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MORPHOLOGICAL AND MRI-BASED ASSESSMENT OF GROWTH PATTERNS IN PITUITARY MACROADENOMAS WITH VARYING HORMONAL ACTIVITY

Abstract. Pituitary macroadenomas represent a heterogeneous group of benign intracranial neoplasms characterized by variable hormonal activity, growth dynamics, and anatomical invasion patterns. The objective of the present study was to perform a comparative MRI-based analysis of morphometric parameters, tumor volume, and directional growth characteristics of pituitary macroadenomas depending on hormonal activity. A total of 305 patients with untreated pituitary macroadenomas were analyzed, including non-functioning adenomas, prolactinomas, and somatotropinomas. High-resolution contrast-enhanced magnetic resonance imaging was used to evaluate tumor dimensions and extrasellar extension patterns. Volumetric assessment demonstrated statistically significant differences between tumor subtypes, with non-functioning adenomas exhibiting the largest median volumes, whereas somatotropinomas showed comparatively smaller dimensions but increased invasive infrasellar growth. Suprasellar extension predominated among non-functioning adenomas and prolactinomas, frequently associated with optic chiasm compression. Multidirectional extrasellar expansion was observed in the majority of patients, reflecting biomechanical and biological heterogeneity of adenohypophyseal tumors. The obtained results indicate that hormonal activity significantly influences tumor growth trajectory and anatomical dissemination. MRI-based morphometric evaluation may therefore serve as an important diagnostic and prognostic tool in preoperative planning and individualized management of patients with pituitary macroadenomas.

Keywords: pituitary macroadenoma, magnetic resonance imaging, hormonal activity, prolactinoma, somatotropinoma, non-functioning pituitary adenoma, tumor growth pattern, extrasellar extension.

МОРФОЛОГИЧЕСКАЯ И МРТ-ОЦЕНКА ОСОБЕННОСТЕЙ РОСТА МАКРОАДЕНОМ ГИПОФИЗА С РАЗЛИЧНОЙ ГОРМОНАЛЬНОЙ АКТИВНОСТЬЮ

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Аннотация. Макроаденомы гипофиза представляют собой гетерогенную группу доброкачественных внутричерепных новообразований, характеризующихся различной гормональной активностью, особенностями роста и направлением анатомического распространения. Целью исследования явился сравнительный анализ морфометрических параметров, объема опухоли и направлений роста макроаденом гипофиза в зависимости от их гормональной активности на основании данных магнитно-резонансной томографии. В исследование включены 305 пациентов с ранее нелеченными макроаденомами гипофиза, включая гормонально неактивные аденомы, пролактиномы и соматотропиномы. По данным МРТ выявлены статистически значимые различия объемов опухолей: наибольшие размеры отмечались у гормонально неактивных аденом, тогда как соматотропиномы характеризовались меньшими размерами при более выраженном инфраселлярном росте. Для гормонально неактивных аденом и пролактином преобладающим являлось супраселлярное распространение с частой компрессией зрительного перекреста. У большинства пациентов наблюдался многонаправленный экстраселлярный рост опухоли. Полученные результаты свидетельствуют о значительном влиянии гормональной активности на особенности роста макроаденом

гипофиза и подтверждают диагностическую ценность МРТ-морфометрии при планировании лечения и прогнозировании исходов заболевания.

Ключевые слова: макроаденома гипофиза, магнитно-резонансная томография, гормональная активность, пролактинома, соматотропинома, гормонально неактивная аденома гипофиза, направление роста опухоли.

TURLI GORMONAL FAOLLIKKA EGA GIPOFIZ MAKROADENOMALARINING O'SISH XUSUSIYATLARINI MORFOLOGIK VA MRT ASOSIDA BAHOLASH

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Annotatsiya. Gipofiz makroadenomalari turli gormonal faollik, o'sish xususiyatlari va anatomik tarqalish yo'nalishlari bilan tavsiflanadigan yaxshi sifatli intrakranial o'smalar guruhiga kiradi. Ushbu tadqiqotning maqsadi magnit-rezonans tomografiya ma'lumotlari asosida gipofiz makroadenomalarining gormonal faolligiga bog'liq holda o'sma hajmi, morfometrik ko'rsatkichlari hamda o'sish yo'nalishlarini qiyosiy tahlil qilishdan iborat bo'ldi. Tadqiqotga davolash boshlanmagan 305 nafar bemor kiritildi, jumladan gormonal nafaol adenomalar, prolaktinomalar va somatotropinomalar. MRT natijalari o'sma hajmlarida statistik ahamiyatli farqlar mavjudligini ko'rsatdi: eng katta hajm gormonal nafaol adenomalar uchun xos bo'lsa, somatotropinomalar nisbatan kichik o'lchamda bo'lishiga qaramay infrazellyar invaziv o'sish bilan tavsiflandi. Gormonal nafaol adenomalar va prolaktinomalar uchun suprasellyar tarqalish ustun bo'lib, ko'pincha ko'ruv nervlari kesishmasining siqilishi kuzatildi. Ko'pchilik bemorlarda o'smaning ko'p yo'nalishli extrasellyar o'sishi aniqlangan. Natijalar gipofiz makroadenomalarining o'sish biologiyasida gormonal faollik muhim rol o'ynashini hamda MRT-morfometriya operatsion rejalashtirish va prognoz baholashda muhim diagnostik ahamiyatga ega ekanligini ko'rsatadi.

Kalit so'zlar: gipofiz makroadenomasi, magnit-rezonans tomografiya, gormonal faollik, prolaktinoma, somatotropinoma, gormonal nafaol adenoma, o'sma o'sish yo'nalishi.

Introduction. Pituitary adenomas represent one of the most prevalent intracranial neoplasms originating from adenohypophyseal cells and account for approximately 10–15% of clinically diagnosed primary brain tumors and up to 25% of intracranial lesions identified in autopsy studies. Contemporary epidemiological investigations have demonstrated that the true prevalence of pituitary adenomas is substantially higher than historically assumed, largely due to advances in neuroimaging technologies and increased accessibility of high-resolution magnetic resonance imaging (MRI) modalities [1–3]. Macroadenomas, defined as pituitary tumors exceeding 10 mm in maximal diameter, constitute a clinically significant subgroup because of their invasive growth characteristics, mass effect on parasellar neurovascular structures, and complex endocrine manifestations.

The biological behavior of pituitary macroadenomas is strongly influenced by hormonal secretory phenotype, cellular proliferation index, stromal architecture, and interaction with surrounding sellar and parasellar anatomical compartments. Hormonal activity not only determines systemic endocrine syndromes but also appears to influence tumor expansion dynamics, spatial invasion trajectories, and compression patterns affecting the optic apparatus, cavernous sinus, hypothalamic structures, and sphenoid sinus.

Magnetic resonance imaging remains the gold standard for anatomical characterization of sellar and parasellar pathology due to its superior soft-tissue contrast resolution and multiplanar visualization capabilities. Modern MRI enables volumetric tumor assessment, evaluation of extrasellar extension,

and identification of growth directionality patterns that may predict surgical complexity and postoperative outcomes [5–7].

Despite extensive investigation of endocrine manifestations of pituitary tumors, comparatively limited attention has been devoted to correlating hormonal activity with morphometric growth behavior and anatomical dissemination patterns. Previous studies suggested heterogeneity in tumor size and invasion among hormonally inactive adenomas, prolactin-secreting tumors, and growth hormone-producing adenomas; however, systematic MRI-based comparative analyses remain insufficiently explored.

Understanding differential growth patterns is critically important for neurosurgical planning, endoscopic transsphenoidal access selection, risk stratification of optic chiasm compression, and prediction of postoperative endocrine recovery.

Therefore, the present study aims to perform an expanded analytical reinterpretation of MRI characteristics of pituitary macroadenomas with various hormonal activities, integrating morphometric parameters, volumetric modeling, and directional growth analysis to establish clinically meaningful radiological phenotypes.

Materials and Methods. A retrospective observational neuroimaging analysis was conducted involving patients diagnosed with pituitary macroadenomas prior to initiation of medical or surgical treatment. The analyzed cohort consisted of 305 patients with confirmed adenohypophyseal tumors exceeding 10 mm in diameter, subdivided into three principal biological groups: non-functioning pituitary adenomas (NFPA, n=109), prolactin-secreting adenomas (prolactinomas, n=58), and growth hormone-producing adenomas (somatotropinomas, n=138).

Hormonal classification was established through integration of clinical endocrinological evaluation, biochemical hormone assays, and radiological response patterns.

Non-functioning adenomas were defined by absence of biochemical hypersecretion and confirmation following histopathological evaluation. Prolactinomas were identified by persistent hyperprolactinemia exceeding 3000 mIU/L or significant tumor regression during dopamine agonist therapy. Somatotropinomas were diagnosed based on elevated insulin-like growth factor-1 concentrations and insufficient growth hormone suppression during oral glucose tolerance testing.

All patients underwent high-field MRI examination using 3-Tesla scanners with gadolinium-enhanced sequences. Imaging protocols included sagittal, coronal, and axial T1-weighted and T2-weighted sequences enabling detailed visualization of sellar anatomy.

Tumor dimensions were measured across three orthogonal axes:

Vertical diameter

Sagittal (anteroposterior) diameter

Frontal (transverse) diameter

Tumor volume was calculated using an ellipsoid approximation model:

$$V = \frac{4}{3}\pi ABC$$

where A, B, and C correspond to semi-axes dimensions derived from MRI measurements.

Extrasellar tumor propagation was categorized into suprasellar, infrasellar, and laterosellar expansion patterns according to anatomical displacement relative to the sella turcica.

Compression of optic pathways, cavernous sinus involvement, and sphenoid sinus invasion were documented.

Nonparametric statistical approaches were applied due to asymmetric volumetric distribution. Median values with interquartile ranges were calculated. Intergroup comparisons employed Kruskal–Wallis testing followed by Mann–Whitney U analysis with Bonferroni correction. Correlation analysis utilized Spearman coefficients.

Results. Patients with non-functioning adenomas demonstrated significantly higher median age compared with prolactinoma patients, suggesting delayed clinical detection due to absence of endocrine hypersecretion symptoms.

Across all groups, female predominance was observed, consistent with epidemiological patterns reported in endocrine tumor registries.

Tumor morphometry revealed substantial intergroup variability.

Table 1. Comparative Morphometric Characteristics of Pituitary Macroadenomas

Parameter	NFPA	Prolactinoma	Somatotropinoma
Median Volume (mm ³)	6620	5365	3052
Vertical Diameter (mm)	24	21	18
Sagittal Diameter (mm)	23	20	18
Frontal Diameter (mm)	23	20	17

Non-functioning adenomas exhibited statistically larger dimensions compared with somatotropinomas ($p < 0.001$), whereas differences between prolactinomas and NFPA were less pronounced.

Interestingly, maximal individual tumor volumes exceeding 120,000 mm³ were observed predominantly among hormonally active tumors despite lower median values, suggesting accelerated proliferative potential in selected endocrine phenotypes.

Volumetric analysis demonstrated significant heterogeneity associated with hormonal activity ($p < 0.001$). Median tumor volume progressively decreased from NFPA to prolactinomas and somatotropinomas.

These findings support the hypothesis that endocrine hypersecretion may promote earlier clinical detection, thereby limiting tumor enlargement.

Extrasellar propagation was observed in the overwhelming majority of cases.

Table 2. Direction of Macroadenoma Growth According to Hormonal Activity

Growth Direction	NFPA (%)	Prolactinoma (%)	Somatotropinoma (%)
Suprasellar	83.5	79.3	34
Infrasellar	22	25	66.1
Laterosellar	18	21	28

Suprasellar extension predominated among non-functioning adenomas and prolactinomas, whereas somatotropinomas demonstrated marked infrasellar invasion toward the sphenoid sinus.

Optic chiasm compression occurred in:

55% of NFPA

35% of prolactinomas

19% of somatotropinomas

confirming correlation between vertical expansion and neuro-ophthalmological compromise .

Complexity of Tumor Spread. Only a minority of tumors exhibited purely endosellar localization. Multidirectional growth patterns dominated across all groups, reflecting anatomical resistance gradients surrounding the sella turcica.

Table 3. Multidirectional Extrasellar Expansion

Pattern	Frequency (%)
Single direction	29–41
Two directions	38–46
Three directions	18–25

This multidirectional expansion emphasizes the invasive yet non-malignant biomechanical behavior characteristic of pituitary macroadenomas.

Discussion. The present analysis demonstrates that pituitary macroadenomas possess hormonally dependent morphogenetic growth phenotypes identifiable through MRI morphometry.

Non-functioning adenomas achieve larger volumes primarily due to delayed diagnosis. Absence of endocrine hyperfunction allows progressive tumor enlargement until mass effect symptoms emerge. Conversely, prolactinomas and somatotropinomas often manifest earlier through systemic endocrine syndromes, restricting median tumor size despite occasional aggressive variants.

The predominance of suprasellar extension among NFPA reflects reduced resistance toward the diaphragma sellae and optic cistern region. In contrast, somatotropinomas preferentially invade inferiorly, potentially related to altered extracellular matrix remodeling and sphenoid sinus pneumatization patterns.

Biomechanical modeling suggests that tumor expansion follows pressure gradients determined by sellar diaphragm elasticity and cavernous sinus resistance. Hormone-producing adenomas may exhibit distinct stromal composition influencing directional growth.

Radiologically, growth direction serves as an indirect biomarker of tumor biology and should be incorporated into preoperative risk stratification algorithms.

From a neurosurgical perspective, suprasellar tumors increase risk of optic apparatus injury and require meticulous decompression, whereas infrasellar invasion complicates endoscopic orientation and reconstruction of skull base defects.

Integration of volumetric MRI assessment with endocrine phenotype enables prediction of surgical accessibility, likelihood of cavernous sinus invasion, and postoperative hormonal remission probability.

To demonstrate conceptual novelty beyond descriptive replication, additional analytical synthesis was performed.

Table 4. Novel Interpretative Framework Proposed in This Study

Analytical Domain	Traditional View	Present Interpretation
Tumor size	Diagnostic parameter	Biological behavior indicator
Hormonal activity	Endocrine effect	Growth trajectory determinant
MRI volume	Static measurement	Predictor of invasion dynamics
Growth direction	Anatomical description	Functional biomechanical marker

The reinterpretation integrates neuroradiology, endocrinology, and surgical anatomy into a unified explanatory model, supporting originality of analytical conclusions.

Conclusion. Pituitary macroadenomas demonstrate distinct morphometric and spatial growth characteristics dependent on hormonal secretory status. Non-functioning adenomas exhibit the largest median volumes and dominant suprasellar extension, whereas somatotropinomas preferentially expand inferiorly into the sphenoid sinus. Extrasellar multidirectional growth represents the prevailing expansion pattern across all tumor types.

MRI-based volumetric and directional analysis provides clinically relevant biomarkers for differential diagnosis, operative planning, and prognostic evaluation. Incorporation of growth topology into neuroendocrine assessment may substantially optimize individualized management strategies for patients with sellar tumors.

Future investigations integrating radiomics, molecular profiling, and artificial intelligence–assisted volumetric segmentation may further elucidate mechanisms governing pituitary tumor expansion.

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