



Radiomics and artificial intelligence in pituitary adenomas (PitNETs): from imaging biomarkers to clinical translation

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Abstract

Pituitary neuroendocrine tumors (PitNETs) are common intracranial neoplasms with heterogeneous hormonal activity, invasiveness, and treatment response. Conventional MRI is central to diagnosis, but is limited in quantifying tumor heterogeneity and predicting clinically relevant features such as consistency, molecular subtype, proliferation, and clinical outcomes. To review current evidence on MRI-based radiomics and artificial intelligence (AI) in PitNETs, focusing on clinical applications, methodological quality, and future integration into precision medicine. Narrative review of studies published between 2019 and 2025 evaluating radiomics, machine learning, and deep learning applied to PitNETs, highlighting tumor consistency, molecular and histological subtypes, proliferation, invasiveness, treatment response, recurrence, visual outcomes, and differential diagnosis of sellar lesions. Radiomics has been applied across the PitNET clinical trajectory. Texture- and shape-based features from T2-weighted and multiparametric MRI predict intraoperative tumor consistency with AUCs often >0.80, outperforming conventional radiology. Radiomic signatures allow non-invasive differentiation of functional vs. non-functional adenomas, somatotroph granulation patterns, silent corticotroph adenomas, prolactinomas, and prediction of Ki-67 and PIT-1 expression. Models also predict cavernous sinus invasion, postoperative regrowth, recurrence, visual outcomes, and treatment response, including dopamine-agonist therapy. Differential diagnosis of hypophysitis and Rathke's cleft cyst has also been explored. Methodological quality remains heterogeneous, with frequent single-center, retrospective designs, limited external validation, and suboptimal adherence to reporting guidelines. Radiomics and AI show promise for risk stratification and personalized therapy in PitNETs, particularly for predicting tumor consistency, molecular subtypes, and recurrence. Clinical implementation requires standardized imaging protocols, multicenter datasets, reproducible segmentation, interpretable models, and prospective validation.

Keywords Pituitary adenoma · PitNET · Radiomics · MRI · Precision medicine

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1 Introduction

Pituitary neuroendocrine tumors (PitNETs) represent approximately 15–20% of intracranial neoplasms and display marked heterogeneity in hormonal activity, proliferation, and invasiveness [1–3]. The 2022 WHO classification emphasizes lineage-based subtyping and recognizes clinically relevant categories, including silent corticotroph tumors and clinically aggressive lactotroph tumors, such as large or invasive macroprolactinomas, particularly in men [4]. Yet, in everyday practice, clinicians still rely largely on conventional MRI and intraoperative findings to anticipate surgical difficulty, choose adjuvant therapy, and provide patient counseling [5, 6].

Radiomics -high-throughput extraction of quantitative features from medical images- offers a means to decode intratumoral heterogeneity, potentially linking imaging phenotypes to histomolecular traits and clinical outcomes [7, 8]. Combined with machine learning (ML) and deep learning (DL), radiomics can generate predictive models that may outperform conventional human visual assessment for specific tasks, even in expert centers [7–9]. These models have shown promise in refining the characterization of tumors, including the identification of subtle features that may not be apparent through conventional radiological methods [10]. In recent years, applications in neuro-oncology have expanded rapidly, and pituitary tumors are now a prominent field of experimentation, as highlighted in recent general radiomics reviews and endocrine-focused analyses [7, 11–13].

This review synthesizes current evidence on radiomics and AI in PitNETs, focusing on the following clinically relevant questions: (1) Can radiomics reliably predict tumor consistency and surgical difficulty? (2) Can it non-invasively infer molecular and hormonal subtypes, proliferation, and invasion? (3) Does it add value in predicting treatment response, recurrence, and functional outcomes? (4) What are current methodological limitations and translational barriers?

2 Methods

Because this was conceived as a clinically oriented narrative review rather than a formal systematic review, no *de novo* meta-analysis was undertaken. However, to improve the content, we performed an updated targeted search of PubMed/MEDLINE and reference lists of recent systematic reviews and meta-analyses [7, 11, 12, 14] from January 2019 to March 2025. Original MRI-based radiomics, machine-learning or deep-learning studies in PitNETs [13, 15] were included when they evaluated clinically relevant

endpoints such as consistency, subtype, proliferation, invasion, recurrence, treatment response, visual outcome, segmentation, or differential diagnosis of sellar lesions. A flow diagram summarizing study identification and selection has been added as Fig. 1.

Due to methodological heterogeneity across studies, performance metrics (AUC, sensitivity, specificity) are described qualitatively rather than meta-analyzed, except where prior meta-analyses are available.

2.1 Radiomics workflow and methodological considerations in PitNETs

A standard radiomics pipeline includes image acquisition, segmentation, feature extraction and selection, modelling, and validation [7, 8]. In PitNETs, most studies rely on pre-operative MRI with T2WI and T1WI with or without contrast administration and DWI (diffusion-weighted imaging), given their widespread availability and their ability to capture tumor heterogeneity and microstructural properties. The sellar region's small size and frequent artifacts impose specific and important challenges in spatial resolution, motion, and susceptibility [7, 14], which may significantly affect feature stability and reproducibility across scanners and acquisition protocols.

Segmentation -outlining the tumor on MRI images- is typically manual or semi-automatic (Fig. 2A, B and C), and usually performed on post-contrast T1WI or T2WI [16]. Even small differences in where observers draw the tumor border can alter the extracted radiomic features, particularly texture features that depend on voxel intensity patterns. This is why inter-observer variability can reduce reproducibility [17]. Automatic segmentation using DL, particularly convolutional neural networks, algorithms trained to identify imaging patterns and distinguish tumor tissue from surrounding structures, has been successfully explored in macroadenomas. These approaches have achieved high DICE coefficients, indicating a high degree of agreement between automated segmentation and expert-defined reference, and have supported the development of fully automated pipelines [18]. Nevertheless, the performance of automated methods in microadenomas and complex invasive tumors remains less consistent.

Feature extraction yields hundreds to thousands of descriptors, including first-order intensity statistics, shape-based features, and higher-order texture features derived from gray-level co-occurrence matrices, run-length matrices, and wavelet transformations. To mitigate overfitting and improve model generalizability, robust feature selection and dimensionality reduction techniques (e.g. LASSO -Least Absolute Shrinkage and Selection Operator-, which selects the most informative variables by shrinking less

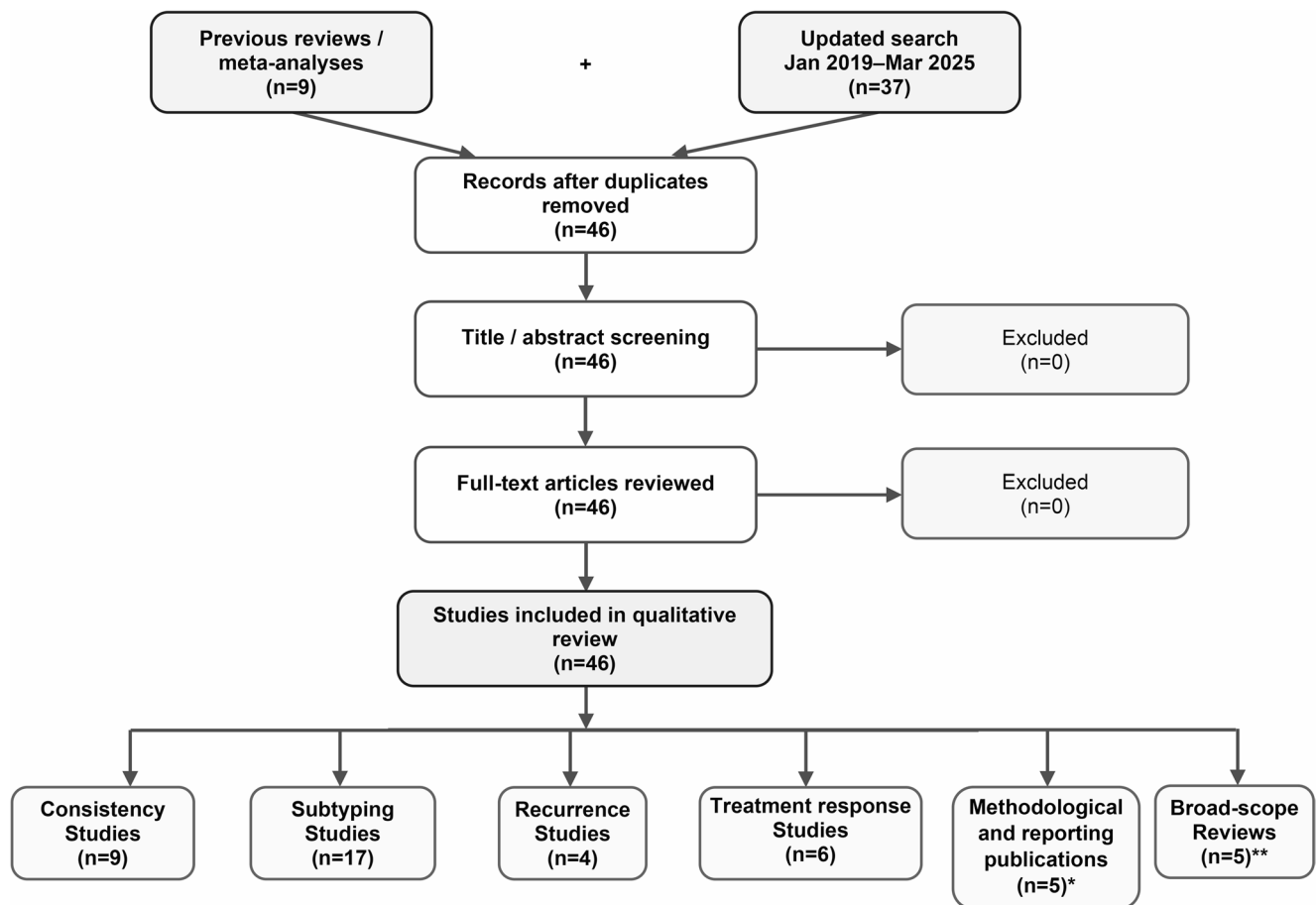


Fig. 1 Literature selection workflow. Flow diagram summarizing the inclusion of studies discussed in this review. Recent systematic reviews and meta-analyses served as the foundation of the evidence synthesis and were complemented by an updated search for original studies published between 2019 and 2025. *Methodological and reporting publications included papers addressing radiomic feature reproducibility,

segmentation methodology, dataset development, methodological quality and reporting standards. **Broad-scope reviews comprised reviews synthesizing multiple applications of radiomics and artificial intelligence in pituitary tumors, without being limited to a single clinical endpoint

relevant features toward zero, thereby reducing model complexity and minimizing overfitting) combined with appropriate cross-validation strategies are essential [7, 13]. However, several reviews have highlighted that adherence to standardized reporting and methodological guidelines (e.g., Radiomics Quality Score, Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD-AI) guideline, Image Biomarker Standardisation Initiative (IBSI) feature definitions) remains suboptimal in PitNET radiomics studies. Common limitations include small single-center cohorts, insufficient harmonization of imaging protocols, lack of external validation, and limited availability of open-source code and data, all of which hinder reproducibility and clinical translation [7, 11, 12, 19]. Harmonization is of particular importance, which refers to statistical or technical methods used to reduce unwanted differences caused by scanner vendor, magnetic field strength, acquisition parameters, or reconstruction

methods. Without harmonization, a model may learn scanner-specific differences rather than true biological tumor characteristics.

2.2 Clinical Applications (Table 1-2)

1. Prediction of Tumor Consistency and Surgical Difficulty.

Tumor consistency is a critical determinant of resectability in endoscopic endonasal surgery, influencing complication risk and the likelihood of gross total resection (GTR) [14, 44]. While radiologists typically infer tumor softness versus hardness from T2WI, cystic components, and contrast enhancement patterns, these visual indicators are subjective and provide only an approximate assessment [7, 45].

Several radiomics studies have quantified MRI heterogeneity to predict intraoperative consistency. Early work using T2WI radiomics showed that texture features could distinguish soft from firm macroadenomas with AUCs around

Fig. 2 **A)** Semi-automated segmentation of the pituitary gland on T2WI, showing the outlined contour (blue line) and the resulting segmented volume (shaded area) corresponding to a representative anonymized preoperative MRI image from the authors' institutional pituitary imaging archive, used to illustrate segmentation and radiomics workflow. (All images were anonymized in accordance with institutional requirements). **B)** Semi-automated segmentation of the entire pituitary gland on T2WI, showing the segmented contour (blue line) and the resulting segmented volume (shaded area), with a spontaneously hyperintense lesion at the right anterolateral margin of the gland, corresponding to a representative anonymized preoperative MRI image from the authors' institutional pituitary imaging archive, used to illustrate segmentation and radiomics workflow. (All images were anonymized in accordance with institutional requirements). **C)** Semi-automated segmentation of a pituitary macroadenoma on T2WI, showing the segmented contour (blue line) and the resulting segmented volume (shaded area); heterogeneous lesion, Knosp grade 3a, displacing the optic chiasm without signal alteration corresponding to a representative anonymized preoperative MRI image from the authors' institutional pituitary imaging archive, used to illustrate segmentation and radiomics workflow. (All images were anonymized in accordance with institutional requirements)

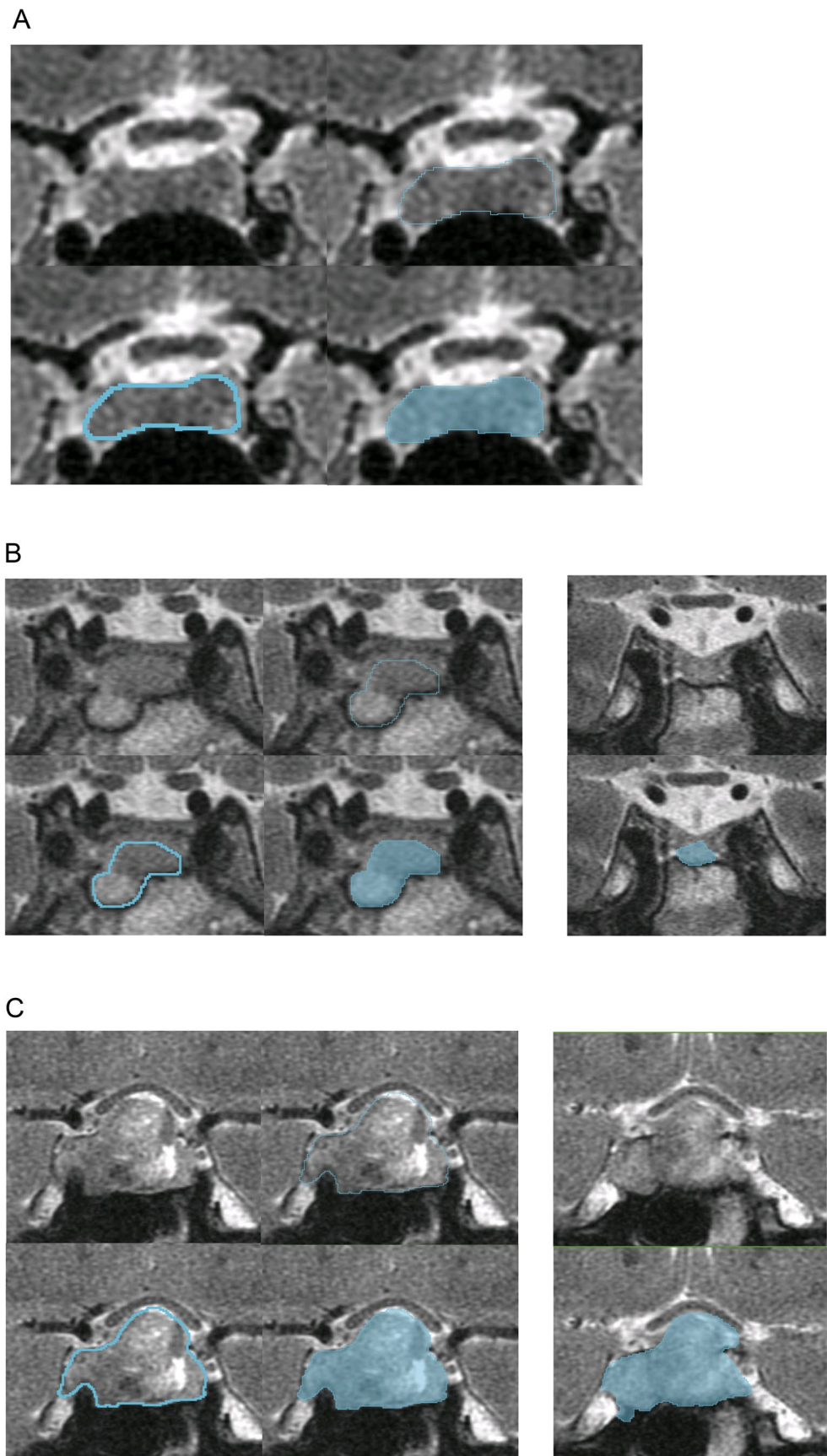


Table 1 Representative clinical applications of MRI-based radiomics in pituitary adenomas (PitNETs) characterization, diagnosis and prognostic stratification

Clinical application	Representative clinical endpoint / question	Study (reference)	Patients (n)	MRI scans (n)	MRI sequences	Validation method	Best model performance	Key limitations	Potential clinical impact
Tumor consistency	Soft vs. firm consistency; gross total resection (GTR)	Cuocolo 2020 (20)	89	89	T2WI	Internal validation	AUC 0.99, Acc. 93%, Sens 100%, Spec. 87%	Small, class-imbalanced cohort; no external validation	Preoperative counseling; surgical planning
		Wan 2022 (21)	156	156	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.90, Acc. 87%, Sens 83%, Spec. NR	Preliminary study; no external validation	choice of approach and instruments
		Mendi 2023 (22)	52	52	T2WI	Internal validation	AUC 0.96, Acc. NR, Sens 96%, Spec. 84%	Small cohort; cross-validation only	
		Liang 2025* (23)	350	350	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.92, Acc. 84%, Sens NR, Spec. NR	No external validation	
		Yang 2025* (24)	147	147	T1WI, CE-T1WI and T2WI	Internal and external validation	AUC 0.86, Acc. 80%, Sens 67%, Spec. 86%	Small external validation cohort (n = 10)	
Histological / molecular subtype	Somatotroph granulation; silent corticotroph; prolactinoma identification	Peng 2020 (25)	235	235	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.96, Acc. NR, Sens NR, Spec. NR	No independent validation	Choice of medical therapy; risk stratification; personalized management
		Park 2020 (16)	69	69	T2WI	Internal validation	AUC 0.83, Acc. 74%, Sens 74%, Spec. 74%	Small, class-imbalanced cohort; no external validation	
		Rui 2022 (9)	302	302	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.93, Acc. 87%, Sens 87%, Spec. 87%	No external validation	
		Wang 2023 (19)	295	295	T1WI, CE-T1WI and T2WI	External validation	AUC 0.94, Acc. NR, Sens NR, Spec. NR	Small external validation cohort (n = 35)	
		Fan 2025* (26)	212	212	T1WI, CE-T1WI and T2WI	Internal and external validation	AUC 0.91, Acc. NR, Sens NR, Spec. NR	Retrospective design; combined clinic-radiomic model.	
Proliferation markers	High Ki-67; PIT-1 expression	Ugga 2019 (13)	89	89	T2WI	Internal validation	AUC 0.87, Acc. 92%, Sens 80%, Spec. 96%	Small cohort; no external validation	Prognostic stratification; follow-up planning; indication for adjuvant therapy
		Li 2024 (15)	1214	1214	T1WI, CE-T1WI and T2WI	Internal and external validation	AUC 0.83, Acc. NR, Sens NR, Spec. NR	Retrospective design; Small external validation cohort (n = 65)	
		Liu 2025 (18)	247	247	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.83, Acc. 79%, Sens 79%, Spec. 78%	Single-center; no external validation	

Table 1 (continued)

Clinical application	Representative clinical endpoint / question	Study (reference)	Patients (n)	MRI scans (n)	MRI sequences	Validation method	Best model performance	Key limitations	Potential clinical impact
Invasion and aggressiveness	Cavernous sinus invasion; high Knosp grade; extent of resection (EOR)	Niu 2019 (27)	194	194	CE-T1WI and T2WI	Internal validation	AUC 0.87, Acc. NR, Sens NR, Spec. NR	Knosp 2–3 only; no external validation	Anticipating incomplete resection; planning staged or adjuvant therapy
		Wang 2023 (28)	246	246	CE-T1WI	Internal validation	AUC 0.94, Acc. NR, Sens 94%, Spec. 83%	Single-center; combined model; no external validation	
		Fiore 2023 (29)	Not reported in abstract	Not reported in abstract	T2WI	No independent validation	AUC 0.88, Acc. NR, Sens NR, Spec. NR	No validation	
Differential diagnosis	Rathke cleft cyst vs. cystic adenoma; hypophysitis vs. non-functioning pituitary adenoma; posterior pituitary tumour vs. PitNET/craniopharyngioma	Wang 2021 (30)	215	215	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.85, Acc. 77%, Sens 74%, Spec. 80%	No external validation	Avoidance of unnecessary surgery; improved preoperative diagnostic confidence
		Taslicay 2024 (31)	65	65	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.98, Acc. 0.94, Sens 98%, Spec. 89%	Small, single-center cohort; no external validation	
		Sahin 2022 (32)	34	34	CE-T1WI	No independent validation reported	AUC 0.91, Acc. 85%, Sens 74%, Spec. 97%	Small cohort; no independent validation	
		Jin 2025* (33)	165	165	CE-T1WI	Internal validation	AUC 0.91, Acc. NR, Sens NR, Spec. NR	Retrospective design; no external validation	
		Liu 2025* (34)	174	174	T1WI and CE-T1WI	Internal and prospective validation	AUC 0.82, Acc. 79%, Sens 79%, Spec. 78%	Single-center; small validation cohort (n=42)	

Studies marked with an asterisk represent additional primary studies that were not included in the prior systematic reviews or meta-analyses used as the basis for this narrative review but were identified through the authors' updated targeted search. Acc.: accuracy; AUC: area under the receiver operating characteristic curve; NR: not reported; Sens.: sensitivity; Spec.: specificity

0.80, outperforming qualitative T2 signal [20, 21]. Subsequent single- and dual-center studies integrating T1WI- and T2WI-based features with clinical variables further improved discriminatory accuracy, sometimes exceeding AUC of 0.85 and providing interpretable models highlighting features related to homogeneity and shape irregularity [23]. From a reproducibility standpoint, shape features may be more stable than higher-order texture features when the tumor boundary is clearly identified; however, they are still affected by segmentation of parasellar extension, cystic or hemorrhagic components, and the choice of whether to include necrotic regions. Texture features are particularly sensitive to acquisition parameters, voxel resampling, intensity normalization, gray-level discretization, and scanner-related variability. Therefore, reproducibility should be assessed using inter-observer segmentation experiments,

test–retest imaging comparisons, feature stability analysis, and external validation.

A recent systematic review and meta-analysis dedicated to PitNET consistency pooled radiomics studies and found that ML-based models significantly improved prediction over conventional MRI alone, with pooled AUCs around 0.85 and acceptable calibration [14]. Another meta-analysis focusing on benign central nervous tumors, including pituitary adenomas, similarly supported the added value of radiomics, while highlighting limitations such as small sample sizes and lack of external validation [11].

Most tumor-consistency studies were performed in macroadenoma cohorts, with sample sizes generally ranging from several dozen to a few hundred patients. In the recent dedicated meta-analysis, 9 studies comprising 935 patients were included, of whom 67.8% had soft and 32.2% hard

Table 2 Representative clinical applications of MRI-based radiomics for treatment individualised and patient outcomes in pituitary adenomas

Clinical application	Representative clinical endpoint / question	Study (reference)	Patients (n)	MRI scans (n)	MRI sequences	Validation method	Best model performance	Key limitations	Potential clinical impact
Recurrence / regrowth	Residual regrowth; 3-5-year recurrence	Machado 2020 (35)	27	27	CE-T1WI	Internal validation	AUC 0.96, Acc. 96%, Sens 92%, Spec. 100%	Very small cohort; no external validation	Tailored follow-up imaging; early radiotherapy consideration
		Zhang 2022 (36)	168	168	CE-T1WI	Internal validation	AUC 0.78, Acc. 80%, Sens 83%, Spec. 79%	Single-center; combined model	
		Shen 2023 (37)	114	228	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.88, Acc. 82%, Sens 82%, Spec. 83%	No external validation	
		Zhao 2025* (38)	415	415	T1WI, CE-T1WI and T2WI	Internal and external validation	AUC 0.86, Acc. 68%, Sens 80%, Spec. 82%	Retrospective; combined model	
Treatment response	DA response in prolactinomas; multimodal therapy	Fan 2019 (39)	163	163	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.81, Acc. 75%, Sens 61%, Spec. 92%	Single center; combined model	Early identification of resistant disease; optimization of systemic and radiosurgical strategies
		Park 2021 (40)	177	177	T2WI	Internal validation	AUC 0.81, Acc. 78%, Sens 79%, Spec. 77%	No external validation	
		Fan 2025* (8)	315	315	CE-T1WI and T2WI	Internal and external validation	AUC 0.92, Acc. NR, Sens NR, Spec. NR	Retrospective; combined model	
		Speckter 2025* (GK response) (41)	81	81	T1WI, CE-T1WI and T2WI	Internal validation	AUC 0.93, Acc. 85%, Sens 82%, Spec. 85%	Small cohort; no external validation	
Visual and endocrine outcomes	Visual recovery; DI risk	Zhang 2023 (42)	130	260	T2WI	Internal validation	AUC 0.84, Acc. 77%, Sens 69, Spec. 92%	Postoperative MRI required; No external validation	Counselling regarding postoperative visual prognosis and risk of DI
		Mastantuoni 2025* (43)	30	30	CE-T1WI and T2WI	Internal validation	PR-AUC 0.68, Acc. 63%, Sens NR, Spec. NR	Very small cohort	

Studies marked with an asterisk represent additional primary studies that were not included in the prior systematic reviews or meta-analyses used as the basis for this narrative review but were identified through the authors' updated targeted search. Acc.: accuracy; AUC: area under the receiver operating characteristic curve; NR: not reported; Sens.: sensitivity; Spec.: specificity

tumors. The radiomic predictors were not simple visual T2 signal descriptors but quantitative features reflecting heterogeneity and spatial organization, including first-order intensity statistics, gray-level co-occurrence matrix-derived entropy and contrast, gray-level run-length and size-zone features, wavelet-derived texture features, and shape descriptors. Biologically, these features are presumed to reflect differences in water content, collagen/fibrosis, cellularity, necrosis, and internal architectural heterogeneity, although direct histological correlation remains incomplete. However, these values may also derive from heterogeneous MRI protocols and mainly from manual segmentation procedure, and that none of the included studies had true external validation. Moreover, most favorable performance estimates were obtained in macroadenomas. Translation to microadenomas is substantially more challenging

because small tumor volume increases partial-volume effects, reduces the number of voxels available for stable feature extraction, and makes manual or automated segmentation less reproducible. Therefore, current radiomic models should not be assumed to perform equally well in microadenomas unless specifically validated in that setting.

Notably, prediction of tumor consistency using radiomic features has been correlated with surgical outcomes: tumors characterized as harder by radiomic signatures demonstrate reduced likelihood of achieving GTR and an increased frequency of intraoperative complications, indicating that preoperative radiomic evaluation may provide valuable guidance for surgical strategy and patient counseling [29, 46].

2. Histological and Molecular Subtyping.

The 2022 WHO classification emphasizes lineage-specific markers and recognizes subtypes with distinct prognoses, such as sparsely vs. densely granulated somatotroph tumors and silent corticotroph adenomas [4]. Non-invasive identification of these subtypes could influence both surgical strategy and adjuvant therapy [47].

Radiomics has also been applied to classify immunohistochemical subtypes. Peng et al. used multiparametric MRI radiomics to differentiate hormone-secreting subtypes, achieving high accuracy for GH-, PRL-, and ACTH-secreting adenomas [25]. More recently, a multicenter clinic-radiomic model has accurately differentiated somatotroph subtypes, with implications for predicting response to somatostatin receptor ligands [26]. Silent corticotroph adenomas—often more aggressive than classical non-functioning PitNETs—have been identified by radiomics models trained on non-functioning cohorts, reaching AUCs above 0.85 [9, 19, 48].

Radiomics has also been combined with clinicopathological data to aid in prolactinoma identification among PitNETs, both for diagnostic purposes and for predicting response to dopamine agonists [8, 40]. These approaches mirror other multiomics efforts in acromegaly and pituitary disease, where integration of imaging, transcriptomics, and metabolomics is being explored to define precision medicine algorithms [49, 50].

3. Proliferation Markers and Biological Aggressiveness.

Several groups have pursued radiomics-based prediction of Ki-67 labeling index and other markers of proliferative and lineage-specific transcription factors. Early work by Ugga et al. showed that MRI-based features could predict high Ki-67 ($\geq 3\%$) in macroadenomas with promising AUCs [13]. Subsequent models incorporating DL-based segmentation and radiomics improved performance and robustness for Ki-67 prediction [15]. Liu et al. expanded this approach to simultaneous prediction of Ki-67 and PIT-1 expression using multiple radiomics algorithms, reporting balanced performance and highlighting the potential of “multi-label” imaging biomarkers [18].

Radiomics has also been linked to broader concepts of aggressiveness. Quantitative assessments of shape and texture have been shown to correlate with Knosp grade, dural invasion, and radiological markers of aggressive growth [28]. These imaging phenotypes could eventually complement histological markers (e.g., TP53, ATRX, MGMT) in integrated prognostic scores [7].

4. Invasion and Extent of Resection.

Cavernous sinus (CS) invasion is a major determinant of surgical outcome. Morphological classifications such as Knosp and Hardy remain imperfect in predicting true invasion [51]. Using radiomics-based models, Niu et al. developed a radiomics-based nomogram using CE-T1WI and

T2WI to enable individualized preoperative prediction of CS invasion in patients with Knosp grade 2 and 3 pituitary adenomas and showed improved prediction of CS invasion compared with standard Knosp grading, with AUCs exceeding 0.85²⁷. Later studies have confirmed that radiomics can refine prediction of dural and parasellar invasion and may better anticipate the likelihood of GTR [27, 46].

Radiomics models have been explored to predict postoperative regrowth of residual tumor and long-term recurrence in clinically non-functioning macroadenomas [35, 36, 38]. Combining radiomics with conventional radiological features and clinical variables yields nomograms capable of stratifying 5-year recurrence risk, potentially guiding follow-up intensity and indications for early radiotherapy. Notably, combined models, which integrate clinical and radiomics features, demonstrate superior predictive performance compared with either the standalone clinical or radiomics models [38].

5. Pharmacologic Treatment Response and Radiosurgery Outcomes.

Beyond diagnosis and surgical planning, radiomics has shown promise in predicting response to medical therapy. Radiomics combined with ensemble ML has predicted dopamine-agonist (DA) response in prolactinomas with good accuracy, outperforming conventional MRI metrics and offering early identification of resistant tumors [8, 40]. These two studies were performed with cohorts comprising 255 and 177 patients respectively and the AUCs obtained ranged from 0.81 to 0.95. Thus, although these models predicting DA response in prolactinomas show promising discrimination results, the available evidence is still based on relatively small retrospective cohorts, requiring external validation in independent cohorts. Reproducibility remains also uncertain because harmonized preprocessing pipelines are required in addition to validation in different scanner environments.

In invasive functional PitNETs, imaging signatures have been linked to response to multimodal therapy, suggesting a role for radiomics in tailoring adjuvant treatments [39].

In the radiosurgical setting, MRI-based radiomics has been used to predict volumetric response to gamma knife radiosurgery, identifying imaging phenotypes associated with greater tumor shrinkage and allowing refinement of patient selection and dose planning [41, 52].

6. Visual Outcomes and Complications.

Visual impairment due to optic chiasm compression is a key driver of surgical decision-making. Delta-radiomics—the analysis of imaging feature longitudinal changes over time—applied to the optic chiasm on serial MRI has been linked to postoperative visual recovery, with radiomic changes outperforming baseline morphology alone. This

approach may help identify patients at risk of persistent or worsened visual deficits despite decompression [42].

Mastantuoni et al. showed that texture-based radiomic features can provide meaningful preoperative information regarding diabetes insipidus risk, although initial models mixed PitNETs with other lesions and thus require further validation before clinical implementation [43].

7. Differential Diagnosis of Sellar and Parasellar Lesions.

The sellar region harbors a broad spectrum of entities including Rathke's cleft cysts, hypophysitis, cystic PitNETs, posterior pituitary tumors, and craniopharyngiomas. Several radiomics studies have tackled this diagnostic challenge. Radiomics can extract high-dimensional features from MRI across different sequences, providing quantitative information that may improve diagnostic accuracy, in particular, CE-T1W has shown promise in enhancing the reliability of lesion classification, potentially supporting clinical decision-making and improving patient outcomes [53].

Texture-based models have achieved high accuracy in discriminating cystic PitNETs from Rathke's cleft cysts, outperforming conventional radiology [30, 31]. ML models using radiomic features have also differentiated non-functioning PitNETs from hypophysitis with promising performance, potentially avoiding unnecessary surgery in some if not in all patients with hypophysitis [32]. Recently, radiomics has been used to differentiate posterior pituitary tumors from PitNETs and craniopharyngiomas, using multiclass ML pipelines and external validation cohorts [34].

These differential-diagnosis tools are particularly attractive in multidisciplinary pituitary boards, where specialists from radiology, endocrinology, and neurosurgery must reach consensus on management in the face of diagnostic uncertainty. In this context, the application of radiomic analysis in the study of PitNETs has begun to demonstrate its potential to support diagnosis, characterization, and treatment planning and so highlight the growing role of radiomics as a complementary tool to guide multidisciplinary decision-making in pituitary disease [7].

2.3 Segmentation, datasets, and data sharing

Robust radiomics relies critically on accurate and reproducible segmentation, as segmentation errors, generated when manually performed, propagate through the entire feature extraction and modeling process. DL-based segmentation models, particularly convolutional neural networks and U-Net-derived architectures, have demonstrated high performance for macroadenomas and show strong potential for standardizing volumes of interest across institutions. Nevertheless, most published studies continue to depend on manual segmentation in relatively small, single centre

cohorts, which is time consuming and prone to inter- and intra-observer variability [54, 55].

To facilitate model generalization, reproducibility, and objective benchmarking, open and well-annotated datasets have begun to emerge [56], although their number remains limited. An annotated MRI dataset profiling PitNETs and adjacent carotid characteristics was recently released, providing expert-defined contours, multiparametric MRI sequences, and accompanying clinical metadata to support the development and validation of radiomics and ML models [56]. Such resources are essential for enabling external validation and comparative evaluation of algorithms.

Systematic reviews of pituitary segmentation algorithms and radiomics studies confirm that the field is expanding but still fragmented, with substantial heterogeneity in acquisition protocols, segmentation strategies, feature extraction workflows, and reporting practices. Limited harmonization of acquisition protocols and feature definitions continues to impede reproducibility and cross-study comparison, underscoring the need for standardized pipelines, multicenter collaborations, and broader adoption of open data and code-sharing practices [7, 54].

2.4 Methodological quality, challenges, and reporting standards

Multiple methodological reviews have highlighted recurrent limitations of PitNET radiomics, including small, single-center cohorts, retrospective designs, lack of pre-registered protocols, insufficient calibration and decision-curve analysis and scarce external validation [7, 11, 12, 54]. Rigor in segmentation practices, feature stability testing, and model interpretability is often suboptimal. The Radiomics Quality Score and IBSI-compliant feature definitions are not consistently reported [54, 57]. From a ML perspective, sample size should be driven by the number of outcome events rather than the total number of MRI studies alone. For common binary endpoints such as soft versus firm consistency, a prospective multicenter study would ideally include several hundred patients with balanced outcome categories and an independent external validation cohort. For less frequent endpoints, such as recurrence, silent corticotroph subtype, treatment resistance, or postoperative diabetes insipidus, larger registry-based datasets are likely required. A practical minimum would be to predefine a limited feature set, avoid high-dimensional unrestricted modelling in small cohorts, and ensure at least 100–200 of cases for model development whenever possible, followed by external validation.

A focused assessment of reporting quality in pituitary radiomics underscored poor adherence to TRIPOD guidelines [58], incomplete description of ML pipelines, and limited availability of source code and trained models.

Furthermore, direct comparison across studies should be interpreted cautiously because of differences in endpoints, model development strategies and validation procedures. These shortcomings compromise reproducibility and hinder clinical translation [57].

MRI radiomics is highly sensitive to how images are acquired and processed. A model trained on images from one center may perform poorly in another if scanner type, field strength, slice thickness, contrast timing, or reconstruction methods differ. Statistical harmonization methods, such as ComBat, attempt to reduce these scanner-related differences so that the remaining features are more likely to reflect tumor biology. However, these methods have rarely been tested in PitNET radiomics, and their use should be prospectively evaluated before clinical implementation [54]. Other analytical post-processing approaches, including Weighted Harmonization Parameters (WHARMPA) [59], have demonstrated improved correction of inter-site variability compared with conventional Boolean site covariates in multi-site MRI datasets. However, such techniques have not yet been widely adopted in PitNET radiomics, representing a missed opportunity to enhance harmonization and robustness of predictive models [54].

2.5 Future directions and clinical integration

In order to move radiomics research from proof-of-concept to clinical implementation, several strategies are needed:

1. Prospective, multicenter studies with standardized imaging protocols, pre-specified endpoints (e.g., consistency, Ki-67, recurrence), and external validation cohorts [7, 12, 54].
2. Integration with clinical and molecular data, building multiomics models combining radiomics with genomics, transcriptomics, and epigenetics—aligned with evolving precision medicine frameworks in pituitary disease [7, 11, 49, 54].
3. User-friendly decision support tools, such as web-based calculators or PACS-integrated software, providing explainable outputs (e.g., probability of hard consistency, silent corticotroph subtype, or early recurrence) [36].
4. Regulatory and ethical considerations, including transparency of algorithm development, continuous performance monitoring, and bias mitigation [57].

Radiomics should be regarded not as an independent solution but as a complementary tool integrated with expert neuroradiological and endocrine assessment within multidisciplinary pituitary boards. For instance, combined models might use baseline radiomics to predict hard consistency and CS invasion, thereby prompting early involvement of

experienced skull-base surgeons and intraoperative tools. Similarly, radiomic signatures associated with tumor proliferation and recurrence could inform individualized follow-up schedules and adjuvant radiotherapy [7].

An additional limitation concerns the risk of AI hallucination or overconfident unsupported output, particularly for generative AI systems used in reporting or clinical decision support. Although classical radiomics models do not ‘hallucinate’ in the same way as large language models, any AI system may produce misleading predictions when applied to out-of-distribution images, poorly segmented lesions, uncommon tumor subtypes, or scanners and protocols not represented in the training data. Therefore, radiomics outputs should be presented as probabilistic decision-support information, remain interpretable to clinicians, and never replace expert multidisciplinary review. Finally, a further limitation is the geographic concentration of the available evidence. A substantial proportion of PitNET radiomics studies have been conducted in Asian, particularly Chinese, cohorts. This may introduce domain shift related not only to scanner vendors and MRI protocols but also to referral patterns, tumor size at diagnosis, pathology procedures, treatment strategies, and population characteristics. Multi-national validation across European, North American, Latin American and African cohorts is needed before assuming global applicability.

Thus, at present, PitNET radiomics remains primarily a research tool. No radiomics model for PitNET characterization, consistency prediction, recurrence prediction, or treatment-response selection has yet been incorporated into routine guideline-based clinical practice. The main barriers are insufficient prospective validation, limited external reproducibility, lack of standardized acquisition and segmentation pipelines, uncertain regulatory pathways, poor integration into PACS or multidisciplinary workflows, and absence of interventional studies showing that radiomics-guided decisions improve outcomes.”

3 Conclusions

MRI-based radiomics and AI have rapidly expanded in the field of pituitary adenomas. Current evidence supports their value in predicting tumor consistency, histomolecular subtype, proliferative activity, invasiveness, treatment response, recurrence, and functional outcomes, as well as in refining the differential diagnosis of sellar lesions. Nonetheless, the integration of radiomics into routine clinical practice remains constrained by methodological heterogeneity, insufficient external validation, and suboptimal reporting quality.

Future efforts should prioritize robust, multi-institutional, prospective studies, standardized and harmonized analytical pipelines, and the integration of radiomic information with clinical and molecular data within precision medicine frameworks. At present, radiomics should be regarded as a powerful research tool and an emerging complement to conventional imaging and pathological assessment, with substantial potential to transform PitNET diagnosis, characterization and management in the coming years.

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Data availability No datasets were generated or analysed during the current study.

Declarations

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in this manuscript.

Competing interests The authors declare no competing interests.

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