Original Article

Radiomics for Preoperative Assessment of Pituitary Adenoma Consistency with T2-Weighted MRI: A Multicenter Study

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Abstract

Introduction Pituitary adenoma (PA) consistency significantly influences the outcomes of endoscopic endonasal surgery. Radiomics represents a promising tool for objective and quantitative assessment using T2-weighted magnetic resonance imaging (MRI).
Methods A multicenter retrospective database was collected (2012–2023), including 394 patients with preoperative T2-weighted MRI and histologically confirmed PAs after endoscopic endonasal surgical removal. Tumor segmentation was performed manually on coronal T2-weighted images using ITK-SNAP software. Radiomic features were extracted with Pyradiomics. A 60:40 dataset split was used to train an Extra Trees classifier, and recursive feature elimination was used to select features. Model performance was assessed using sensitivity, specificity, and the area under the curve of receiver operating characteristic (AUC-ROC) curve metrics.
Results From 1,106 extracted radiomic features, 65 were identified as most predictive following variance and correlation filtering. The sensitivity, specificity, and accuracy of the ET classifier were 74%, 74%, and 63% (±10%), respectively. The AUC-ROC curve was 0.59.

Keywords
- pituitary adenoma
- consistency
- preoperative MRI
- radiomics
- machine learning

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Conclusion Despite its moderate accuracy and AUC-ROC curve, the ET model showed promising performance to predict preoperative PA consistency, underlying the power of radiomics-driven models in PA surgical planning.

Introduction

Pituitary adenoma (PA) consistency is a critical factor in determining the success of endoscopic endonasal surgery.[1] Soft tumors are generally easier to resect, while fibrous or harder tumors pose significant challenges due to their close relation with surrounding neurovascular structures and increased risk of postoperative complications.[2,3] Therefore, preoperative prediction of PA consistency is paramount in planning the surgical approach, potentially reducing surgical time, minimizing complications, and improving patient outcomes.[4,5]

Traditional magnetic resonance imaging (MRI) techniques are limited in their ability to provide reliable qualitative assessments of PA consistency. Despite advances in imaging technologies, the determination of tumor texture, especially whether a tumor is soft or fibrous, remains challenging.[3]

Radiomics, an emerging field in medical imaging, involves the conversion of medical images into a high-dimensional array of quantitative data, from which texture features can be extracted and analyzed.[5,6] This approach allows for the assessment of tumor heterogeneity at a pixel level, far surpassing the capabilities of traditional imaging interpretation. The rise of machine learning (ML) algorithms has further propelled the application of radiomics in radiology.[6] By analyzing vast amounts of radiomic features from MRI scans, these algorithms can develop predictive models that classify tumor consistency and other clinically relevant characteristics.[7] This data-driven approach represents a shift toward personalized medicine, where preoperative planning is tailored to individual patient characteristics based on advanced imaging analysis.[8]

Radiomics has been applied to various aspects of PAs, including classification of PA types and subtypes,[9] assessment of tumor consistency,[10] evaluation of cavernous sinus invasion,[11] and prediction of surgical remission.[12] It has also been explored in predicting responses to medical therapies,[13] radiotherapy outcomes,[14] visual prognosis,[15] and recurrence risks.[16] However, the predictive strength of current models remains limited due to single-center studies and small sample sizes, highlighting the need for larger, multicenter research to improve reliability and clinical applicability.[7]

This study aimed to assess the accuracy of radiomics-based models for the preoperative prediction of PA consistency.

Methods

Multicenter Retrospective Registry

This retrospective study was conducted in accordance with the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments.[17] The study protocol received approval from the Institutional Review Board (approval code: IRB-5924). Given the retrospective design of the study, the requirement for patient consent was waived by the Institutional Review Board, as all data were anonymized to protect patient privacy.

Data were collected from patients diagnosed with PAs who underwent preoperative MRI and subsequent endoscopic endonasal surgery at four collaborating institutions. The participating centers included the University of Brescia, Spedali Civili of Brescia, Italy; the University of Naples "Federico II," University Hospital Federico II, Naples, Italy; Ca' Foncello Hospital, Treviso, Italy; and the University of Insubria, Circolo Hospital and Macchi Foundation of Varese, Italy.

The study encompassed a patient selection period from January 2012 to December 2023. Only patients with complete medical records, including preoperative T2-weighted MRI scans and subsequent surgical documentation, were included. All collected data were anonymized to ensure patient privacy and confidentiality.

Exclusion criteria were defined to ensure the dataset's clarity and consistency. Patients were excluded if they were under 18 years old, had a history of prior treatments for sellar or parasellar diseases, had undergone radiotherapy or medical therapy for PA at the time of the MRI, or had lesions smaller than 10 mm. Additionally, cases with extensive tumor necrosis, hemorrhage, or significant imaging artifacts that could compromise radiomic analysis were also excluded from the study.[18]

MRI Data Acquisition

All patients included in the study underwent MRI scans using either a 1.5-T or 3-T magnetic resonance scanner, depending on the availability at the respective center. Scanners utilized in the study included models from Philips (Gyroscan Intera) and Siemens (Magnetom Trio). The imaging protocol was standardized across all centers and consistently incorporated a coronal T2-weighted Turbo Spin Echo (T2-w TSE) sequence, which served as the primary imaging modality for radiomic feature extraction. The specific acquisition parameters, such as repetition time (TR), echo time (TE), slice thickness, and field of view (FOV), were adjusted to ensure optimal image quality, enabling consistent texture analysis across different MRI platforms (►**Table 1**).

In addition to the T2-weighted sequence, standard pituitary imaging protocols often include other sequences, such as T1-weighted pre- and postcontrast images. However, these were not utilized in the texture analysis for this study. The focus remained on non-contrast T2-weighted images, as prior research has demonstrated their particular

Table 1 Coronal T2-weighted Turbo Spin Echo sequence parameters for 1.5- and 3-Tesla scanners

	TR (ms)	TE (ms)	FOV (mm)	Matrix	Thk (mm)	ETL	Slice gap	Acquisition time
1.5 T	2,600	89	180 × 180	288 × 288	3	17	No gap	2 min 17 s
3 T	3,000	98	200 × 200	384 × 384	3	18	No gap	3 min 22 s

Abbreviations: ETL, echo train length; FOV, field of view; TE, echo time; Thk, slice thickness; TR, repetition time.

utility in capturing tissue heterogeneity associated with PA consistency.[19,20]

Consistency Evaluation

The consistency of PAs was documented in the operative reports and further evaluated through intraoperative videos. Two experienced neurosurgeons, each with over a decade of specialization in pituitary surgery, independently reviewed the videos to confirm the reported consistency. In cases where their evaluations differed, a consensus was reached through joint analysis of the videos with the primary surgeon.

Lesions classified as soft were characterized by their ease of removal using standard surgical instruments, such as suction and curettage. These tumors tended to deform and fragment readily, allowing for quick and uncomplicated resection. In contrast, fibrous adenomas exhibited a denser structure, necessitating more meticulous extracapsular dissection, often requiring additional effort or alternative instruments such as microdissectors to ensure complete resection.[21–24]

The classification relied on observable intraoperative properties, including tumor texture, resistance to surgical manipulation, and the instruments required for effective resection.[25] For educational purposes, the surgical features of both soft and fibrous PAs are demonstrated in ►**Videos 1** and **2, respectively.**

Video 1

Endoscopic video demonstrating surgical removal of a soft pituitary adenoma. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-2607-0735.

Video 2

Endoscopic video demonstrating surgical removal of a fibrous pituitary adenoma. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-2607-0735.

Radiomics Analysis

Tumor segmentation was performed manually by an experienced neuroradiologist using ITK-SNAP (v4.0.2), an open-source software for medical image annotation. A two-dimensional polygonal region of interest (ROI) was delineated on the coronal slice that exhibited the largest cross-sectional area of the lesion (►**Fig. 1**). Two additional readers, both with more than 5 years of experience in neuroradiology, independently performed the segmentation of the same images. These readers were blinded to the initial neuroradiologist's annotations to ensure unbiased radiomic feature extraction and to validate the reproducibility of the segmentation process.

To ensure consistency in radiomic analysis, interobserver variability was measured using the intraclass correlation coefficient (ICC), with an acceptable threshold of $\geq$0.75, ensuring stability across the features extracted from the multiple segmentations. This multireader approach was implemented to guarantee robust and reliable radiomic feature extraction for subsequent analysis.

A widely used, open-source Python software platform (Pyradiomics, v2.2.0) was utilized for image preprocessing and radiomic feature extraction. Initially, images and ROIs were resampled to an isotropic voxel size of $2 \times 2 \times 2$ mm to ensure compatibility with subsequent preprocessing steps, such as the correct application of image filters. Voxel intensity values were normalized by subtracting the mean intensity and dividing by the standard deviation, with a voxel array shift of 300, followed by discretization using a fixed bin count of 32.

Feature extraction was performed not only on the preprocessed original images but also on filtered images. Specifically, a Laplacian of Gaussian filter was applied with sigma values ranging from 2.0 (capturing finer textures) to 6.0 (capturing coarser textures) in 2.0 increments. Additionally, all possible combinations of high- and low-pass wavelet decompositions were applied along the x, y, and z dimensions.

Data Mining and Machine Learning

The initial evaluation and processing of the extracted data were conducted in Python, utilizing the *numpy*, *pandas*, and *scikit-learn* libraries. Non-informative features with low variance ($\leq$0.01) were excluded from further analysis. To address multicollinearity, a pairwise correlation matrix was generated, and features exhibiting an intercorrelation of $\geq$0.8 were removed. Then, a Recursive feature elimination (RFE) with 10-fold cross-validation was employed to select the final feature subset.

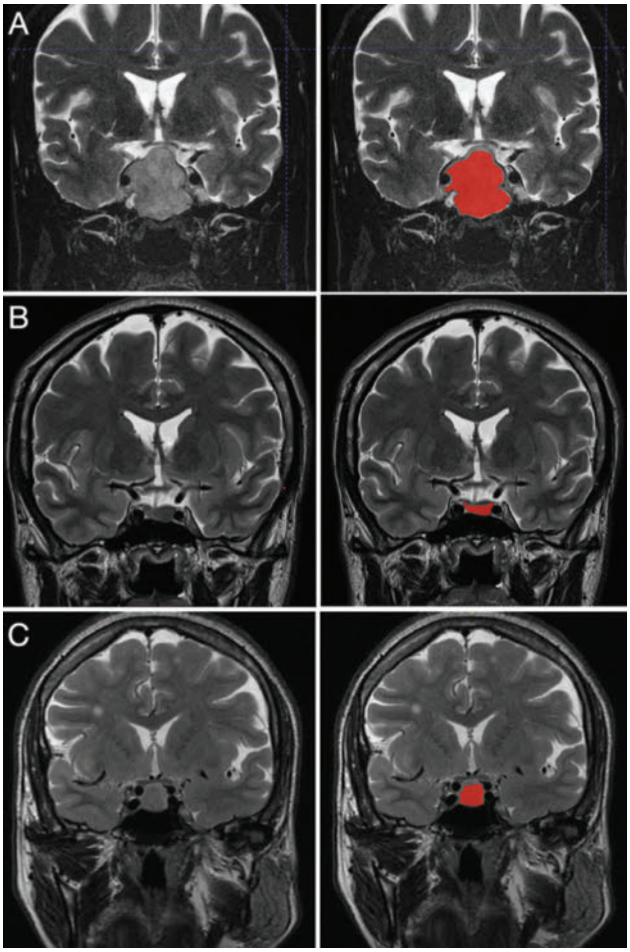

Fig. 1 Example of pituitary adenoma segmentation on coronal T2-weighted, displaying ROI placement by hand. (**A**) Coronal T2-weighted MRI of a pituitary macroadenoma with the corresponding ROI (**B**). (**C**) Coronal T2-weighted MRI of a pituitary microadenoma with the corresponding ROI (**D**). (**E**) Coronal T2-weighted MRI of a pituitary microadenoma with the corresponding ROI (**F**). MRI, magnetic resonance imaging; ROI, region of interest.

For model training and evaluation, 60% of the data was allocated for hyperparameter tuning through stratified five-fold cross-validation, while the remaining 40% served as a hold-out test set for performance assessment on unseen data. Within the training set, a normalization scaler was first computed to mitigate feature scale biases and subsequently applied to the test set. Given the expected class imbalance due to the relative rarity of fibrous adenomas compared with soft ones, the Synthetic Minority Oversampling Technique was employed to balance the training dataset.

The selected features were used to train an ensemble learning meta-algorithm, the ET Classifier, which has demonstrated strong performance in radiomic-based medical imaging studies. The model's predictive performance was evaluated on the test set, with accuracy metrics computed using *scikit-learn* and further analyzed in *R* (version 3.4.4, R Foundation for Statistical Computing, 2014). Specifically, DeLong's test (*pROC* package) was applied to estimate 95% confidence intervals (95% CIs) for the area under the curve of the receiver operating characteristic (AUC-ROC) curve, while the confusion matrix function (*caret* package) was used to assess classifier accuracy and compare it to the no-information rate.

Results

A total of 1,106 texture features were extracted, encompassing both first- and higher-order texture features derived from the original and filtered images. A correlation cluster map of the extracted features is presented in ►**Fig. 2**, while a detailed description of these features is available in the *Pyradiomics* online documentation (https://pyradiomics.readthedocs.io/en/latest/features.html). Among these, 167 exhibited low variance, and 767 showed high intercorrelation. RFE subsequently identified a refined subset of 65 features as the most predictive (►**Fig. 3**; the full feature list is provided in ►**Supplementary Material S1** [available in the online version only]).

The Extra Trees (ET) model achieved an overall accuracy of 63% (±10%) in the test set, correctly classifying most lesions with a sensitivity of 74% and a specificity of 74%. The optimized classifier parameters are detailed in ►**Supplementary Material S2** (available in the online version only). The AUC-ROC curve was 0.59 (►**Fig. 4**). The classifier's performance was significantly superior to the no-information rate. The confusion matrix and a detailed breakdown of accuracy metrics are provided in ►**Tables 2** and **3**.

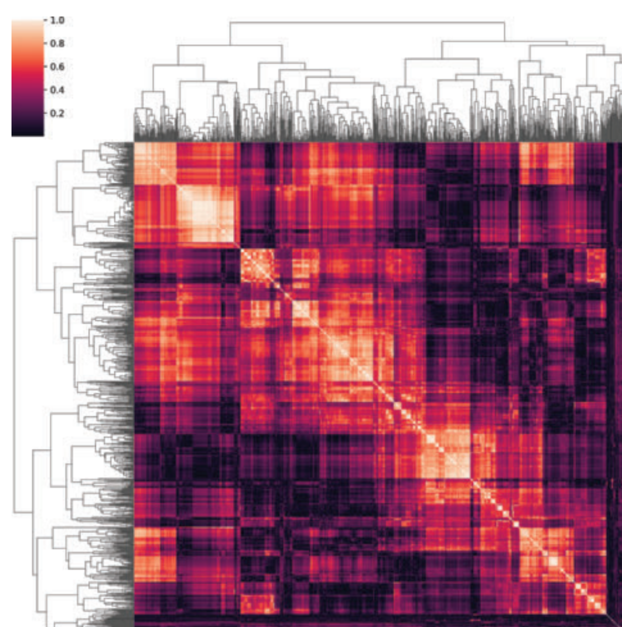

Fig. 2 Heatmap of the feature correlation matrix using hierarchical clustering. The dataset was cleansed of features whose intercorrelation was greater than the chosen threshold (≥1).

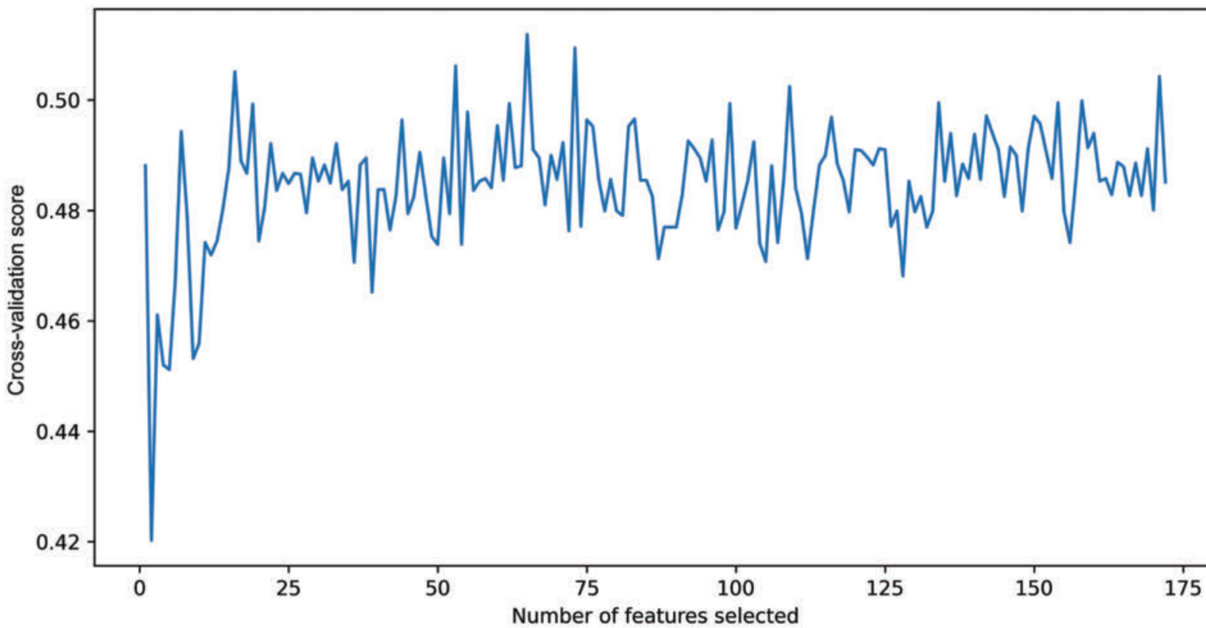

Fig. 3 Recursive feature removal plot of the feature selection procedure. At each iteration, one feature is eliminated from the total number of features on the x-axis. The average cross-validation score for each feature total is shown on the y-axis.

Discussion

Various imaging modalities have previously been investigated to predict PA consistency prior to surgery. Unlike most previous studies on predicting tumor consistency, which only relied on qualitative MRI assessments, our approach incorporated high-dimensional quantitative data, offering an objective method to predict PA consistency.[5,26,27]

Černý et al.[28] reviewed 54 articles on methods for preoperative prediction of PA consistency based on dynamic MRI intensity, enhancement patterns, radiomics, MR elastography, or CT evaluations. None demonstrated sufficient accuracy and reliability for clinical use. For instance, statistically significant relationships were found in only 55% of studies that explored T2-weighted signal intensity with tumor consistency. Most studies have reported a negative correlation between T2-weighted signal intensity and tumor consistency,[29–32] often attributing this to a higher water content in the extracellular space of softer adenomas. Only one study associates firm consistency with a hyperintense T2-weighted signal.[4] Also, analyses of apparent diffusion coefficient values yielded inconsistent results, with some studies reporting positive, negative, or no correlation with tumor firmness. Similarly, the utility of elastography has not been confirmed by the literature, with only half of the studies demonstrating a statistically significant difference in mean stiffness between soft and firm tumors.[33,34] These discrepancies underscore the challenges in developing reliable imaging biomarkers for PA consistency.

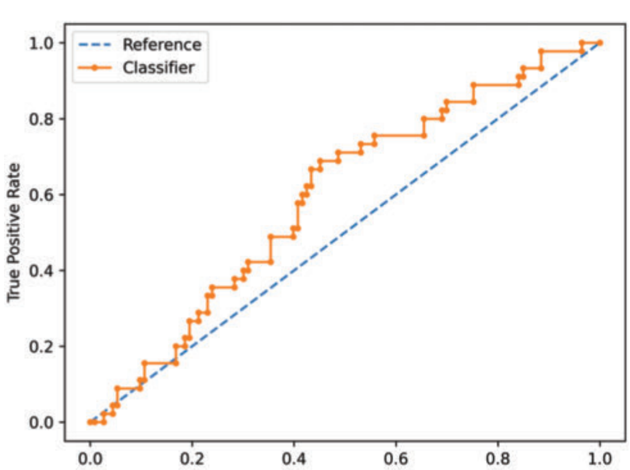

Fig. 4 The accuracy of the Extra Trees classifier's receiver operating characteristic curve.

Table 2 The test group's confusion matrix

		Predicted class	
		Soft	Fibrous
Actual class	Soft	84	29
	Fibrous	29	16

Table 3 Accuracy metrics for the Extra Trees classifier

		Precision	Recall	*F*-score
Soft		0.74	0.74	0.74
Fibrous		0.36	0.36	0.36
Accuracy	Macro Avg	0.55	0.55	0.55
	Weighted Avg	0.63	0.63	0.63

Abbreviation: Avg, average.

Zeynalova et al.[35] T2-weighted MRI-based model achieved an accuracy of 72.5% and an AUC of 0.71. However, their study focused solely on first-order histogram-derived features, which are more reproducible but provide less detailed information on tissue texture compared with higher-order features. Furthermore, they based their findings on the amount of collagen found during histopathological examination of the tumor, as a reference for consistency. While these data can aid in surgical planning, we argue that intraoperative consistency evaluation is a more practical and relevant reference, as the neurosurgeon is the primary user of this information. Additionally, due to their limited patient sample, they did not perform a separate validation but instead employed a nested 10-fold cross-validation.

Besides the limited cohort, Cuocolo et al.[20] were able to show that radiomic texture analysis combined with ML could predict PA consistency with an AUC value of 0.99. The use of ensemble-based classifiers and a comprehensive feature selection method in their study likely contributed to enhanced performance.

Among the models developed by Wan et al.,[10] the best one achieved AUC and accuracy values, respectively, of 0.90 and 0.87. They employed a fully automatic convolutional neural network-based model for tumor segmentation, along with support vector machines and random forest classifiers. Support vector machine classifier works by identifying a hyperplane that best separates data points from different classes, maximizing the margin between the closest points from each class. In contrast, the random forest classifier, as ET, uses an ensemble of decision trees, with each tree deciding based on feature thresholds. The final prediction is made by combining the decisions of all the trees, making the random forest classifier robust to overfitting. The best performances were shown by both classifiers in the models based on combined T1-weighted, T1-weighted contrast-enhanced, and T2-weighted, demonstrating the superiority of combined sequence-based models over the single sequence-based ones.

In the study by Wang et al.,[36] consistency prediction was treated as a secondary objective, with the primary aim focused on developing automated segmentation models and comparing their performance to those trained on manually segmented data. The authors found that models using automated segmentation slightly outperformed manual ones, achieving an AUC of 0.840 versus 0.821. However, these models demonstrated a tendency toward overfitting and faced challenges in generalizing to unseen data. This underscores the need for further validation using larger, multicenter datasets to ensure clinical applicability, given that imaging equipment and protocols can vary significantly between institutions.[37,38] In this context, a key strength of our study is the use of a relatively large dataset compiled from four different centers, enhancing the robustness and generalizability of our findings.

A study by Yao et al.[39] investigated the correlation between ultrahigh field 7-T MRI and histological study of PA consistency, and again, the potential validation of complex imaging technology emerged. Moreover, Bioletto et al.[7] and Zheng et al.[40] demonstrated the significance of radiomics in assessing invasiveness, secretory patterns, histopathological features, and treatment response, in addition to consistency. They propose integrating radiomics with clinical, histopathological, and genomic data to improve outcomes. Additionally, they emphasize the need for studies with larger patient cohorts as well as better standardization of tumor segmentation and feature extraction protocols for consistent clinical practice implementation.

Since fibrous tumors tend to require more complex resection modalities and are associated with more surgical complications,[41] the ability to assess PA consistency preoperatively is fundamental to surgical management. Whereas qualitative MRI assessment is still widely used alongside subjective judgment, radiomics offers a quantitative, objective assessment that is also independent from personal judgment and can lend support to the surgeon's decision-making. In addition to consistency prediction, radiomics in pituitary surgery has wider implications. Radiomics enables a more individualized surgical approach by offering a comprehensive assessment of tumor heterogeneity, allowing for the preoperative identification of challenging cases that may require alternative strategies, such as extended transsphenoidal approaches or supplementary therapies. Studies, such as those conducted by Romano et al.,[42] have emphasized the importance of preoperative imaging in predicting surgical difficulty and outcomes, while Fan et al.[43] suggest that incorporating radiomics into daily clinical workflows would enhance intraoperative preparation and reduce complications, and thus, should further improve the standard imaging analysis.

Radiomics may also provide valuable new information on tumor fibrosis and vascularity, both of which are determinants of surgical complexity. Preoperative diagnosis of very fibrous tumors may facilitate the application of adjuvant therapy, intraoperative assistive methods, or neoadjuvant factors when designing treatment plans to increase the rate of R0 resections and improve patient prognosis. As radiomics models evolve, they will make pituitary surgery even more precise, owing to their ability to predict other elements of surgery, such as the likelihood of a residual tumor, perioperative complications, and long-term recurrence risk.[44,45]

Limitations

Despite its promise, there are several challenges to the application of radiomics in PA consistency prediction. Our study has a lower classification accuracy than several published models, likely due to the consistency assessment method, classifier selection, and feature selection techniques. While the model demonstrated a sensitivity and specificity of 74%, the AUC-ROC of 0.59 indicates limited discriminative ability, only slightly better than chance. This highlights a key limitation of our current radiomics-based approach and underscores the inherent challenges in predicting PA consistency using T2-weighted MR imaging alone. The modest AUC-ROC diminishes the model's immediate clinical utility, particularly in guiding surgical planning where precision is critical. To improve predictive performance and clinical relevance, further methodological refinement, such as optimizing feature selection strategies or integrating relevant clinical parameters, will be essential.

One fundamental difficulty lies in the subjective nature of intraoperative consistency assessment, which lacks a universally accepted quantitative standard. Additionally, PAs do not always have uniform consistency, and in this study, grading was based on the main consistency of the tumor, which may have influenced the classification and contributed to the model's relatively low predictive accuracy. Future studies need to explore deeper learning approaches and more standardized methods for PA consistency assessment to enhance performance. Additionally, automated rather than manual segmentation can improve the accuracy of the model.[36]

The use of T2-weighted MRI alone is another limitation. However, the use of contrast-enhanced MRI and other imaging sequences has not, to date, demonstrated superior performance in developing a more robust predictive model.[10,44] Future studies looking at radiomics in combination with other imaging modalities should be performed to improve the consistency of prediction.

Conclusion

Preoperative prediction of PA consistency is of crucial importance, and our study suggests the promise of radiomics-based analysis of T2-weighted MRI for this purpose. Given the modest classification performance of the ET model, these results suggest that ML has the potential to identify clinically relevant imaging signatures in neuroimaging data that may yield superior performance than traditional MRI-based assessments.

Ethical Approval

This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The IRB approved this study.

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Conflict of Interest

None declared.

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