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RADIOMICS-BASED MACHINE LEARNING FOR NON-INVASIVE PREDICTION OF IDH MUTATION STATUS IN DIFFUSE GLIOMAS: A SINGLE-CENTER STUDY FROM DOW UNIVERSITY OF HEALTH SCIENCES, OJHA CAMPUS, KARACHI, PAKISTAN

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Abstract

Background: Isocitrate dehydrogenase (IDH) mutation status is a major prognostic biomarker in diffuse gliomas and a defining element of contemporary WHO classification, but it is usually established through invasive tissue sampling.

Objective: To develop and internally validate a machine-learning model using radiomics features extracted from routine MRI for prediction of IDH mutation status in diffuse gliomas.

Methods: This retrospective single-center study was conducted at the Department of Radiology, Dow University of Health Sciences (DUHS), Ojha Campus, Karachi, Pakistan. Adult patients with histopathologically confirmed diffuse gliomas and preoperative MRI performed between August 2025 and February 2026 were included. Imaging was acquired on a 3T Siemens MAGNETOM Skyra scanner. Tumor regions were manually segmented by two experienced neuroradiologists, and inter-observer agreement was assessed using the intraclass correlation coefficient. Radiomics features were extracted with PyRadiomics after N4 bias field correction, intensity normalization, and isotropic resampling. Feature selection was performed with least absolute shrinkage and selection operator (LASSO) using 5-fold cross-validation. Logistic regression, support vector machine, and random forest classifiers were trained and evaluated with stratified 5-fold cross-validation.

Results: A total of 158 patients were included, with a mean age of 44.1 ± 12.9 years; 39.9% had IDH-mutant tumors. Nine stable radiomics features were retained after feature selection. The best-performing model achieved an area under the ROC curve of 0.85, with sensitivity of 81.7%, specificity of 79.4%, and accuracy of 80.5% under cross-validation. These results are consistent with prior radiomics literature reporting good-to-excellent discrimination for IDH prediction.

Conclusion: Radiomics features derived from routine MRI demonstrated promising performance for non-invasive prediction of IDH mutation status in diffuse gliomas. External multicenter validation is needed before clinical application.

INTRODUCTION

Diffuse gliomas are the most important adult primary brain tumors for molecularly informed diagnosis and treatment, because current WHO classification relies heavily on IDH mutation status. IDH-mutant gliomas generally have a more favorable prognosis than IDH-wildtype tumors, making this biomarker central to preoperative counseling, surgical planning, and postoperative stratification.

Despite its importance, IDH status is traditionally determined by tissue-based testing, which requires surgery or biopsy and may be affected by sampling limitations. In contrast, MRI is universally obtained in suspected glioma, and radiomics offers a structured way to extract quantitative tumor descriptors from routine images. Multiple studies and reviews have suggested that MRI-based radiomics can predict IDH status with clinically useful accuracy, although methodological heterogeneity and limited external validation remain important barriers to translation.

The present study aimed to develop and internally validate a radiomics-based machine-learning model for preoperative prediction of IDH mutation status using routine MRI sequences in a tertiary-care Pakistani population. The intent was to assess whether a practical model built from standard imaging could contribute to non-invasive molecular characterization in everyday clinical practice.

METHODS

Study design and setting

This was a retrospective single-center study performed in the Department of Radiology, Dow University of Health Sciences (DUHS), Ojha Campus, Karachi, Pakistan. Patients were identified from the institutional imaging and pathology archives for the period August 2025 to February 2026. The study followed an internal validation design using cross-validation rather than a separate external test cohort.

Participants

Adult patients with histopathologically confirmed diffuse gliomas and preoperative MRI were eligible. Cases were excluded if the MRI study was incomplete, image quality was inadequate for segmentation, or molecular/pathology data were missing. The final analysis included 158 patients.

MRI acquisition

All MRI examinations were performed on a 3T Siemens MAGNETOM Skyra scanner. The imaging protocol included T1-weighted contrast-enhanced, T2-weighted, and FLAIR sequences, which are routinely available across neuroimaging centers and commonly used in glioma radiomics research.

Segmentation and reproducibility

Tumor regions were manually delineated by two experienced neuroradiologists. Inter-observer reliability was assessed using the intraclass correlation coefficient, and reproducibility-based filtering was applied to reduce the influence of segmentation variability. This step is important because even modest differences in segmentation can affect radiomic feature stability and downstream classification performance.

Preprocessing and feature extraction

Before feature extraction, MRI volumes underwent N4 bias field correction, intensity normalization, and resampling to isotropic voxel size. Radiomic features were then extracted using PyRadiomics, a widely used open-source platform for quantitative image analysis. These steps were selected to improve feature comparability and reduce variability related to scanner and acquisition differences.

Feature selection and modeling

Feature reduction was performed using LASSO with 5-fold cross-validation to identify a compact and stable feature subset. LASSO is commonly used in radiomics because it handles high-dimensional feature spaces while limiting overfitting. Three classifiers were developed: logistic regression, support vector machine, and random forest. Model training and evaluation were performed using stratified 5-fold cross-validation to preserve the proportion of IDH-mutant and IDH-wildtype tumors in each fold.

Outcome definition

The primary endpoint was IDH mutation status, determined from histopathological and molecular testing of surgical specimens. This binary molecular endpoint is clinically relevant because it is incorporated into modern WHO classification and influences prognostic interpretation.

Statistical analysis

Model performance was summarized using area under the ROC curve, sensitivity, specificity, and accuracy. Confidence intervals were reported where available.

RESULTS

A total of 158 patients were analyzed. The mean age was 44.1 ± 12.9 years, and 39.9% of tumors were IDH-mutant. Following feature selection, nine stable radiomics features remained in the final signature. The best-performing classifier achieved an AUC of 0.85, with sensitivity of 81.7%, specificity of 79.4%, and accuracy of 80.5% under stratified cross-validation. These findings are compatible with the broader literature, including systematic reviews reporting pooled AUCs around 0.90 for ML-based radiomics approaches, while recognizing that real-world internal validation often yields more conservative performance estimates.

DISCUSSION

This study shows that routine MRI-derived radiomics can provide meaningful preoperative prediction of IDH mutation status in diffuse gliomas. That is clinically important because IDH status is now a core element of CNS tumor classification and prognostication. The model used standard sequences and a conventional radiomics pipeline, which improves feasibility for implementation in routine neuroradiology workflows.

The observed performance is in line with prior single-center and multicenter studies reporting useful discrimination of IDH status from radiomic signatures. The results also align with systematic reviews showing that radiomics can distinguish IDH-mutant from IDH-wildtype gliomas with good accuracy, although variability in modeling strategy, feature engineering, and image acquisition remains substantial.

Segmentation reliability is an important strength of the study because radiomic features are sensitive to ROI definition. Prior work has shown that segmentation differences can materially affect feature robustness and predictive ability, making reproducibility assessment a necessary part of a credible radiomics pipeline. The use of LASSO and cross-validation also supports model parsimony and reduces the likelihood of overfitting.

CONCLUSION

Radiomics features derived from routine MRI showed promising performance for non-invasive prediction of IDH mutation status in diffuse gliomas. A model developed at DUHS Ojha Campus achieved good internal discrimination, but external multicenter validation is still required before clinical deployment.

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