A Novel CLEAR Nomenclature System for Radiographic Assessment of Pituitary Microadenomas in Cushing's Disease

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Introduction

Interpretation of pituitary microadenomas (≤6 mm) in Cushing's disease remains inconsistent, creating uncertainty in clinical decision-making.

We introduce the Cushing's Lesion Evaluation and Reporting (CLEAR) criteria, a simple and reproducible nomenclature designed to standardize MRI reporting and communicate diagnostic certainty.

Methods and Materials

Patients with biochemically confirmed Cushing's disease that underwent surgical resection with an MRI report of no tumor or tumor ≤6mm were reviewed. Additional cases of normal MRIs in patients without pituitary pathology were included to avoid bias in rater scoring but not included in the analysis.

Three blinded neuroradiologists scored MRIs using a proposed nomenclature.

Any lesion identified on imaging was evaluated on two criteria:

1) whether the lesion was visible in >1 orthogonal plane (axial, coronal, sagittal), and 2) whether the lesion was visible on >1 sequence (T1 pre-contrast, T1 post-contrast, T2/
2) CISS).

Based on these criteria, we defined four categories:

- ''Definite': lesion meets both criteria;
- 'Probable': meets one of the two criteria;
- 'Possible': a lesion seen only in one orthogonal plane and sequence that does not meet either criterion; or
- 'Negative': no lesion identifiable

Cases were scored first on a standard pituitary protocol (including 3 mm slices in coronal and sagittal T1 pre-, T1 post-contrast fat-saturated, and T2 coronal), then after a 4-week washout on a skull base protocol (0.8 mm axial isotropic acquisition with coronal and sagittal reconstructions on high resolution T1 weighted volumetric gradient echo sequence (VIBE) pre/post and high resolution T2 weighted steady state free procession sequence (CISS).

Statistical Analysis
- Inter-rater reliability was examined using intraclass correlation coefficients (ICC) for ordinal data using a two-way random-effects model (absolute agreement). ICC values were interpreted per conventional thresholds: <0.5 poor, 0.5–0.75 moderate, 0.75–0.9 good, >0.9 excellent.
- Sensitivity and specificity of Definite scoring were calculated using intraoperative identification/pathologic confirmation as reference standards in separate analyses.

Table 1. Accuracy of CLEAR MRI nomenclature in identifying tumor intraoperative, on pathology report and postoperative remission (nomenclature based on MRI skull base protocol).

Outcome	Definitive (n=17)	Probable (n=10)	Possible (n=4)
Tumor present on operative report (n=30)	16 (94.1%)	9 (90%)	2 (50%)
Tumor present on pathology report (n=25)	13 (76.5%)	8 (80%)	2 (50%)
Postoperative remission achieved postop (n=33)	17 (100%)	9 (90%)	3 (75%)

Figure 1: Bar chart showing the distribution of MRI scoring by nomenclature categories for the skull base and pituitary protocol.
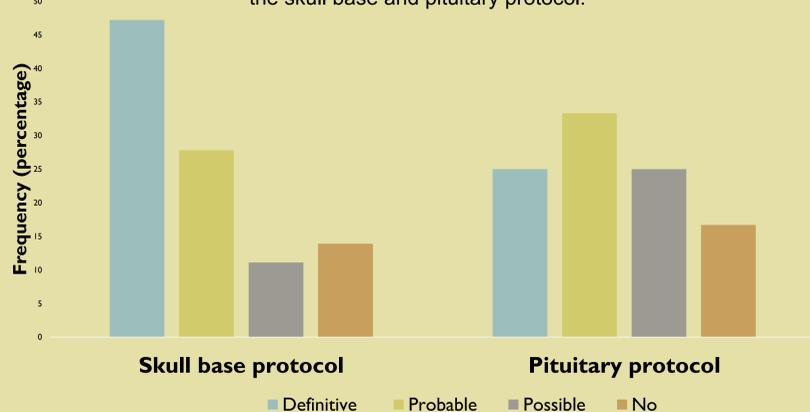
Results

A total of 36 patients were included in the final analysis.

On the standard pituitary MRI protocol, across raters, cases were scored as: Definitive 25.0% (n=9), Probable 33.3% (n=12), Possible 25.0% (n=9), and Negative 16.7% (n=6).

Using the high-resolution skull base MRI protocol, Definite categorizations significantly increased to 47.2% (n=17, p<0.01), with Probable, Possible, and Negative scores of 27.8% (n=10), 11.1% (n=4), and 13.8% (n=5), respectively.

Operative reports documented a tumor in 83.3% of patients (n=30), pathology confirmed a tumor in 69.4% (n=25), and 91.7% (n=33) achieved postoperative biochemical remission.

Inter-rater reliability for the CLEAR nomenclature was good, with ICC values of 0.76 for the pituitary protocol and 0.79 for the skull base protocol (p<0.001).

Across raters, tumor was identified intraoperatively in 94% of Definitive, 90% of Probable, 50% of Possible, and 60% of Negative cases.

The Definitive MRI category showed the highest positive predictive value (77–94%) and moderate sensitivity (52-53%), indicating it reliably confirms tumor presence and postoperative remission.

Discussion

- In this study, we present the CLEAR criteria, a four-tier radiographic nomenclature for reporting pituitary microadenomas.
- The proposed categories: Definite, Probable, Possible, and Negative, demonstrated good inter-rater reliability across neuroradiologists.
- Implementation of a high-resolution skull base MRI protocol substantially increased the frequency of Definite categorizations compared with the standard pituitary protocol and modestly improved agreement among readers, suggesting that enhanced spatial resolution contributes to more consistent interpretation.
- The Definite category was most predictive of intraoperative tumor identification, pathology confirmation, and postoperative biochemical remission.
- These findings indicate that when a lesion is labeled Definite, it is highly reliable for confirming tumor presence.
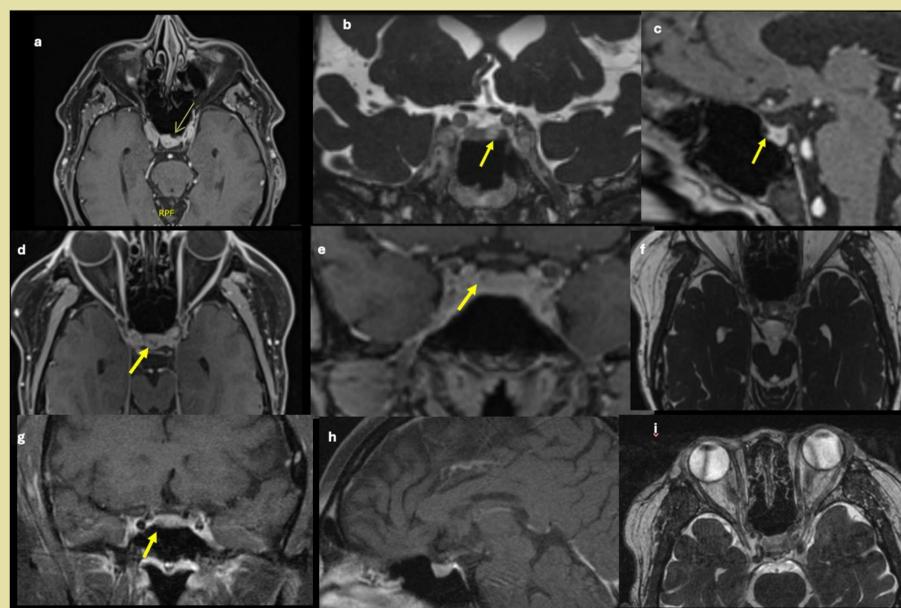
Figure 2. MRI skull base protocol demonstrates various lesion types (yellow arrows). A Definite lesion (a,b,c). A Probable lesion (d,e,f)–A Possible lesion (g,h.i)

Conclusions

- The proposed CLEAR nomenclature for small microadenomas demonstrates good inter-rater reliability and provides a standardized approach to MRI interpretation.

- In patients with Cushing's disease and tumors ≤6mm, use of the skull base protocol increased the detection of definitive tumors compared with a pituitary protocol.
- Scoring a definitive tumor reliably confirms tumor presence, though some microadenomas may still be missed.
- This system may improve preoperative assessment, guide surgical treatment, and aid in consistent communication and reporting in patients with Cushing's microadenomas.

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