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PITUITARY MICROADENOMA: MOLECULAR GENETIC BASIS AND POSSIBILITIES OF EARLY MRI DIAGNOSIS

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ABSTRACT
The article presents an analytical review of current possibilities of magnetic resonance imaging (MRI) in the early diagnosis of pituitary microadenoma, reflecting the evolution of imaging methods from standard protocols to high-field and functional technologies. The pathogenetic and morphological features of microadenomas are considered, along with the comparative effectiveness of MRI and other neuroimaging methods in the context of early detection of tumor changes. Particular attention is paid to the prospects for using dynamic contrast-enhanced MRI, radiomics, and multi-omics approaches, which make it possible to improve diagnostic accuracy and reproducibility. The analysis highlights the relevance of standardizing MRI protocols and integrating artificial intelligence into clinical practice. The findings may be useful for specialists in neuroradiology, endocrinology, and neurosurgery in improving the diagnosis and treatment strategy for pituitary neoplasms.

KEYWORDS: magnetic resonance imaging, pituitary microadenoma, dynamic contrast-enhanced MRI, radiomics, neuroimaging, endocrinology, early diagnosis.

INTRODUCTION
The pituitary gland is a key regulator of the endocrine system, coordinating the activity of most endocrine glands and maintaining the body's homeostasis [1]. Despite its small size, this organ has a complex morphology and high functional activity, which makes it vulnerable to tumor processes. Among pituitary neoplasms, adenomas are the most common; in some cases, they remain microscopic in size and clinically "silent" until substantial progression occurs [2–4]. According to international epidemiological studies, the prevalence of pituitary microadenomas ranges from 10 to 20% in the general population, with approximately 40% of cases detected incidentally during neuroimaging performed for other indications [10]. In the Russian Federation, according to endocrinological registries for 2024, the diagnostic rate of pituitary adenomas was approximately 70 cases per 100,000 population; however, the actual incidence is estimated by experts to be significantly higher due to difficulties in early detection [5]. The main problem remains the low sensitivity of traditional diagnostic methods, which do not allow reliable differentiation of microadenomas at an early stage or assessment of their functional activity.

Modern magnetic resonance imaging (MRI) technologies offer fundamentally new possibilities in this field, providing high spatial resolution and enabling visualization of even minimal changes in the structure of the pituitary gland [6–9]. The development of dynamic contrast-enhanced MRI, high-field scanners of 3.0 T and higher, and specialized protocols has significantly improved diagnostic accuracy and reduced the proportion of false-negative results. Despite the achievements of recent years, early detection of pituitary microadenomas remains insufficiently studied: there is no unified standard for MRI protocols, and the interpretation of results depends on the radiologist's experience and the technical characteristics of the equipment [10–15].

Thus, the aim of this review is to analyze the current capabilities of magnetic resonance imaging in the early diagnosis of pituitary microadenoma, determine its diagnostic value, and identify unresolved aspects requiring further research.

Pathogenetic and Morphological Features of Pituitary Microadenoma

Pituitary microadenomas are benign neuroendocrine lesions originating from the adenohypophysis. They are characterized by slow growth and high morphological variability of cellular composition. According to Astafyeva L.I. et al. [3], the key pathogenetic factor in their formation is impaired regulation of cell proliferation against the background of hypothalamic-pituitary system imbalance, which is manifested by hormone hypersecretion while maintaining local autonomy of the tumor node. At the same time, as noted by Lukyanenok P.I. and Usov V.Yu. [6], microadenomas often have no clear morphological boundaries and may include both functionally active and non-functioning cell populations, which complicates their differentiation at early stages.

Modern studies based on high-field MRI data show that even minimal changes in the architecture of the pituitary gland may reflect deep biochemical shifts and initial signs of neoangiogenesis, which serve as an early marker of tumor growth [10]. At the same time, comparative analysis of different MRI technologies demonstrates that conventional protocols often do not provide sufficient contrast between pituitary tissue and microadenoma, as emphasized by Grober et al. [11] and Bonneville et al. [12]. These data indicate the need for further improvement of imaging techniques, including the use of contrast-enhanced 3D-FLAIR and STIR sequences, which increase diagnostic accuracy in assessing the morphological characteristics of pituitary microlesions.

Thus, the accumulated data convincingly demonstrate that the development of pituitary microadenomas requires not only improved imaging quality, but also a comprehensive revision of diagnostic approaches taking into account molecular biological and radiomorphological characteristics. Against this background, the analysis of the current capabilities of magnetic resonance imaging (MRI) as the leading tool for non-invasive assessment of the structure and functional state of the pituitary gland becomes particularly important.

Current Capabilities of Magnetic Resonance Imaging (MRI)

Pituitary adenomas (PAs), or pituitary neuroendocrine tumors (PitNETs), are among the most common intracranial pathologies, accounting, according to Agustsson et al. [24], for approximately 10–15% of all primary brain tumors. Despite their predominantly benign nature, these neoplasms are often associated with pronounced endocrine disorders, hypersecretion syndromes, and compression of vital structures, which significantly reduces patients' quality of life [20]. The current capabilities of magnetic resonance imaging (MRI) have radically changed the approach to early diagnosis and morphological classification of these lesions by enabling visualization of microscopic pituitary changes even before the onset of clinical symptoms. According to Butz and Petrossians [26], high-field MRI systems make it possible to assess in detail not only the size and topography of a microadenoma, but also signs of invasive growth, which previously could only be detected intraoperatively. In addition, the use of advanced MRI protocols, such as T2-weighted, contrast-enhanced, and dynamic sequences, opens new prospects for assessing the functional activity of the tumor and its relationship with surrounding structures [30].

Recent WHO and IEA classifications [29] have emphasized the role of MRI visualization as a key diagnostic tool that allows non-invasive correlation of the morphological and hormonal phenotypes of PAs. Thus, modern MRI technologies are becoming not only a method for primary detection of pituitary microadenomas, but also a basis for predicting their biological behavior, assessing aggressiveness, and selecting an individualized treatment strategy. Table 1 presents the main current MRI capabilities used by various authors for early diagnosis and classification of pituitary microadenomas.

Table 1. Current Capabilities of Magnetic Resonance Imaging in Early Diagnosis

№	Author(s), year	Research area	MRI type / protocol	Main diagnostic capabilities	Key findings
1	Agustsson T.T. et al. [24]	Epidemiology and visualization of pituitary adenomas	1.5 T contrast-enhanced MRI	Early differentiation of microscopic pituitary lesions	The prevalence of microadenomas was 94 per 100,000; they were predominantly non-invasive
2	Molitch M.E. [25]	Diagnosis and treatment of pituitary adenomas	Dynamic contrast-enhanced MRI (DCE-MRI)	Detection of microadenomas smaller than 5 mm	DCE-MRI improves diagnostic accuracy
3	Butz L.B. et al. [26]	Subclinical acromegaly and pituitary micromorphology	High-field 3 T MRI	Detailed assessment of pituitary structure	Occult lesions were detected despite normal GH levels
4	Petrossians P. et al. [27]	Large cohort study involving 3,173 patients	3 T MRI with T2 and T1CE sequences	Correlation between tumor size and hormonal activity	The role of MRI in differentiating hormonally

					active PAs was confirmed
5	Beck-Peccoz P., Giavoli C., Lania A. [28]	TSH-secreting adenomas	T1CE + DCE-MRI	Assessment of vascular activity and invasiveness	MRI helps distinguish TSHomas from secondary hyperthyroidism
6	Rindi G. et al. [29]	Classification of neuroendocrine tumors	Multiparametric MRI: T1, T2, FLAIR	Non-invasive typing of PitNETs	MRI supports the WHO tumor classification system
7	Asa S.L. et al. [30]	Modern classification of PitNETs	3D STIR-FLAIR, 3 T	Differentiation of microadenomas and hormonally active forms	Visualization sensitivity increased by 25–30%

The data presented in Table 1 clearly demonstrate that the development of magnetic resonance imaging technologies has significantly expanded diagnostic capabilities in the assessment of pituitary microadenomas, from basic morphological verification to functional and vascular analysis. The accumulated experience with various MRI protocols confirms that diagnostic accuracy directly depends on the choice of scanning parameters and the level of spatial resolution. These findings emphasize the need for further improvement of MRI mapping techniques aimed at standardizing imaging criteria and increasing the sensitivity of detecting minimal pathological changes in pituitary tissue.

Diagnostic Criteria and Features of MRI Mapping of Pituitary Microadenoma

Modern diagnostic criteria for pituitary microadenomas are based on the principles formulated in the fifth edition of the WHO classification (2021–2022), which emphasizes not only the hormonal activity of the tumor, but also its molecular genetic and morphofunctional profile [17; 20]. A key direction in current imaging diagnostics is MRI mapping of the pituitary gland, which includes high-resolution 3D protocols such as VIBE, SPACE, and STIR-FLAIR, as well as dynamic contrast enhancement, making it possible to detect lesions less than 3 mm in diameter that are not visible using standard methods [Savlaev et al., 2017].

Dynamic DCE-MRI series are of particular importance in the diagnosis of microadenomas, as they capture the phase of early contrast enhancement and thereby increase the contrast between normal pituitary tissue and the area of hypovascular lesion [Micko et al., 2020]. According to recent studies, the use of 3 T MRI increases the sensitivity of microadenoma detection to 85–90%, especially when thin slices of 1–1.2 mm and reconstruction based on deep learning algorithms are applied [Özütemiz et al., 2023].

In addition to morphological assessment, functional MRI mapping is becoming increasingly important. It includes diffusion-weighted and perfusion imaging modes, which make it possible to evaluate microcirculation, cell density, and tumor consistency — parameters that were previously available only through histological examination [Savlaev et al., 2017]. These data are especially important for surgical planning, as they allow prediction of tumor firmness and the risk of intraoperative complications.

Comparative Assessment of MRI and Other Neuroimaging Methods

Although contrast-enhanced and dynamic MRI remain the main tools for preoperative mapping of pituitary microadenomas, even high-field scanners, including 3 T systems, do not always allow reliable visualization of small or hypovascular lesions [Kinoshita et al., 2021]. This is due to the fact that microadenomas, especially ACTH-secreting ones, may have contrast enhancement dynamics similar to normal pituitary tissue, which masks pathological areas and reduces the sensitivity of MRI diagnostics.

In such cases, dynamic contrast-enhanced multislice CT (DCE-MCT) is considered a promising approach, as it provides significantly higher temporal resolution, up to 3 seconds per phase, and allows reconstruction of 3D contrast enhancement curves using AUC analysis, or Area Under the Curve. According to Kinoshita et al. (2021), DCE-MCT correctly localized microadenomas in 93% of cases, whereas standard MRI did so in only 54%, indicating its additional diagnostic value. Therefore, the combination of high-field MRI and dynamic CT imaging can be regarded as an optimal strategy for early detection and accurate topographic analysis of functional pituitary microadenomas.

Problems, Prospects, and Directions for Further Research

Current radiomic studies demonstrate significant potential in the early diagnosis and prediction of pituitary adenoma behavior; however, issues related to the standardization of imaging protocols, data reproducibility, and cross-platform consistency remain unresolved. Differences in scanning parameters, scanner types, and image reconstruction methods substantially affect the stability of extracted features, which limits the clinical applicability of radiomics in multicenter studies. Insufficient integration of clinical, histopathological, and radiomic data also remains an important problem, preventing the development of truly personalized diagnostic algorithms.

A promising direction is the development of a multi-omics approach that combines radiomic, genomic, and metabolomic tumor characteristics for more accurate risk stratification and prediction of treatment response. At the same time, the active implementation of deep learning and neural network models may reduce dependence on manual ROI segmentation and improve prediction accuracy; however, this requires large representative datasets and transparent algorithmic interpretation. Researchers pay particular attention to the creation of a unified open-access database containing anonymized images and radiomic labels, which would improve the reproducibility of results and accelerate the development of clinical standards. In the long term, the key direction of development will be the translation of radiomics from research into clinical practice, with an emphasis on model validation, automated analysis, and interdisciplinary cooperation among radiologists, neurosurgeons, and machine learning specialists.

Thus, further development of radiomics in pituitary adenomas requires the systematic integration of technological, methodological, and clinical efforts aimed at creating reproducible, clinically meaningful, and interpretable diagnostic tools.

CONCLUSION

The present review systematizes current data on the capabilities of magnetic resonance imaging (MRI) in the early diagnosis of pituitary microadenoma, including an analysis of pathogenetic features, a comparative assessment of various neuroimaging methods, and prospects for the application of radiomics. The summarized findings emphasize the importance of an integrated approach combining morphological, functional, and molecular assessment of pituitary tumors, which makes it possible to improve diagnostic accuracy and optimize the choice of treatment strategy. This review may serve as a methodological basis for further clinical studies and for the development of imaging standards for microadenomas. The findings are particularly relevant in the context of improving neuroendocrinological diagnostics and interdisciplinary cooperation among specialists in radiology, endocrinology, and neurosurgery.

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