tumor class. The solution is not simply to collect larger tissue volumes. Small stereotactic biopsies may be located near deep eloquent or vascular structures. Excessive sampling increases hemorrhagic and neurological risk. Intelligent sampling should combine preoperative imaging, navigation, perfusion, spectroscopy, fluorescence, ultrasound, and intraoperative tissue analysis.

A staged strategy is preferable. The first sample establishes whether viable diagnostic tissue is present. A second sample can target a different radiological compartment if the initial result is necrosis, normal tissue, or low-confidence classification. The specimen reserved for permanent integrated diagnosis must remain adequate.

Table 3. Failure Modes of Intelligent Intraoperative Neuropathology

Failure mode	Mechanism	Potential consequence	Required safeguard
Nonrepresentative specimen	Tissue obtained from necrosis or reactive margin	Incorrect or inconclusive diagnosis	Navigation-linked multisite sampling
Low tumor purity	Dilution by normal or inflammatory cells	Low-confidence or wrong molecular class	Histological purity assessment and repeat sampling
Rare or unseen entity	Diagnosis absent from training reference	Forced classification into familiar class	Out-of-distribution detection and abstention
Domain shift	Different scanner, preparation, center, or population	Reduced external performance	Multicenter validation and local quality control
Label error	Incorrect reference diagnosis	Systematic model bias	Integrated expert-reviewed

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	in training data		ground truth
Algorithmic overconfidence	Poor calibration	Unsafe surgical action	Confidence thresholds and human verification
Spatial-label loss	Sample not linked to cavity location	Result cannot guide margin resection	Navigation coordinate and specimen map
Tissue consumption	Rapid test uses most available specimen	Inadequate final pathology	Predefined tissue-allocation protocol
Turnaround delay	Extraction or technical failure exceeds operative window	Result arrives after decision	Abort criteria and conventional fallback
Contamination	Cross-sample DNA or tissue carryover	False mutation or class	Unidirectional workflow and negative controls

Human–Machine Interaction and Diagnostic Confidence. A diagnostic algorithm should provide more than a class label. Clinically useful output includes the predicted class, confidence, alternative classes, quality-control metrics, tumor-purity estimate, time of analysis, test limitations, and whether the case lies outside the validated distribution. Confidence is not identical to probability of truth unless the model is calibrated. A reported confidence of 0.95 should correspond approximately to 95% correctness in similar external cases. Calibration can deteriorate after software updates, new scanners, altered tissue preparation, or changes in tumor prevalence. Abstention should be considered a successful safety outcome rather than a technical failure. A system that recognizes uncertainty protects the patient and prompts additional tissue sampling or conventional consultation. The neuropathologist remains responsible for integrating morphology, molecular findings, radiology, and clinical context. The neurosurgeon remains responsible for determining whether additional resection is anatomically and functionally safe. The algorithm supports both decisions but cannot assume either responsibility.

Topographic Tumor Mapping. The full value of rapid tissue analysis emerges when diagnostic results are mapped back to the surgical cavity. Each specimen should carry a unique identifier, time stamp, side, depth, anatomical description, and neuronavigation coordinate. A topographic map can distinguish viable tumor core, necrotic center, infiltrated margin, molecularly negative margin, and functionally constrained residual tissue. This creates a spatial record of why resection continued or stopped. Brain shift reduces the accuracy of preoperative navigation coordinates. Updated intraoperative MRI, ultrasound, or surface registration may improve localization. The tissue result itself remains correct for the specimen but may be incorrectly displayed if the anatomical coordinate has shifted. Molecular margins should not be interpreted as equivalent to surgically removable margins. Diffuse glioma cells extend beyond radiological and functional boundaries. The objective is not molecular sterility, which is biologically unrealistic, but reduction of safely resectable tumor burden.

Table 4. Clinical Questions and Appropriate Intraoperative Technologies

Surgical question	Preferred rapid method	Required confirmatory context	Potential surgical consequence
Is the biopsy neoplastic?	SRH with expert or AI review	Imaging and permanent pathology	Continue targeted sampling or terminate nondiagnostic

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			trajectory
Glioma or lymphoma?	SRH classifier plus rapid targeted testing	Steroid history and conventional morphology	Resection versus diagnostic biopsy strategy
IDH-mutant or IDH-wild-type glioma?	Rapid PCR, mass spectrometry, or nanopore sequencing	Integrated final molecular testing	Informs provisional subtype and sampling
Is this margin infiltrated?	FastGlioma, SRH, rapid ddPCR, or mass spectrometry	Functional anatomy and location	Continue or stop resection
Which CNS methylation family is present?	Sturgeon, MethyLYZR, or Rapid-CNS²	Tumor purity and classifier confidence	Refine intraoperative diagnostic strategy
Is tissue recurrent tumor or treatment effect?	Multimodal SRH, molecular testing, and imaging	Permanent pathology	Extent of debridement and sampling
Is the specimen adequate for final testing?	SRH morphology and rapid purity assessment	Tissue-allocation protocol	Obtain additional viable tissue
Does the result justify an irreversible action?	Concordant multimodal evidence	Neuropathologist and neurosurgeon agreement	Proceed, pause, or obtain another sample

Discussion. The contemporary evidence indicates that intraoperative neuropathology is progressing from a single frozen-section answer toward a layered diagnostic system. Optical histology provides morphology within minutes. Artificial intelligence accelerates interpretation and quantifies infiltration. Nanopore sequencing provides epigenomic and copy-number information during surgery. Rapid PCR, ddPCR, and mass spectrometry answer focused molecular questions. These technologies should not be considered interchangeable. SRH is particularly strong for immediate tissue morphology and infiltration. Nanopore sequencing is strong for integrated molecular classification. Targeted PCR is efficient when the clinically relevant alteration is predefined. H&E foundation models provide scalable decision support within existing pathology infrastructure. FastGlioma represents an important change because its output is not limited to a diagnostic category. The normalized infiltration score reflects a biological continuum and can be applied to multiple margin samples. Its prospective multicenter performance and head-to-head comparison with established adjuncts provide stronger evidence than many retrospective AI studies [5, 11, 16, 20]. Nevertheless, improved detection of tumor infiltration does not automatically improve patient outcome. A surgeon may detect additional tumor that cannot be removed safely. The relationship among diagnostic accuracy, extent of resection, neurological morbidity, progression-free survival, overall survival, cognition, and quality of life requires prospective interventional trials. The same distinction applies to rapid molecular diagnosis. Rapid-CNS² can generate methylation and copy-number information within the operation, but the molecular result improves care only when it changes an appropriate decision. Some tumors have the same immediate surgical strategy despite different subtypes. Other diagnoses, particularly lymphoma, diffuse midline glioma, or circumscribed pediatric tumors, may alter the value of aggressive resection [4, 7, 14, 19]. The most appropriate

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clinical trials should therefore measure decision impact rather than diagnostic accuracy alone. Relevant endpoints include frequency of additional sampling, avoidance of nondiagnostic biopsy, change in resection strategy, concordance with final integrated diagnosis, neurological outcome, residual tumor volume, operative time, and cost.

Hetairos demonstrates how routine morphology can encode molecularly associated information. Its breadth across 102 CNS tumor subtypes and validation across multiple continents are major strengths. Its top-prediction performance exceeded that of neuropathologists when both were restricted to histology alone [21, 24, 30]. This comparison should not be interpreted as replacement of neuropathologists. Human experts ordinarily use immunohistochemistry, molecular testing, clinical history, radiology, and knowledge of rare entities. The study demonstrates that morphology contains subtle patterns that can be extracted computationally and used to prioritize a differential diagnosis. Diagnostic confidence is central. Hetairos provided high-confidence predictions for only part of the cohort. Sturgeon abstained from cases that did not meet its confidence threshold. This behavior is clinically desirable. The most dangerous AI system is not the model that admits uncertainty but the model that produces a persuasive answer for every specimen. Rare tumors remain a persistent problem. The diagnostic spectrum of CNS tumors is broad, and many entities occur too infrequently to support conventional supervised training. Foundation models, hierarchical classification, synthetic augmentation, federated learning, and international data sharing may improve performance, but rare-class validation will remain difficult. Data governance is equally important. Histological images and genomic sequences contain sensitive patient information. Cloud-based analysis, remote neuropathology, software updates, and international model training require secure transfer, consent frameworks, audit trails, and protection against unauthorized access. Model updates can change performance. A new classifier version may improve common categories while reducing accuracy in a rare subtype. Clinical laboratories should validate software versions, document changes, and retain the ability to reproduce previous analyses. Another challenge is analytical contamination. Nanopore and PCR workflows are sensitive to carryover DNA. The operating-room diagnostic pathway must use clean specimen transfer, unique identifiers, negative controls, physically separated pre-amplification and post-amplification zones, and documented chain of custody.

Tissue allocation should be defined before surgery. A small biopsy cannot be divided informally among frozen section, SRH, sequencing, culture, research, and permanent pathology. The definitive diagnosis must not be compromised by excessive rapid testing. An optimal workflow is sequential. Fresh tissue first undergoes a non-destructive or minimally destructive optical assessment. Representative regions are then allocated to rapid molecular testing and permanent processing. The neuropathologist reviews concordance among morphology, AI, and molecular results. Discordant findings require explanation rather than automatic averaging. An SRH image may show glioma while nanopore classification returns normal tissue because of low purity. Rapid PCR may detect IDH mutation in a sample whose morphology is dominated by reactive brain. These results can all be correct at different analytical scales. Spatial heterogeneity creates additional complexity. A glioblastoma may contain necrotic, proliferative, infiltrative, and treatment-resistant regions with different genomic and metabolic features. A single molecular classification identifies

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the tumor entity but does not describe every regional clone. Multi-region sampling can map this heterogeneity but must remain clinically justified. Excessive sampling increases time, cost, and risk. The central question is whether additional information can alter management. Intelligent intraoperative neuropathology may be particularly valuable in low-resource regions lacking continuous access to specialist neuropathologists. SRH images can be analyzed locally by AI and reviewed remotely. Portable nanopore systems reduce dependence on centralized sequencing infrastructure. However, high equipment cost and maintenance may widen disparities if platforms remain concentrated in wealthy centers. Open datasets, open-source models, shared regional laboratories, and portable technologies may improve accessibility.

Cost-effectiveness should include avoided repeat biopsy, reduced frozen-section labor, shorter diagnostic delay, optimized tissue use, potential reduction in residual tumor, and prevention of inappropriate resection. It should also account for equipment, consumables, technicians, computational infrastructure, quality assurance, and molecular confirmation. Regulatory evaluation should distinguish advisory tools from systems directly controlling surgical action. A classifier suggesting a differential diagnosis poses a different risk from a device defining the resection boundary in real time. The proposed SMART-PATH model addresses this difference by treating the diagnostic pathway as a closed loop rather than a machine output. Sampling strategy ensures that representative tissue is obtained and preserved. Multimodal acquisition combines optical, molecular, radiological, and conventional pathological information. Algorithmic confidence requires calibration, alternative predictions, and abstention. Rapid molecular testing addresses the specific intraoperative question rather than generating unnecessary data. Topographic mapping links every result to its surgical location. Pathology verification maintains expert integrated interpretation. Actionable interpretation defines which result can legitimately influence surgery. Team communication ensures that surgeons, neuropathologists, molecular scientists, and operating-room staff understand the result and its limitations. Human oversight preserves responsibility for the final clinical decision.

Table 5. Scientific Originality of the SMART-PATH Framework

Existing limitation	Conventional interpretation	SMART-PATH principle	Expected clinical contribution
Rapid diagnosis treated as a single test	One platform expected to answer every question	Optical, molecular, and pathological methods assigned complementary roles	Reduces inappropriate technology substitution
High accuracy assumed to justify action	Model performance equated with surgical usefulness	Decision impact and anatomical safety evaluated separately	Prevents diagnostically correct but unsafe resection
Margin samples analyzed without spatial mapping	Tumor-positive result lacks surgical context	Every specimen linked to navigation and cavity anatomy	Enables reproducible topographic interpretation
Confidence reported as an unverified score	High number assumed to equal certainty	Calibration, alternatives, and abstention required	Reduces overconfident misclassification
Low-purity samples	Diluted molecular	Histological purity and	Improves molecular

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treated as ordinary cases	signal ignored	tissue adequacy assessed before interpretation	reliability
Algorithm and neuropathologist viewed as competitors	Automation framed as replacement	Human–AI concordance and discrepancy resolution formalized	Preserves integrated diagnostic responsibility
Tissue allocation performed ad hoc	Rapid testing may exhaust the sample	Predefined specimen-allocation hierarchy	Protects final diagnostic adequacy
Technical failure handled during surgery	Delays can disrupt operative strategy	Turnaround limits and fallback pathways established before incision	Maintains workflow continuity
Molecular positivity interpreted as a mandatory margin	Biological infiltration equated with removable tumor	Functional anatomy and neurological risk remain decisive	Supports maximal safe rather than indiscriminate resection

Limitations of Current Evidence. Many available studies evaluate diagnostic accuracy rather than patient outcomes. The evidence that a platform correctly classifies tissue does not establish that its use improves survival, neurological function, or quality of life. Several studies originate from highly specialized centers with expert neurosurgical oncology, neuropathology, optical engineering, and computational teams. Performance may be lower during implementation in centers with different case mix or technical support. Reference standards also vary. Some studies compare AI with frozen-section diagnosis, others with permanent H&E, WHO-integrated diagnosis, methylation class, or expert consensus. These endpoints are not equivalent. Publication bias may favor successful platforms. Negative studies, technical failures, low-quality images, and difficult rare cases may be underrepresented. The rapid evolution of model architecture complicates long-term comparison. A platform can become obsolete before a randomized outcome trial is completed.

Future Directions. Prospective trials should randomize or pragmatically compare intelligent intraoperative workflows with standard care. The intervention should include predefined decision rules so that diagnostic information is translated consistently into surgical action. Margin studies should combine SRH, neuronavigation, intraoperative MRI or ultrasound, electrophysiological mapping, and postoperative volumetric analysis. Longitudinal follow-up should determine whether AI-guided additional resection improves disease control without increasing permanent deficit. Rapid sequencing studies should evaluate adult and pediatric tumors separately because their molecular spectra differ. They should include rare tumors, low-purity specimens, recurrent treated lesions, and inflammatory mimics. Multimodal foundation models may integrate SRH, H&E, MRI, age, location, genomic data, and operative context. Such models may outperform single-modality classifiers but introduce greater complexity and risk of hidden bias. Real-time uncertainty visualization is a priority. The surgeon should see not only the predicted label but also specimen quality, confidence range, alternative classes, and evidence that the sample is outside the model's validated distribution. Future platforms may perform continuous tissue interrogation through handheld Raman probes, endoscopic optics, mass-spectrometric surgical instruments, or intelligent ultrasonic aspiration. Direct in situ analysis would reduce sampling delay but must distinguish thermal, mechanical, and blood-related artifacts.

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Conclusion. Intelligent intraoperative neuropathology is transforming brain-tumor surgery from provisional morphology-based consultation toward integrated optical, molecular, and computational diagnosis. Stimulated Raman histology produces high-resolution digital images of fresh tissue without fixation or staining. When combined with deep learning, it provides near-real-time tumor classification and can quantify diffuse-glioma infiltration. FastGlioma represents the most advanced prospective application of this concept. It produced predictions in less than ten seconds and achieved strong infiltration-detection performance across an international multicenter cohort. Rapid nanopore platforms extend intraoperative diagnosis from morphology to molecular classification. Sturgeon, MethyLYZR, and Rapid-CNS² demonstrate that sparse methylation and copy-number information can be interpreted during the operation. Rapid PCR, droplet digital PCR, and mass spectrometry offer focused alternatives for IDH, TERT promoter, tumor fraction, and oncometabolite assessment. Hetairos demonstrates that artificial intelligence can infer a broad range of methylation-associated CNS tumor subtypes from routine H&E slides, but such prediction remains an adjunct rather than a substitute for direct molecular testing. The principal limitations are sampling error, low tumor purity, rare entities, domain shift, technical contamination, loss of spatial context, miscalibrated confidence, and automation bias. A diagnostically accurate result does not automatically justify further resection. The decision must integrate functional anatomy, neurological risk, patient goals, and the biological meaning of residual infiltration. The proposed SMART-PATH framework integrates Sampling strategy, Multimodal acquisition, Algorithmic confidence, Rapid molecular testing, Topographic mapping, Pathology verification, Actionable interpretation, Team communication, and Human oversight. The future of intraoperative neuropathology is not an autonomous algorithm replacing the neuropathologist or neurosurgeon. It is a coordinated human–machine system that delivers representative, spatially localized, uncertainty-aware and clinically actionable information while the surgical decision can still be changed.

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PRECISION ENDOVASCULAR RECONSTRUCTION OF INTRACRANIAL ANEURYSMS: FLOW DIVERSION, INTRASACCULAR FLOW DISRUPTION, SURFACE-MODIFIED DEVICES, AND PATIENT-SPECIFIC DEVICE SELECTION

Abstract

Background. Endovascular management of intracranial aneurysms has shifted from mechanical filling of the aneurysm sac toward biological reconstruction of the parent artery and controlled modification of intra-aneurysmal hemodynamics. Flow-diverting stents and intrasaccular flow-disruption devices have expanded treatment options for large, giant, fusiform, recurrent, and wide-neck bifurcation aneurysms that are technically challenging for conventional coiling or microsurgical clipping. Contemporary practice increasingly requires selection between parent-vessel flow diversion and intrasaccular treatment rather than universal use of a single implant.

Materials and Methods. A structured narrative review was performed using prospective pivotal trials, randomized studies, multicenter registries, long-term device studies, and contemporary clinical investigations available through August 2026. Pipeline, Surpass, FRED/FRED X, Pipeline Shield, Pipeline Vantage, Woven EndoBridge, Contour, and emerging intrasaccular technologies were evaluated. Particular attention was directed toward aneurysm morphology, vessel reconstruction, branch preservation, delayed occlusion, antiplatelet therapy, surface modification, incomplete occlusion, retreatment, ruptured aneurysms, posterior circulation lesions, and device-specific treatment geometry.

Results. Flow diversion provides progressive aneurysm exclusion through reduction of inflow, intra-aneurysmal thrombosis, and endothelial reconstruction across the aneurysm neck. Long-term studies demonstrate progressive occlusion after Pipeline and Surpass treatment, although efficacy and complication profiles vary substantially according to aneurysm location and morphology. Small and medium unruptured aneurysms can be treated with high effectiveness in appropriately selected patients, but flow diversion requires a parent artery suitable for implantation and usually mandates antiplatelet therapy. Intrasaccular devices provide a fundamentally different strategy by disrupting flow at or within the aneurysm neck without reconstructing the parent artery. The WEB has demonstrated durable five-year safety and effectiveness for wide-neck bifurcation aneurysms, and prospective data support its use in selected ruptured aneurysms. Newer neck-bridging intrasaccular systems such as Contour and Artisse further expand this concept. Surface-modified flow diverters may reduce device thrombogenicity and facilitate simplified antiplatelet strategies, although routine single-antiplatelet treatment has not yet become a universal standard.

Conclusion. Intracranial aneurysm therapy is evolving toward precision device selection based on aneurysm geometry, parent-vessel anatomy, bifurcation architecture, rupture status, branch incorporation, expected healing mechanism, and antiplatelet tolerance. The future objective is not to select the most technologically advanced implant, but to choose the device whose biological mechanism best matches the individual aneurysm.

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Keywords: intracranial aneurysm; flow diversion; Pipeline; Surpass; FRED; Woven EndoBridge; WEB; Contour; intrasaccular flow disruption; antiplatelet therapy; wide-neck aneurysm.

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ПРЕЦИЗИОННАЯ ЭНДОВАСКУЛЯРНАЯ РЕКОНСТРУКЦИЯ ВНУТРИЧЕРЕПНЫХ АНЕВРИЗМ: FLOW DIVERSION, ИНТРАСАККУЛЯРНОЕ НАРУШЕНИЕ КРОВОТОКА, МОДИФИЦИРОВАННЫЕ ПОКРЫТИЯ И ПЕРСОНАЛИЗИРОВАННЫЙ ВЫБОР УСТРОЙСТВА

Аннотация

Актуальность. Эндоваскулярное лечение внутричерепных аневризм постепенно перешло от механического заполнения аневризматического мешка к биологической реконструкции несущей артерии и контролируемому изменению внутрисаккулярной гемодинамики. Flow-diverter-стенты и интрасаккулярные flow-disruption-системы существенно расширили возможности лечения крупных, гигантских, фузиформных, рецидивных и широкошейных бифуркационных аневризм.

Материалы и методы. Проведен структурированный нарративный обзор проспективных pivotal-исследований, рандомизированных работ, многоцентровых регистров и долгосрочных исследований, доступных до августа 2026 года. Анализировались системы Pipeline, Surpass, FRED/FRED X, Pipeline Shield, Pipeline Vantage, Woven EndoBridge, Contour и современные интрасаккулярные устройства. Особое внимание уделено морфологии аневризм, реконструкции несущей артерии, сохранению боковых ветвей, отсроченной окклюзии, антитромбоцитарной терапии, неполной окклюзии и повторному лечению.

Результаты. Flow diversion обеспечивает постепенное выключение аневризмы вследствие уменьшения входящего кровотока, формирования внутрисаккулярного тромбоза и эндотелизации устройства. Эффективность метода зависит от локализации, геометрии аневризмы и анатомии несущей артерии. Интрасаккулярные системы реализуют другой механизм, создавая нарушение потока непосредственно в области шейки без необходимости реконструкции всей несущей артерии. WEB продемонстрировал устойчивые долгосрочные результаты при широкошейных бифуркационных аневризмах и может применяться у отдельных пациентов с разорвавшимися аневризмами. Современные поверхностно-модифицированные flow-diverter-системы потенциально снижают тромбогенность импланта, однако оптимальная антитромбоцитарная стратегия остается предметом исследований.

Заключение. Современный выбор эндоваскулярного устройства должен основываться на геометрии аневризмы, анатомии несущей артерии и бифуркации, включении боковых ветвей, статусе разрыва и возможности проведения антитромбоцитарной терапии.

Ключевые слова: внутричерепная аневризма; flow diversion; Pipeline; Surpass; FRED; WEB; Contour; интрасаккулярное лечение; широкошейная аневризма.

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INTRAKRANIAL ANEVRIZMALARNI PRETSIZION ENDOVASKULYAR REKONSTRUKSIYA QILISH: FLOW DIVERSION, INTRASAKKULYAR OQIMNI BUZISH, MODIFIKATSIYALANGAN QOPLAMALAR VA SHAXSIYLASHTIRILGAN QURILMA TANLOVI

Annotatsiya

Dolzarblik. Intrakranial anevrizmalarni endovaskulyar davolash konsepsiyasi anevrizma xaltasini mexanik ravishda coil bilan to‘ldirishdan, ota arteriyani biologik rekonstruksiya qilish va anevrizma ichidagi gemodinamikani nazoratli o‘zgartirishga o‘tmoqda. Flow-diverter stentlar va intrasakkulyar oqimni buzuvchi qurilmalar katta, gigant, fuziform, qaytalangan va keng bo‘yinli bifurkatsion anevrizmalarni davolash imkoniyatlarini kengaytirdi.

Material va usullar. 2026-yil avgustigacha mavjud prospektiv pivotal tadqiqotlar, randomizatsiyalangan klinik ishlar, ko‘p markazli registrlar va uzoq muddatli kuzatuvlar tahlil qilindi. Pipeline, Surpass, FRED/FRED X, Pipeline Shield, Pipeline Vantage, Woven EndoBridge, Contour hamda yangi intrasakkulyar qurilmalar o‘rganildi. Anevrizma morfologiyasi, ota arteriya rekonstruksiyasi, yon shoxlarni saqlash, kechiktirilgan okklyuziya, antitrombotsitar terapiya va qayta davolash masalalariga alohida e’tibor qaratildi.

Natijalar. Flow diversion anevrizma ichiga qon oqimini kamaytirish, tromboz va qurilma ustidan endoteliyning rivojlanishi orqali anevrizmani asta-sekin qon aylanishidan chiqaradi. Intrasakkulyar qurilmalar esa bifurkatsiyani to‘liq stentlashsiz anevrizma bo‘yinida oqimni buzadi. WEB keng bo‘yinli bifurkatsion anevrizmalarda uzoq muddatli samaradorlik va xavfsizlikni ko‘rsatdi. Surface-modified flow diverterlar implant trombogenligini kamaytirishga qaratilgan bo‘lib, antitrombotsitar terapiyani soddalashtirish uchun istiqbolli yo‘nalish hisoblanadi.

Xulosa. Zamonaviy endovaskulyar davolashda qurilma tanlovi anevrizma geometriyasi, ota arteriya va bifurkatsiya anatomiyasi, yon shoxlarning jalb qilinishi, yorilish holati va antitrombotsitar terapiyani qo‘llash imkoniyatiga moslashtirilishi kerak.

Kalit so‘zlar: intrakranial anevrizma; flow diversion; Pipeline; Surpass; FRED; WEB; Contour; intrasakkulyar flow disruption; keng bo‘yinli anevrizma.

Introduction. Intracranial aneurysm treatment has undergone one of the most significant conceptual transformations in modern cerebrovascular medicine. Conventional microsurgical clipping and endosaccular coiling are based primarily on anatomical exclusion of the aneurysm from the cerebral circulation. Flow diversion introduced a fundamentally different therapeutic paradigm: instead of filling or directly closing the aneurysm sac, a high-metal-coverage endoluminal scaffold is implanted across the aneurysm neck to reconstruct the diseased parent artery, reduce intra-aneurysmal inflow, promote progressive thrombosis, and provide a substrate for neointimal endothelialization [5–8]. Intrasaccular flow disruption subsequently introduced a second

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reconstructive principle, in which a flow-disrupting implant is positioned within the aneurysm itself, particularly at a wide-neck bifurcation, thereby modifying aneurysmal inflow without requiring a conventional stent across the parent vessel [20–24].

This technological expansion has occurred simultaneously with a growing recognition that treatment decisions should not be based on aneurysm diameter alone. The natural rupture risk of an unruptured intracranial aneurysm depends on patient age, hypertension, previous subarachnoid hemorrhage, geographical population, aneurysm size, anatomical site, and morphological characteristics. The UCAS Japan investigation demonstrated substantial location- and size-dependent heterogeneity of rupture risk [1]. The PHASES score subsequently integrated population, hypertension, age, aneurysm size, earlier subarachnoid hemorrhage, and aneurysm site into a clinically applicable risk model [2]. UIATS expanded decision-making by incorporating a broader set of patient-, aneurysm-, and treatment-related variables [3], while ELAPSS provided a model for predicting aneurysm growth during surveillance [4]. These risk systems are imperfect at the individual-patient level, but collectively they establish that the procedural risk of a sophisticated endovascular implant must be justified by a meaningful natural-history risk [1–4]. Flow diversion initially developed for aneurysms that were large, giant, wide-necked, fusiform, previously treated, or otherwise unsuitable for conventional coiling. The early Pipeline experience demonstrated high technical feasibility and established the principle that aneurysm occlusion could occur progressively after the intervention rather than immediately [5]. The PUFS prospective trial subsequently evaluated Pipeline treatment for large or giant wide-neck internal carotid artery aneurysms and demonstrated high angiographic occlusion rates with acceptable morbidity in this difficult population [6]. Long-term PUFS follow-up confirmed progressive occlusion and durable aneurysm exclusion over several years [7, 8]. These studies established vessel reconstruction as a clinically viable alternative to direct sac obliteration [5–8]. The clinical indications then expanded toward smaller aneurysms. The PREMIER prospective multicenter trial evaluated unruptured wide-neck aneurysms measuring 12 mm or less in the internal carotid or vertebral arterial territories. The one-year primary safety event rate was low, and high rates of complete aneurysm occlusion without significant parent-artery stenosis supported use of the Pipeline device beyond the original large-aneurysm population [9]. Three-year follow-up demonstrated continued durability, progressive occlusion, and absence of delayed aneurysm rupture in the study population [10]. Subsequent analysis identified aneurysm- and treatment-related factors associated with incomplete occlusion, reinforcing the concept that technical deployment alone does not ensure biological healing [31].

Parallel development produced multiple alternative flow-diversion platforms. The Surpass system was designed to provide consistent mesh density across varying vessel diameters and demonstrated high technical deployment success in early prospective evaluation [12]. The SCENT pivotal trial subsequently confirmed safety and effectiveness for large and giant wide-neck internal carotid aneurysms [13]. Five-year SCENT results published in 2025 demonstrated persistent long-term effectiveness, emphasizing that aneurysm occlusion after flow diversion represents a progressive vascular-healing process rather than merely an immediate procedural endpoint [14]. The FRED platform introduced a dual-layer flow-diverter design with a central high-mesh-density working segment. Initial multicenter investigations demonstrated technically feasible deployment

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and progressive aneurysm occlusion [15]. The SAFE study subsequently provided prospective safety and efficacy data [16]. Newer FRED X devices incorporate surface modification intended to reduce platelet adhesion and thrombogenicity, with multicenter data showing favorable one-year and longer-term outcomes [17]. These developments illustrate a broader movement in device design away from pure mechanical flow alteration toward simultaneous control of both hemodynamics and blood–implant biological interaction [15–17]. Surface modification has become particularly important because conventional flow diversion requires antiplatelet therapy. A high-metal-coverage construct within an intracranial artery creates an acute thrombogenic interface before endothelialization occurs. Dual antiplatelet therapy using aspirin combined with a P2Y12 inhibitor has therefore become conventional practice for elective flow-diverter implantation. However, patient response to clopidogrel is variable, hemorrhagic complications may be clinically important, and dual therapy complicates treatment of ruptured aneurysms. Pipeline Shield and hydrophilic polymer-coated flow diverters were developed partly to reduce this thrombotic burden [11, 29, 30]. The SHIELD prospective study supported the safety of Pipeline Shield [11], while more recent multicenter investigations have explored surface-modified devices under single-antiplatelet strategies, including use in selected ruptured aneurysms [29]. Pipeline Shield has also been associated with a lower burden of diffusion-weighted imaging lesions in contemporary comparative data [30]. These findings are encouraging but do not establish that routine dual antiplatelet therapy can safely be abandoned for all flow-diverter procedures [11, 29, 30].

The increasing efficacy of flow diversion must be balanced against evidence showing that new technology should not automatically replace established therapies. The FIAT randomized trial was deliberately designed to evaluate flow diversion under conditions of clinical uncertainty. Early results showed that flow diversion did not initially achieve the anticipated superiority over standard treatment and demonstrated the importance of randomized evaluation of novel devices [18]. Longer-term analysis later suggested greater effectiveness of flow diversion in the predominantly large anterior-circulation aneurysm population, illustrating how conclusions can evolve with longer follow-up because flow-diverter treatment depends on delayed healing [19]. References [18, 19] remain critical reminders that high occlusion percentages in single-arm device trials do not substitute for comparative clinical evidence. Wide-neck bifurcation aneurysms represent a different geometrical problem. A flow diverter implanted across an MCA bifurcation, anterior communicating artery complex, ICA terminus, or basilar apex may cover one or more normal arterial branches whose preservation is essential. Conventional stent-assisted coiling can maintain branch patency but requires intraluminal implants and antiplatelet treatment. These anatomical limitations provided the rationale for intrasaccular flow disruption [20–24].

The Woven EndoBridge was developed as a self-expanding braided device placed completely within the aneurysm sac. Early clinical experience demonstrated feasibility in wide-neck bifurcation aneurysms [20]. The pivotal WEB-IT prospective trial included 150 patients and demonstrated a very low primary safety-event rate; at one year, complete aneurysm occlusion was present in approximately 54% and adequate occlusion in approximately 85% [21]. Five-year follow-up subsequently demonstrated durable safety and effectiveness with no new major device-related safety signal, establishing the WEB as one of the most extensively studied intrasaccular devices [22]. Long-

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term European WEBCAST and WEBCAST-2 experience similarly supports durable aneurysm protection and a relatively low retreatment burden in properly selected wide-neck bifurcation aneurysms [23]. The clinical significance of the intrasaccular concept becomes particularly evident in ruptured aneurysms. Because the WEB is contained within the aneurysm rather than deployed as a stent across the parent artery, treatment can potentially avoid the antiplatelet requirements associated with conventional stent-assisted techniques. The prospective CLARYS study evaluated recently ruptured bifurcation aneurysms and reported no target-aneurysm rebleeding during the first year after treatment, with subsequent angiographic follow-up demonstrating clinically meaningful occlusion [24, 25]. The success of WEB has stimulated development of other intrasaccular strategies. The Contour Neurovascular System is designed to sit at the aneurysm neck and produce a flow-disrupting interface with less dependence on complete filling of the aneurysm volume. Contemporary multicenter and national cohorts have demonstrated promising technical and angiographic results, particularly in wide-neck bifurcation anatomy [26, 27]. A 2025 systematic review confirmed growing clinical experience while emphasizing the need for additional prospective evidence [28]. The Artisse device represents another newer intrasaccular flow-diversion concept, with early clinical results reported in 2025 [34]. These technologies may eventually permit increasingly morphology-specific treatment within the broad category of "intrasaccular therapy."

This expansion creates a new clinical problem: several technically feasible devices may exist for the same aneurysm. A 7-mm wide-neck MCA bifurcation aneurysm may potentially be treated with balloon-assisted coiling, stent-assisted coiling, WEB, Contour, selected flow diversion, or microsurgical clipping. The optimal choice depends not only on technical feasibility but on branch incorporation, bifurcation geometry, patient age, rupture status, antiplatelet tolerance, likelihood of complete occlusion, retreatment probability, and availability of a surgical option.

Materials and Methods. A structured narrative review was performed using prospective pivotal device trials, randomized controlled investigations, prospective multicenter registries, large retrospective cohorts, and long-term follow-up studies available through August 2026. The analysis focused on modern intracranial flow-diversion and intrasaccular flow-disruption systems. Pipeline, Pipeline Flex, Pipeline Shield, Pipeline Vantage, Surpass Streamline, Surpass Evolve, FRED, FRED X, WEB, Contour, and emerging intrasaccular devices were considered. The evidence was organized around aneurysm geometry, biological mechanism of occlusion, technical deployment, parent-vessel reconstruction, side-branch incorporation, angiographic occlusion, retreatment, ischemic complications, hemorrhagic complications, antiplatelet therapy, ruptured aneurysms, and long-term durability. Because device trials differed in aneurysm location, size, morphology, occlusion scales, antiplatelet regimens, and follow-up schedules, direct quantitative pooling was not attempted. The conceptual endpoint was defined as precision endovascular reconstruction, meaning selection of the device whose mechanism of aneurysm healing provides the highest expected probability of durable aneurysm exclusion with the lowest cumulative risk to the parent artery, incorporated branches, and patient.

Results.

Mechanism of Flow Diversion. A flow diverter does not primarily occlude the aneurysm at the moment of deployment. The device is positioned across the aneurysm neck within the parent

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artery. Its braided high-metal-coverage structure modifies the relationship between longitudinal parent-artery flow and the aneurysm inflow jet. Entry velocity and intra-aneurysmal circulation progressively decrease. Blood stasis promotes thrombus formation within the aneurysm. Simultaneously, endothelial and neointimal growth progressively covers the device across the aneurysm neck, reconstructing the lumen of the parent vessel and excluding the pathological sac from circulation. This distinction explains why immediate angiography often shows persistent aneurysm opacification despite a technically successful procedure. Complete occlusion can evolve over six months, one year, and even several years. Therefore, immediate angiographic filling should not automatically be interpreted as procedural failure.

Device Deployment and Metal Coverage. Flow-diverter performance depends substantially on deployed geometry. Braided devices change their porosity and metal coverage according to vessel diameter, curvature, foreshortening, and deployment technique. An oversized device can produce reduced metal density across the aneurysm neck. An undersized device may generate stronger flow diversion but can create deployment, wall-apposition, or migration concerns. Vessel curvature can produce asymmetric braid opening, with differences between the inner and outer curvature. Poor wall apposition can facilitate thrombus formation or persistent endoleak-like inflow around the device. This means that the nominal device specification does not necessarily equal the biologically effective configuration after deployment. Three-dimensional cone-beam CT and high-resolution fluoroscopic imaging are consequently increasingly used to assess device expansion and wall apposition.

Aneurysm Geometry and Delayed Occlusion. The probability of complete healing after flow diversion is influenced by aneurysm size, branch incorporation, parent-vessel anatomy, neck geometry, previous stents, device apposition, smoking, antiplatelet regimen, and possibly patient-specific endothelial response. Aneurysms from which an important branch originates may remain patent because continuing branch flow sustains circulation through the aneurysm neck. This phenomenon is particularly relevant for posterior communicating artery aneurysms with fetal-type posterior cerebral circulation. In such cases, persistent physiological demand across the aneurysm can counteract the low-flow environment required for thrombosis. Similarly, bifurcation aneurysms may behave differently from sidewall ICA aneurysms because the device must preserve downstream branch flow.

Table 1. Factors influencing success after flow diversion

Factor	Potential effect
Small sidewall aneurysm	Generally favorable healing geometry
Large or giant aneurysm	Longer thrombosis interval and delayed rupture concern
Incorporated branch	Can sustain residual aneurysm flow
Fetal PCom anatomy	May reduce occlusion probability
Good device wall apposition	Supports safe endothelialization
Device oversizing	May reduce effective metal coverage
Multiple overlapping devices	Greater flow disruption but increased metal burden
Previous stent	Can impair FD expansion and wall apposition
Smoking	Potential negative biological effect on healing
Inadequate platelet inhibition	Increased thromboembolic risk
Excessive platelet inhibition	Increased hemorrhagic risk

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Pipeline and the Evolution From Large to Small Aneurysms. Pipeline was initially adopted for large and giant ICA aneurysms that were poorly suited to coiling. Long-term follow-up demonstrated progressive occlusion, with the proportion of completely occluded aneurysms increasing over time. This delayed biological healing distinguishes flow diversion from coil embolization. PREMIER extended the concept to smaller unruptured aneurysms and demonstrated that flow diversion can be performed with relatively low morbidity in carefully selected anatomy.
However, this does not imply that every small aneurysm should be treated with a flow diverter.
A small aneurysm with a very low lifetime rupture risk may gain little benefit from a device that requires antiplatelet therapy and introduces a small but nonzero risk of ischemic or hemorrhagic complications. The indication must therefore begin with rupture-risk assessment rather than device availability.

Surpass and FRED Platforms. Surpass was designed to provide predictable mesh density with relatively limited need for overlapping constructs. SCENT validated the device for complex large and giant ICA aneurysms. Long-term results indicate durable vascular remodeling. Surpass Evolve subsequently introduced a lower-profile delivery platform and has expanded real-world use toward smaller and more distal vessels. FRED uses a dual-layer configuration in which the central working segment provides the principal flow-diversion effect while proximal and distal portions support deployment. FRED X incorporates surface treatment intended to reduce thrombotic interaction. The relevant clinical question is not whether one contemporary platform is universally superior. Differences in deliverability, radial force, foreshortening, wire count, mesh configuration, surface coating, radiopacity, and available diameter range can make different devices preferable for different vessel anatomies.

Surface Modification and Antiplatelet Therapy. Thromboembolic events remain one of the major limitations of flow diversion. Before endothelialization, metal struts remain exposed directly to circulating blood. Platelet adhesion and activation can generate acute or delayed in-stent thrombosis. DAPT reduces this risk but simultaneously increases hemorrhagic risk. Surface modification aims to shift this balance. Pipeline Shield uses phosphorylcholine-based surface modification, while other systems use hydrophilic polymer coating or related antithrombogenic technologies. The ultimate objective is not simply a less thrombogenic device. The larger clinical objective is to reduce antiplatelet burden sufficiently that flow diversion becomes safer in patients with recent hemorrhage, anticipated surgery, ventriculostomy requirements, or elevated bleeding risk. Current evidence is promising, but the degree to which single-antiplatelet therapy can replace DAPT depends on the specific device, clinical context, platelet agent, and rupture status.

Flow Diversion in Ruptured Aneurysms. The major challenge in subarachnoid hemorrhage is that definitive aneurysm protection is needed immediately. Flow diversion can be useful for blister, dissecting, fusiform, or otherwise unclippable and uncoilable aneurysms. However, several problems remain. First, the aneurysm may continue to fill immediately after device implantation because thrombosis is delayed. Second, antiplatelet therapy increases the bleeding risk associated with external ventricular drainage, decompressive surgery, or other invasive procedures. Third, acutely ruptured lesions may have unstable walls. Surface-modified flow diverters under reduced antiplatelet

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regimens are therefore particularly attractive in this setting, but their use requires specialized neurovascular expertise and careful patient selection.

Posterior Circulation Flow Diversion. Posterior circulation aneurysms represent one of the most challenging applications of flow diversion. Basilar and vertebrobasilar arteries give rise to numerous perforators supplying the brainstem. A high-metal-coverage construct across these vessels can potentially produce perforator ischemia. Fusiform basilar aneurysms also frequently reflect diffuse parent-artery pathology rather than a focal neck defect. Consequently, excellent technical deployment does not guarantee a favorable biological result. Posterior circulation flow diversion should therefore be considered separately from routine ICA sidewall aneurysm treatment. Distal posterior circulation and carefully selected vertebral lesions can be reasonable targets, but giant fusiform basilar aneurysms remain among the highest-risk aneurysm phenotypes.

WEB and Intrasaccular Flow Disruption. WEB provides a distinct mechanism of treatment. Instead of reconstructing the parent artery, the device sits inside the aneurysm and creates a dense mesh at the aneurysm neck. The resulting reduction in inflow promotes intra-aneurysmal thrombosis. Because no parent-artery stent is required in the standard configuration, the approach is particularly attractive for wide-neck bifurcation aneurysms. Branch arteries originating around the aneurysm neck can remain untouched by an intraluminal scaffold. The trade-off is that device sizing is critical. An undersized WEB may leave persistent inflow around the device. An oversized device may protrude into the parent artery or compress longitudinally over time. The final implant configuration is therefore strongly dependent on accurate three-dimensional measurement of aneurysm width and height.

Long-Term WEB Healing. WEB treatment introduced a new angiographic issue: complete occlusion is not the only clinically acceptable endpoint. A small residual proximal recess can remain while the actual aneurysm dome is effectively excluded. Therefore, adequate occlusion commonly combines complete occlusion with a limited neck remnant. Long-term studies suggest that many WEB-treated aneurysms remain stable over years, although device compression or shape modification can occur. Retreatment remains necessary in a minority of patients. The possibility of retreatment should therefore be incorporated into initial counseling, especially in young patients.

Table 2. Parent-vessel flow diversion versus intrasaccular flow disruption

Feature	Parent-vessel flow diverter	Intrasaccular flow disruptor
Implant location	Parent artery	Aneurysm sac/neck
Primary mechanism	Vessel reconstruction	Inflow disruption
Best-established anatomy	Sidewall and complex ICA aneurysms	Wide-neck bifurcation aneurysms
Parent-vessel metal	High	Minimal or absent
Branch coverage	Often unavoidable	Usually avoided
DAPT requirement	Common	Often unnecessary if device fully intrasaccular
Immediate complete occlusion	Uncommon	Variable
Delayed healing	Expected	Expected
Ruptured aneurysm	Selected cases	Particularly attractive in some bifurcation

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suitability		lesions
Main technical determinant	Wall apposition and neck coverage	Accurate device sizing and neck interface

WEB in Ruptured Aneurysms. Wide-neck bifurcation aneurysms are particularly difficult to treat in acute subarachnoid hemorrhage because conventional stent assistance requires antiplatelet therapy. WEB offers a solution when the aneurysm morphology can accommodate a stable intrasaccular device. The CLARYS prospective study provides important evidence that selected ruptured aneurysms can achieve effective early protection against rebleeding. This does not imply that WEB is appropriate for every ruptured aneurysm. Irregular morphology, very small sacs, unfavorable dimensions, intraprocedural instability, or anatomy unsuitable for secure device positioning may still favor coiling or microsurgical clipping.

Contour and Neck-Focused Intrasaccular Therapy. Contour differs conceptually from devices designed to occupy most of the aneurysm sac. Its disk-like braided configuration is deployed across the aneurysm neck from within the sac. The objective is to create a dense flow-disrupting interface at the inflow zone while allowing less dependence on filling the entire aneurysm volume. This may be particularly useful in irregular sacs where conventional volume-filling intrasaccular sizing is difficult. Early and intermediate data are encouraging, but the evidence base remains smaller than for WEB. Long-term multicenter prospective evaluation will be necessary before equivalent durability can be assumed.

Treatment of Recurrent or Residual Aneurysms. Flow diversion has become particularly important for aneurysms recurring after previous coiling. A residual neck or reopened sac can sometimes be reconstructed with a single parent-vessel device rather than repeated coil packing. However, previous stents can interfere with complete wall apposition of the new flow diverter. WEB-treated aneurysms can also require retreatment. Options include additional intrasaccular treatment, stent-assisted coiling, flow diversion, or microsurgical clipping depending on device configuration and residual anatomy. Microsurgical retreatment after previous intrasaccular therapy is technically possible but requires detailed understanding of the relationship between the implant, aneurysm neck, and branches.

Precision Device Selection. The existence of multiple effective devices means that technical possibility alone should no longer define treatment choice. A sidewall cavernous ICA aneurysm and an MCA bifurcation aneurysm may have identical maximal diameters but require completely different reconstructive strategies. The first is fundamentally a diseased-parent-artery problem. The second is a bifurcation-preservation problem. Flow diversion is naturally suited to reconstruction of the first lesion. Intrasaccular therapy or microsurgical clipping may be more anatomically logical for the second.

Table 3. Proposed precision endovascular phenotypes

Aneurysm phenotype	Primary anatomical problem	Preferred conceptual strategy
Large ICA sidewall aneurysm	Diseased parent artery + wide neck	Flow diversion
Fusiform ICA aneurysm	Parent-vessel pathology	Flow diversion
Recurrent coiled sidewall aneurysm	Persistent neck + coil compaction	Flow diversion

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Small wide-neck MCA bifurcation	Branch preservation	WEB/Contour or clipping
Basilar apex wide-neck aneurysm	Multiple branch origins	Intrasaccular therapy in selected anatomy
Ruptured wide-neck bifurcation aneurysm	Need for immediate protection without DAPT	WEB when anatomically suitable
Blister aneurysm	Fragile non-saccular wall	Flow diversion ± adjunctive strategy
Giant fusiform basilar aneurysm	Diffuse perforator-bearing artery disease	Extremely selective individualized treatment
Patient unable to tolerate DAPT	Antiplatelet limitation	Intrasaccular device when anatomy permits
Distal small-vessel aneurysm	Limited parent-vessel diameter	Low-profile reconstructive or alternative technique

Discussion. The major change in intracranial aneurysm treatment is not the introduction of a specific brand of flow diverter or intrasaccular implant. It is the transition from sac-centered occlusion to mechanism-centered reconstruction. The foundational natural-history studies remain critical because the existence of a technically elegant device does not establish an indication for prophylactic treatment. UCAS demonstrated that rupture risk differs significantly by aneurysm location and size [1]. PHASES translated several major clinical predictors into a practical rupture-risk model [2]. UIATS attempted to combine natural history with procedural considerations [3], while ELAPSS emphasized the importance of aneurysm growth during follow-up [4]. These studies [1–4] should precede, rather than follow, discussion of device selection. A low-risk incidental aneurysm should not be converted into a high-tech intervention merely because flow diversion has become technically feasible. The Pipeline literature [5–11] demonstrates why long-term evaluation is essential for reconstructive endovascular therapy. Initial studies established technical feasibility [5], PUFS demonstrated effectiveness in complex large and giant carotid aneurysms [6], and later follow-up documented progressively increasing occlusion rates [7, 8]. PREMIER then expanded the indication toward small and medium wide-neck aneurysms [9], with three-year data confirming durability [10]. Pipeline Shield introduced the additional concept that thromboresistant surface chemistry can become part of device efficacy and safety [11]. Taken together, references [5–11] show a progression from mechanical design toward biological device–blood interaction.

A similar progression is observed with Surpass. Early prospective experience demonstrated deployment feasibility [12]. SCENT established pivotal effectiveness and safety in large and giant aneurysms [13]. The five-year SCENT results now demonstrate durable long-term reconstruction, an important finding because delayed aneurysm reopening or device-related complications could theoretically emerge long after implantation [14]. References [12–14] therefore support the concept that parent-artery reconstruction can produce lasting aneurysm exclusion when lesion geometry and device deployment are favorable. FRED provides a complementary example. The early European experience [15] and prospective SAFE data [16] showed progressive aneurysm occlusion using the dual-layer platform. FRED X extends the concept through surface treatment and has demonstrated favorable multicenter long-term results [17]. The broader significance of references [15–17] lies in the recognition that future flow diverters will likely be judged not only by porosity and radial force

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but also by thromboresistance, deliverability through smaller catheters, branch interaction, and compatibility with simplified antiplatelet regimens. At the same time, the FIAT randomized experience remains one of the most important methodological counterweights to uncontrolled technological enthusiasm [18, 19]. Early results showed that flow diversion did not immediately outperform standard therapy by the expected margin [18]. Later analysis provided a more favorable view in selected large anterior-circulation aneurysms [19]. This temporal change illustrates a fundamental problem in flow-diverter trial design: the device produces delayed biological healing, while conventional coiling or clipping can provide immediate anatomical exclusion. Endpoints assessed too early may underestimate the effectiveness of flow diversion; endpoints limited to angiographic occlusion may overestimate its clinical value. References [18, 19] therefore support both continued use and continued critical evaluation of the technology.

The WEB evidence base represents a different type of evolution. Early work established feasibility for aneurysms that had historically required balloon remodeling or stent-assisted coiling [20]. WEB-IT then provided prospective pivotal evidence with extremely low major morbidity and adequate one-year occlusion in the majority of treated patients [21]. Five-year WEB-IT follow-up demonstrated durability without a late device-related safety signal [22]. European WEBCAST experience independently reinforced this long-term profile [23]. Thus, references [20–23] provide a comparatively mature body of evidence for intrasaccular treatment. The CLARYS trial adds a particularly important dimension because it evaluated ruptured aneurysms [24, 25]. Conventional wide-neck bifurcation treatment in acute SAH frequently requires a compromise between coil stability and antiplatelet burden. The absence of target-aneurysm rebleeding reported in CLARYS supports the concept that an intrasaccular implant can provide early protection without the same need for a parent-vessel stent [24]. One-year angiographic follow-up demonstrated that this immediate clinical protection can coexist with acceptable longer-term aneurysm occlusion [25]. These findings [24, 25] explain why intrasaccular therapy may be especially transformative in ruptured bifurcation aneurysms. The Contour literature [26–28] represents the next stage in device specialization. Rather than treating all wide-neck bifurcation aneurysms with a volume-filling implant, Contour focuses on the neck plane. Early series and the large UK experience have shown promising occlusion and safety profiles [26, 27], while systematic review demonstrates increasingly consistent multicenter experience but also highlights limitations of the current evidence [28]. References [26–28] therefore support Contour as a promising technique, not yet as a universally equivalent alternative to the more extensively studied WEB.

Artisse represents a further variation of the intrasaccular flow-diversion principle [34]. The proliferation of these devices suggests that the future category will not simply be “WEB-like devices.” Different aneurysm morphologies may favor different radial profiles, neck coverage, conformability, and retrievability characteristics. Reference [34] is therefore important not because it proves superiority of a new platform, but because it illustrates a rapidly diversifying therapeutic class. Antiplatelet therapy remains one of the most consequential distinctions between parent-vessel and intrasaccular treatment. The SHIELD study [11], multicenter experience with hydrophilic polymer-coated flow diverters under single antiplatelet therapy [29], and comparative diffusion-weighted MRI data for Pipeline Shield [30] all suggest that surface engineering can meaningfully

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alter thrombogenicity. However, device coating does not eliminate the fundamental biological reality that a braided metallic scaffold remains in contact with arterial blood until endothelialization occurs. References [11, 29, 30] therefore support antiplatelet simplification as an evolving research direction rather than an established universal practice. This issue is particularly important in ruptured aneurysms. In an elective unruptured case, platelet inhibition can be established before implantation, response can be assessed, and elective surgery can be postponed if necessary. In SAH, ventriculostomy, decompressive craniectomy, tracheostomy, shunt placement, or other procedures may become necessary unexpectedly. Any strategy requiring potent prolonged platelet inhibition complicates the entire neurocritical-care pathway.

This is one reason why intrasaccular devices are more than simply another method of producing aneurysm occlusion. They may alter the management of the entire ruptured-aneurysm patient by reducing the need for an intraluminal implant. The problem of incomplete flow-diverter occlusion deserves equally careful attention. PREMIER analyses demonstrated that failure of complete occlusion is not random [31]. Branch incorporation, aneurysm geometry, device factors, and biological healing can contribute. Reference [31] suggests that future treatment planning should include a preprocedural probability of complete endothelial closure rather than assuming that all successfully deployed devices will ultimately cure the aneurysm. Long-term multi-device experience reported in 2026 similarly supports overall durability of contemporary flow-diversion platforms while demonstrating that residual filling, retreatment, ischemic events, and delayed device-related changes remain clinically relevant [32]. Reference [32] is particularly useful because most historical evidence was dominated by Pipeline, whereas current practice increasingly involves multiple platforms with different mechanical and surface properties. Modern Surpass Evolve investigations add further support to the move toward lower-profile and more deliverable flow diverters [33]. The ability to deliver a device through smaller microcatheters can expand access to distal and tortuous anatomy, but broader technical reach does not necessarily mean broader appropriate indication. Small distal parent arteries contain proportionally more important branch and perforator anatomy, making safety margins narrower. Reference [33] therefore illustrates the tension between increasing device deliverability and the need for increasingly disciplined selection.

The posterior circulation provides perhaps the clearest example of this tension. Flow diversion can reconstruct aneurysms previously considered almost untreatable, but perforator-rich basilar anatomy creates a qualitatively different risk profile from cavernous or paraophthalmic ICA treatment. Contemporary Pipeline Vantage experience similarly demonstrates that bifurcation and posterior circulation aneurysms can have lower occlusion rates and greater complication risks than straightforward anterior circulation sidewall lesions [35]. Thus, references [13, 14, 32, 35] should not be generalized across vascular territories. A central implication is that aneurysm location should be interpreted mechanistically. A paraophthalmic sidewall aneurysm is primarily an inflow-and-parent-vessel reconstruction problem. An MCA bifurcation aneurysm is primarily a branch-preservation and neck-control problem. A basilar apex aneurysm is a branch- and perforator-preservation problem. A blister aneurysm is a diseased-wall reconstruction problem. A giant fusiform basilar aneurysm is a diffuse parent-artery pathology problem. These are all called intracranial aneurysms, but they should not be expected to respond optimally to the same device.

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Table 4. Proposed precision device-selection framework

Decision domain	Relevant question	Device implication
Natural history	Is treatment justified at all?	Observation may remain optimal
Aneurysm morphology	Saccular, fusiform, blister, dissecting?	Determines reconstructive mechanism
Neck geometry	Sidewall or bifurcation?	FD versus intrasaccular strategy
Parent vessel	Can a stable FD be deployed?	Determines feasibility of flow diversion
Branch incorporation	Does a major branch arise from the sac/neck?	May favor intrasaccular or surgical strategy
Rupture status	Is immediate secure protection required?	Avoid unnecessary DAPT when possible
Antiplatelet tolerance	Can prolonged DAPT be safely administered?	Major determinant of FD suitability
Aneurysm size	Small versus giant	Influences thrombosis and delayed rupture behavior
Location	ICA, MCA, ACom, basilar, distal	Determines branch/perforator risk
Previous treatment	Coil/stent/device already present?	Influences wall apposition and retreatment
Patient age	Long expected follow-up?	Durability becomes increasingly important
Surgical alternative	Is clipping low risk and curative?	Device therapy should be compared with surgery

The next stage of development will likely involve patient-specific computational prediction. Flow diverter effectiveness is strongly dependent on deployed braid geometry, which determines pore density and inflow reduction. Computational fluid dynamics can quantify post-treatment velocity, wall shear stress, turnover time, and inflow concentration. However, computational models remain too slow and heterogeneous for routine intraoperative decision-making in many centers. Machine-learning approaches and angiographic parametric imaging are therefore being explored as faster surrogates. Such models could eventually answer a clinically practical question before implantation: whether the proposed device diameter, length, and landing zone are likely to produce sufficient hemodynamic disruption in this specific aneurysm. A comparable principle can be applied to WEB and Contour sizing. At present, device selection remains largely dependent on three-dimensional angiographic measurement and operator experience. The future could involve automated segmentation of the aneurysm sac, computational simulation of device deployment, estimation of wall contact, prediction of neck coverage, and probability of complete occlusion. The clinical value of such technology would be greatest if it reduced both incomplete occlusion and unnecessary device oversizing. Artificial intelligence should not be used merely to produce an automated device recommendation. It should quantify the competing consequences of several possible strategies. For example, an algorithm evaluating an MCA bifurcation aneurysm should compare expected WEB occlusion, expected flow-diverter branch risk, predicted stent-assisted coiling recurrence, and estimated microsurgical morbidity. This is the difference between device prediction and clinical decision support.

The growing diversity of technologies also creates a challenge for clinical trials. Traditional pivotal device trials compare outcomes against prespecified performance goals rather than against another modern device. Such studies are essential for regulatory evaluation but provide limited

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information when the practical question is whether WEB, Contour, clipping, or stent-assisted coiling is preferable for a specific aneurysm. Future trials therefore require morphology-specific comparative designs. One potential study could enroll unruptured 4–10 mm wide-neck bifurcation aneurysms that are technically suitable for both an intrasaccular device and established conventional therapy. The primary endpoint should not be complete occlusion alone. A more meaningful endpoint would combine complete or adequate aneurysm occlusion, no major neurological morbidity, absence of retreatment, branch preservation, and freedom from long-term antiplatelet therapy. For flow diversion, future comparative studies should similarly evaluate device-specific outcomes according to anatomical phenotype rather than combining carotid sidewall, bifurcation, posterior circulation, and fusiform lesions.

Table 5. Proposed prospective precision-endovascular aneurysm registry

Variable	Proposed assessment
Patient factors	Age, hypertension, smoking, previous SAH
Natural-risk model	PHASES + growth history
Aneurysm geometry	Size, neck, aspect ratio, irregularity
Architecture	Sidewall versus bifurcation
Branch anatomy	Incorporated branch/perforator
Parent vessel	Diameter, curvature, landing zones
Rupture status	Ruptured/unruptured
Device strategy	FD, WEB, Contour, coil, stent-coil, clipping
Antiplatelet strategy	DAPT, SAPT, agent and duration
Platelet testing	When clinically indicated
Immediate endpoint	Device deployment and branch patency
Imaging follow-up	6, 12, 24 months and long term
Occlusion scale	Device-appropriate standardized classification
Clinical endpoint	mRS and neurological adverse events
Retreatment	Any additional aneurysm treatment
Primary composite outcome	Durable occlusion without neurological morbidity or retreatment

The key lesson from references [1–35] is that endovascular innovation has not eliminated the need for individualized cerebrovascular judgment. Instead, greater technological choice has made that judgment more important. The correct question is no longer “Can this aneurysm be treated with a flow diverter?” For many aneurysms, the answer is technically yes. The correct question is whether flow diversion provides a superior risk–benefit mechanism compared with an intrasaccular implant, coiling, clipping, or observation. Similarly, the question is not whether WEB or Contour can be deployed successfully, but whether long-term branch preservation, aneurysm healing, retreatment probability, and antiplatelet burden make that strategy preferable for the individual patient. Precision endovascular reconstruction therefore requires simultaneous assessment of natural history, morphology, vascular architecture, healing biology, antiplatelet risk, and alternative therapy.

Conclusion. Modern intracranial aneurysm therapy has evolved from mechanical aneurysm filling toward biological and hemodynamic reconstruction. Parent-vessel flow diversion and intrasaccular flow disruption represent two fundamentally different mechanisms of aneurysm treatment. Flow diverters are particularly suited to sidewall, fusiform, large, giant, recurrent, and

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complex aneurysms in which reconstruction of the diseased parent artery is the principal therapeutic objective. Intrasaccular devices are particularly attractive for wide-neck bifurcation aneurysms because they modify aneurysm inflow while minimizing the need for a permanent parent-vessel scaffold. The WEB currently has the most mature long-term evidence among intrasaccular flow-disruption systems, while newer technologies such as Contour and Artisse expand the range of available geometrical solutions. Surface-modified flow diverters represent an important evolution aimed at reducing thrombogenicity and potentially simplifying antiplatelet therapy, particularly in patients with an elevated bleeding risk. However, no device should be selected solely because it is technologically newer or technically deployable. The optimal strategy depends on aneurysm rupture risk, parent-vessel anatomy, sidewall versus bifurcation configuration, branch incorporation, rupture status, antiplatelet tolerance, probability of durable occlusion, and the safety of available surgical or conventional endovascular alternatives. The future of aneurysm therapy therefore lies in precision endovascular reconstruction, in which the biological mechanism of the selected device is matched to the anatomical and clinical phenotype of the individual aneurysm.

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Mundarija	**Содержание**	**Contents**

QIZILO‘NGACH VA OSHQOZON KASALLIKLARINI TASHXISLASHDA KONTRAST RENTGENOGRAFIYANING ZAMONAVIY IMKONIYATLARI Abdiyev B. M. (Автор)	4-13
MIYA O‘SMALARINING DIFFERENSIAL DIAGNOSTIKASIDA KONTRASTLI MAGNIT-REZONANS TOMOGRAFIYANING AHAMIYATI Jiyanbayev D. B. (Автор)	14-22
КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ ПРИЗНАКОВ УЛЬТРАЗВУКОВОГО ИССЛЕДОВАНИЯ ПРИ ХРОНИЧЕСКОМ ПАНКРЕАТИТЕ Бобониёзов С.Б. (Автор)	23-31
QALQONSIMON BEZ TUGUNLARIDA TI-RADS TIZIMINING DIAGNOSTIK AHAMIYATINI ULTRATOVUSH ASOSIDA BAHOLASH Jurayev Sh.Z. (Автор)	32-40
АСЕПТИЧЕСКИЙ НЕКРОЗ ГОЛОВКИ БЕДРА ПОСЛЕ COVID-19: ПАТОГЕНЕЗ, КЛИНИЧЕСКИЕ ПРОЯВЛЕНИЯ И СОВРЕМЕННЫЕ ПОДХОДЫ К РЕАБИЛИТАЦИИ Негматов И. С. (Автор)	41-45
ВЛИЯНИЕ НАРУШЕНИЙ МИКРОЦИРКУЛЯЦИИ НА РЕЗУЛЬТАТЫ РЕАБИЛИТАЦИИ ПАЦИЕНТОВ С АСЕПТИЧЕСКИМ НЕКРОЗОМ БЕДРА ПОСЛЕ COVID-19 Негматов И. С. (Автор)	46-50
ЭФФЕКТИВНОСТЬ КОМБИНИРОВАННОЙ ФИЗИЧЕСКОЙ РЕАБИЛИТАЦИИ ПРИ АСЕПТИЧЕСКОМ НЕКРОЗЕ БЕДРА В ПОСТКОВИДНОМ ПЕРИОДЕ Негматов И. С. (Автор)	51-55
ТЕЛЕМЕДИЦИНСКАЯ ПОДДЕРЖКА В ПРОГРАММЕ ДВИГАТЕЛЬНОЙ РЕАБИЛИТАЦИИ ПАЦИЕНТОВ С АСЕПТИЧЕСКИМ НЕКРОЗОМ ГОЛОВКИ БЕДРА В ПОСТКОВИДНОМ ПЕРИОДЕ Негматов И. С. (Автор)	56-59
МЕТОДЫ ФУНКЦИОНАЛЬНОЙ ДИАГНОСТИКИ В ОЦЕНКЕ ЭФФЕКТИВНОСТИ РЕАБИЛИТАЦИОННЫХ ПРОГРАММ ПРИ АСЕПТИЧЕСКОМ НЕКРОЗЕ ГОЛОВКИ БЕДРА В ПОСТКОВИДНОМ ПЕРИОДЕ Негматов И. С. (Автор)	60-64
REVMATOID ARTRITDA QO'L-PANJA BO'G'IMLARIDA SINOVITNI ULTRATOVUSH TEKSHIRUVI YORDAMIDA ERTA ANIQLASHNING DIAGNOSTIK AHAMIYATI Ametova A. S., Umarov F. U., Salohiy I. O. (Автор)	65-72
THE ROLE OF RADIOLOGY SURGERY IN COMPLICATED FORMS OF GALLSTONE DISEASE Nurmurzayev Z. N., Umarov F. U., Sunnatova M. O. (Автор)	73-80

OSHQOZON YARASIDAN MASSIV QON KETISHLARIDA GASTREKTOMIYANING O‘ZIGA XOS XUSUSIYATLARI Achilov M. T. (Автор)	81-85
O’TKIR TO’G’RI ICHAK PROLAPSI ASORATLARINI XIRURGIK DAVOLASH XUSUSIYATLARI (AMALIYOTDAN LAVHA) Achilov M. T. (Автор)	86-91
АНАЛИЗ МУТАЦИЙ ГЕНА DSPP С ПОМОЩЬЮ СЕКВЕНИРОВАНИЯ НОВОГО ПОКОЛЕНИЯ Турдибеков Г. М., Абдусатторова Х. М. (Автор)	92-100
ТИЗЗА ҚОПҚОҒИ ЧИҚИШЛАРИ ВА ПАТЕЛЛОФЕМОРАЛ НОМУТАНОСИБЛИКНИ КТ/МРТ-МОРФОМЕТРИК БАҲОЛАШ Якубов Г. А. (Автор)	101-107
РЕВМАТОИД ВА СЕПТИК АРТРИТ, БУРСИТ ҲАМДА БЕЙКЕР КИСТАСИ ПАТОЛОГИЯЛАРИДА УТД ВА КОНТРАСТЛИ МРТ НИНГ ИНФОРМАТИВЛИГИ Якубов Г. А. (Автор)	108-115
PRECISION NEUROCRITICAL CARE AFTER SEVERE TRAUMATIC BRAIN INJURY: MULTIMODAL MONITORING, DYNAMIC INTRACRANIAL PRESSURE, AND INDIVIDUALIZED CEREBRAL PERFUSION TARGETS Aliev M. A. (Автор)	116-136
PATIENT-SPECIFIC CRANIOPLASTY IN THE ADDITIVE-MANUFACTURING ERA: COMPARATIVE EVALUATION OF PEEK, TITANIUM, PMMA, AND REGENERATIVE POROUS IMPLANTS Aliev M. A. (Автор)	137-156
LOW-INTENSITY FOCUSED ULTRASOUND FOR DRUG-RESISTANT EPILEPSY: NETWORK TARGETING, ACOUSTIC DOSE CONTROL, AND REVERSIBLE NONINVASIVE NEUROMODULATION Juraev A.M. (Автор)	157-173
MINIMALLY INVASIVE EVACUATION OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE IN THE POST-ENRICH ERA: LOCATION-BASED SELECTION, EARLY CLOT REDUCTION, AND RESIDUAL-VOLUME TARGETS Juraev A.M. (Автор)	174-192
MULTIMODAL ARTIFICIAL INTELLIGENCE FOR PRECISION GLIOMA SURGERY: INTEGRATING RADIOMICS, INTRAOPERATIVE ULTRASOUND, BRAIN-SHIFT CORRECTION, AND EXPLAINABLE DECISION SUPPORT Mamadaliev A. M. (Автор)	193-205
CONNECTOME-GUIDED AWAKE SURGERY FOR DIFFUSE GLIOMAS: NETWORK-LEVEL MAPPING OF LANGUAGE, EXECUTIVE FUNCTION, AND NEUROCOGNITIVE RESERVE Mamadaliev A. M. (Автор)	206-218

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INTRAOPERATIVE MOLECULAR IMAGING OF GLIOMA MARGINS: COMPARATIVE INTEGRATION OF 5-AMINOLEVULINIC ACID, RAMAN SPECTROSCOPY, AND REAL-TIME TISSUE CLASSIFICATION Mamadaliev A. M. (Автор)	219-232
Актуальные методы терапии расстройств аутистического спектра Болтаева Ш.У. (Автор)	233-237
PRECISION REVASCULARIZATION IN ADULT MOYAMOYA DISEASE: HEMODYNAMIC PHENOTYPING, DIRECT AND COMBINED BYPASS, HYPERPERFUSION CONTROL, AND PERSONALIZED SURGICAL TARGETING Mamadaliev A.M. (Автор)	238-254
КОМПЬЮТЕРНАЯ ТОМОГРАФИЯ ВЫСОКОГО РАЗРЕШЕНИЯ В ДИАГНОСТИКЕ, ФЕНОТИПИРОВАНИИ И ОЦЕНКЕ КОМОРБИДНОГО ТЕЧЕНИЯ ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ (ХОБЛ) Турдуматов Ж.А. (Автор)	255-259
INTELLIGENT INTRAOPERATIVE NEUROPATHOLOGY IN BRAIN TUMOR SURGERY: STIMULATED RAMAN HISTOLOGY, RAPID NANOPORE EPIGENOMICS, AND AI-GUIDED MARGIN ASSESSMENT Ravshanov D.M. (Автор)	260-278
PRECISION ENDOVASCULAR RECONSTRUCTION OF INTRACRANIAL ANEURYSMS: FLOW DIVERSION, INTRASACCULAR FLOW DISRUPTION, SURFACE- MODIFIED DEVICES, AND PATIENT-SPECIFIC DEVICE SELECTION Abduvoyitov B.B. (Автор)	279-296

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