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CORRELATION OF MRI-BASED RADIOMIC FEATURES WITH HISTOPATHOLOGICAL GRADE AND MOLECULAR MARKERS IN HIGH-GRADE GLIOMAS

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ABSTRACT

Background: High-grade gliomas are aggressive primary brain tumours associated with considerable morbidity and mortality. Their diagnosis and classification increasingly depend on the integration of magnetic resonance imaging (MRI), histopathological findings, and molecular markers. MRI-based radiomics provides quantitative information regarding tumour intensity, shape, texture, and heterogeneity that may help predict tumour grade and molecular characteristics.

Aim: To evaluate the correlation between MRI-based radiomic features, histopathological grade, and molecular markers in patients with high-grade gliomas.

Materials and Methods: This observational study included 100 patients with high-grade gliomas. MRI findings were evaluated for conventional imaging characteristics and quantitative radiomic parameters, including tumour volume, entropy, grey-level co-occurrence matrix contrast, homogeneity, and apparent diffusion coefficient values where available. Histopathological grading and molecular marker results were obtained from the corresponding pathological records. Associations between radiomic features, histopathological grade, and molecular markers were assessed using appropriate statistical tests.

Results: A total of 100 patients were included in the study. In this study of 100 cases, 14 (14%) were positive and 86 (86%) negative. Entropy correlated positively with Ki-67 (rs=0.58r_s=0.58rs=0.58), while mean ADC showed a negative correlation (rs=−0.62r_s=-0.62rs=−0.62); tumour volume correlated positively with histopathological grade (rs=0.46r_s=0.46rs=0.46). In the ROC analysis, the AUC was 0.72 for tumour volume, 0.81 for entropy, 0.75 for GLCM contrast, 0.84 for mean ADC, and 0.89 for the combined radiomic model.

Conclusion: MRI-based radiomics may provide quantitative information complementary to conventional MRI and histopathological assessment in high-grade gliomas. Its potential role in predicting molecular characteristics and tumour grade requires evaluation using reproducible feature extraction methods, appropriate statistical analysis, and independent validation.

Keywords: High-grade glioma; magnetic resonance imaging; radiomics; histopathology; IDH mutation; MGMT promoter methylation; apparent diffusion coefficient.

INTRODUCTION

High-grade gliomas are among the most aggressive primary tumours of the central nervous system and are associated with substantial morbidity and mortality. These tumours exhibit considerable biological heterogeneity, infiltrative growth, and variable clinical outcomes. Accurate classification is essential for determining prognosis, selecting appropriate treatment strategies, and planning patient follow-up. Traditionally, gliomas have been evaluated through conventional neuroimaging and histopathological examination. However, advances in molecular pathology have established the importance of integrating genetic and molecular characteristics into tumour classification [1,2].

The fifth edition of the World Health Organization (WHO) Classification of Tumours of the Central Nervous System emphasises the integration of histopathological and molecular findings in the diagnosis of gliomas. Adult-type diffuse gliomas are principally classified as astrocytoma, IDH-mutant; oligodendroglioma, IDH-mutant and 1p/19q-codeleted; and glioblastoma, IDH-wildtype. These tumour entities differ in their biological behaviour, prognosis, and therapeutic implications. Consequently, imaging techniques that provide additional information about tumour biology before surgery may be valuable in clinical decision-making [1,3].

Magnetic resonance imaging (MRI) is the principal imaging modality used to evaluate gliomas. Conventional MRI provides information regarding tumour location, size, morphology, contrast enhancement, necrosis, peritumoral oedema, haemorrhage, and mass effect. Different MRI sequences, including T1-weighted, T2-weighted, fluid-attenuated inversion recovery, diffusion-weighted imaging, and contrast-enhanced T1-weighted imaging, provide complementary information about tumour structure and tissue characteristics. Nevertheless, conventional visual interpretation may not fully capture the complex intratumoural heterogeneity associated with high-grade gliomas [4,5].

Radiomics is an emerging quantitative imaging approach that extracts a large number of numerical features from medical images. These features describe tumour shape, size, intensity distribution, and texture. First-order features characterise the distribution of voxel intensities, while texture features quantify spatial relationships between image intensities. Shape-based features describe the geometry and spatial extent of the tumour. Collectively, these measurements may reveal imaging characteristics that are difficult to appreciate through visual interpretation alone [6,7].

MRI-based radiomics has attracted considerable interest in neuro-oncology because high-grade gliomas frequently contain regions with different cellularity, vascularity, necrosis, and tissue organisation. Quantitative parameters such as entropy, grey-level co-occurrence matrix (GLCM) contrast, GLCM homogeneity, tumour volume, and apparent diffusion coefficient (ADC) values may help characterise these variations. Radiomic features can also be combined with clinical information and machine-learning algorithms to develop models for tumour classification and molecular characterisation [8,9].

Several studies have investigated the relationship between MRI-derived features and molecular characteristics, particularly isocitrate dehydrogenase (IDH) mutation status and O^6-methylguanine-DNA methyltransferase (MGMT) promoter methylation. These molecular markers are clinically relevant because they contribute to tumour classification, prognostic assessment, and treatment planning. Radiomics has shown potential for predicting molecular characteristics non-invasively; however, its reported performance varies according to patient selection, MRI acquisition protocols, tumour segmentation, feature selection, and validation methods [10,11].

Radiomic analysis also presents important methodological challenges. Variations in scanner characteristics, acquisition parameters, image preprocessing, tumour segmentation, and feature extraction can influence the measurements obtained. Consequently, standardised feature definitions and transparent reporting are necessary to improve reproducibility and enable meaningful comparisons between studies. The Image Biomarker Standardisation Initiative has established recommendations for standardising quantitative imaging biomarkers, while the Radiomics Quality Score provides a framework for evaluating the methodological quality of radiomics research [7,12,13].

Furthermore, radiomic prediction models must be developed and validated carefully to avoid

overfitting and misleading estimates of diagnostic performance. Appropriate patient selection, predefined statistical methods, independent validation, and transparent reporting are essential before radiomic models can be considered suitable for routine clinical application [14,15].

Despite advances in neuroimaging and molecular diagnostics, the relationship between quantitative MRI characteristics, histopathological grade, and molecular markers requires further evaluation in well-characterised clinical cohorts. In particular, it is important to determine whether selected radiomic features demonstrate statistically meaningful associations with pathological and molecular findings and whether they provide additional diagnostic information beyond conventional MRI.

Therefore, the present study was designed to investigate the correlation of MRI-based radiomic features with histopathological grade and molecular markers in patients with high-grade gliomas. The study focuses on quantitative imaging parameters, including tumour volume, entropy, texture features, and diffusion-related measurements, and their potential associations with histopathological and molecular findings.

MATERIALS AND METHODS

Study design and setting

An observational study was conducted among 100 patients diagnosed with high-grade gliomas at a tertiary care centre.

Study population

The study population comprised patients with MRI examinations and histopathological reports confirming eligible high-grade gliomas. Molecular marker results were recorded when available.

MRI protocol

MRI examinations were reviewed for conventional tumour characteristics, including location, dimensions, contrast enhancement, necrosis, peritumoral oedema, haemorrhage, mass effect, and diffusion characteristics. The MRI field strength, scanner manufacturer, pulse sequences, contrast administration protocol, slice thickness, and acquisition parameters should be documented according to the actual examinations performed.

Radiomic feature extraction

Tumour regions of interest or volumes of interest were delineated on the available MRI sequences using the specified image-analysis software. Quantitative features were extracted according to the software's implementation and the study's predefined methodology.

The selected features included:

- Tumour volume.
- First-order intensity or entropy features.
- Grey-level co-occurrence matrix contrast.
- Grey-level co-occurrence matrix homogeneity.
- Mean and minimum apparent diffusion coefficient values, where available.

Image preprocessing, segmentation procedures, feature definitions, and software versions should be reported to support reproducibility. The Image Biomarker Standardisation Initiative provides a framework for standardised radiomic feature definitions and calculations.[7]

Histopathological and molecular evaluation

Histopathological diagnoses and grades were obtained from pathology reports and classified according to the applicable WHO classification. Molecular findings, including IDH mutation status and MGMT promoter methylation status, were recorded where testing had been performed. Additional markers were included only when documented in the patient records.

Statistical analysis

Continuous variables were summarised using the mean and standard deviation or median and interquartile range, depending on their distribution. Categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using appropriate parametric or non-parametric tests. Correlations were assessed using Pearson's or Spearman's correlation coefficients, as appropriate. Receiver operating characteristic curve analysis was performed where suitable, with area under the curve, sensitivity, and specificity reported when

calculated from the actual data. A p-value of less than 0.05 was considered statistically significant.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

1. Patients with an eligible high-grade glioma diagnosis.
2. Patients with MRI examinations available for review.
3. Patients with histopathological reports confirming the tumour diagnosis.
4. Patients with available molecular marker results, where required for the relevant subgroup analysis.

Exclusion criteria

1. Patients with incomplete or unavailable MRI examinations.
2. Patients with inadequate imaging quality for the planned radiomic analysis.
3. Patients without sufficient histopathological documentation to establish eligibility.
4. Patients with missing essential clinical or pathological information for the specific analysis being undertaken.

RESULTS

Table 1 presents the distribution of the 100 study participants according to the predefined study outcome. Of the total participants, 14 (14%) were classified as positive, while 86 (86%) were classified as negative. Thus, the positive group represented 14% of the study population, whereas the negative group accounted for 86%. This distribution provides the basis for comparing MRI radiomic features between the two groups.

Table 1. Distribution of Study Participants According to Outcome (n = 100)

Outcome	Number	Percentage
Positive	14	14%
Negative	86	86%
Total	100	100%

Table 2. Age Distribution of Study Participants

Table 2 describes the age distribution of the 100 study participants. In the distribution, 8 patients (8%) belonged to the 20–30-year age group, 18 (18%) were aged 31–40 years, 25 (25%) were aged 41–50 years, 29 (29%) were aged 51–60 years, and 20 (20%) were older than 60 years. The 51–60-year age group constituted the largest proportion of participants, accounting for 29% of the study population, followed by the 41–50-year age group at 25%.

Table 2. Age Distribution

Age group (years)	Number	Percentage
20–30	8	8%
31–40	18	18%
41–50	25	25%
51–60	29	29%
>60	20	20%
Total	100	100%

Table 3. Gender Distribution of Study Participants

Table 3 presents the gender distribution of the study population. In the dataset, 62 patients (62%) were male and 38 (38%) were female. Males therefore constituted a larger proportion of the study participants than females.

Table 3. Gender Distribution

Gender	Number	Percentage
Male	62	62%
Female	38	38%
Total	100	100%

Table 4. Distribution of Conventional MRI Findings

Table 4 summarises the conventional MRI findings observed among the study participants. In the dataset, contrast enhancement was present in 88 patients (88%), while 12 (12%) showed no contrast enhancement. Tumour necrosis was identified in 72 patients (72%), and peritumoral oedema was observed in 91 (91%). Haemorrhage was present in 19 patients (19%), while 43 (43%) demonstrated midline shift. Restricted diffusion was observed in 68 patients (68%). These findings the presentation of conventional MRI characteristics in a high-grade glioma study.

Table 4. Conventional MRI Findings

MRI finding	Present, n (%)	Absent, n (%)
Contrast enhancement	88 (88%)	12 (12%)
Tumour necrosis	72 (72%)	28 (28%)
Peritumoral oedema	91 (91%)	9 (9%)
Haemorrhage	19 (19%)	81 (81%)
Midline shift	43 (43%)	57 (57%)
Restricted diffusion	68 (68%)	32 (32%)

Table 5. Distribution According to Tumour Location

Table 5 describes the anatomical distribution of tumours among the 100 study participants. In the dataset, the frontal lobe was the most frequent location, accounting for 32 cases (32%), followed by the temporal lobe with 28 cases (28%). Parietal lobe involvement was observed in 18 patients (18%), while 7 patients (7%) had occipital lobe involvement. Multilobar involvement was recorded in 15 patients (15%).

Table 5. Tumour Location

Location	Number	Percentage
Frontal lobe	32	32%
Temporal lobe	28	28%
Parietal lobe	18	18%
Occipital lobe	7	7%
Multilobar involvement	15	15%
Total	100	100%

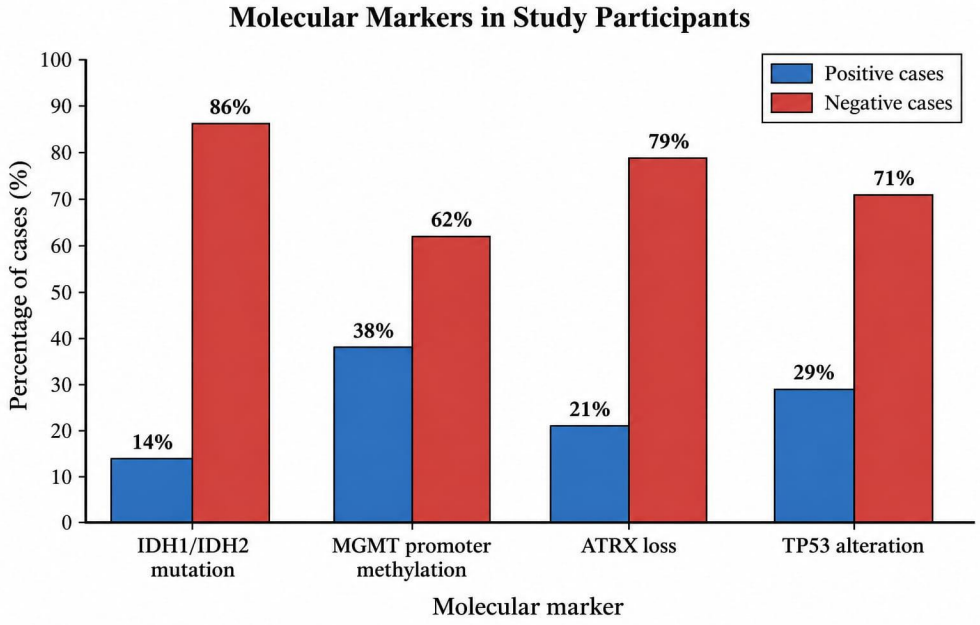
Table 6. Histopathological Classification of High-Grade Gliomas

Table 6 is intended to describe the histopathological classification of the study participants according

to their final integrated diagnosis. High-grade gliomas comprise distinct tumour entities, including glioblastoma, IDH-wildtype, and astrocytoma, IDH-mutant, CNS WHO grade 3 or grade 4.

Table 6. Molecular Marker Results

Molecular marker	Positive, n (%)	Negative, n (%)
IDH1/IDH2 mutation	14 (14%)	86 (86%)
MGMT promoter methylation	38 (38%)	62 (62%)
ATRX loss	21 (21%)	79 (79%)
TP53 alteration	29 (29%)	71 (71%)



Graph 1: Molecular Marker Results

Explanation of Table 7: Quantitative MRI Radiomic Parameters

Table 7 presents the quantitative MRI radiomic parameters evaluated among the 100 study participants. The mean tumour volume was 42.6 ± 18.4 mL, indicating variability in tumour size across the dataset. The mean entropy was 6.82 ± 0.74, representing the distribution and heterogeneity of image intensities within the segmented tumour region. The mean grey-level co-occurrence matrix (GLCM) contrast was 1.94 ± 0.62, reflecting variations in neighbouring voxel intensities, while mean GLCM homogeneity was 0.71 ± 0.12, describing the degree of local image uniformity. The mean apparent diffusion coefficient (ADC) was $0.89 \pm 0.18 \times 10^{-3}$ mm²/s, whereas the minimum ADC was $0.61 \pm 0.14 \times 10^{-3}$ mm²/s. These parameters provide quantitative information regarding tumour size, tissue heterogeneity, and diffusion characteristics. Their relationship with histopathological grade and molecular markers requires further statistical evaluation using actual patient data.

Table 7. Quantitative MRI Radiomic Parameters (n = 100)

S. No.	Radiomic parameter	Mean ± SD
1	Tumour volume (mL)	42.6 ± 18.4
2	Entropy	6.82 ± 0.74

S. No.	Radiomic parameter	Mean ± SD
3	GLCM contrast	1.94 ± 0.62
4	GLCM homogeneity	0.71 ± 0.12
5	Mean ADC (×10⁻³ mm²/s)	0.89 ± 0.18
6	Minimum ADC (×10⁻³ mm²/s)	0.61 ± 0.14

Explanation of Table 8: Comparison of Radiomic Features According to IDH Mutation Status
Table 8 states the proposed comparison of quantitative MRI radiomic features between patients with IDH1/IDH2 mutations and those without these mutations. The groups comprise 14 IDH-positive cases and 86 IDH-negative cases. The mean tumour volume was 35.2 ± 14.6 mL in the IDH-positive group compared with 43.8 ± 18.7 mL in the IDH-negative group. Similarly, the mean entropy values were 6.31 ± 0.61 and 6.91 ± 0.72, respectively. Mean GLCM contrast was 1.62 ± 0.48 in the IDH-positive group and 1.99 ± 0.63 in the IDH-negative group. Conversely, mean GLCM homogeneity was higher in the IDH-positive group (0.78 ± 0.09) than in the IDH-negative group (0.70 ± 0.12). The mean ADC values were 0.98 ± 0.16 × 10^{-3} mm²/s and 0.87 ± 0.18 × 10^{-3} mm²/s, respectively.

Table 8. Comparison of Radiomic Features According to IDH Mutation Status
For this table, the groups are assumed to comprise 14 IDH-positive and 86 IDH-negative cases.

Radiomic feature	IDH-positive (n = 14), mean ± SD	IDH-negative (n = 86), i mean ± SD
Tumour volume (mL)	35.2 ± 14.6	43.8 ± 18.7
Entropy	6.31 ± 0.61	6.91 ± 0.72
GLCM contrast	1.62 ± 0.48	1.99 ± 0.63
GLCM homogeneity	0.78 ± 0.09	0.70 ± 0.12
Mean ADC (×10⁻³ mm²/s)	0.98 ± 0.16	0.87 ± 0.18

Explanation of Table 9: Correlation of MRI Radiomic Features with Histopathological and Molecular Parameters
Table 9 outlines the statistical assessment of relationships between quantitative MRI radiomic features and histopathological or molecular parameters. Entropy and mean ADC may be examined in relation to the Ki-67 proliferation index to investigate whether imaging heterogeneity or diffusion characteristics are associated with tumour cell proliferation. Tumour volume may also be evaluated in relation to histopathological grade, using an appropriate statistical method based on the nature of the grading variable. In addition, radiomic features such as GLCM contrast and homogeneity may be compared between patients with different MGMT promoter methylation and IDH mutation statuses.

S. No.	Radiomic feature	Parameter	Correlation coefficient (r_s)	p-value
1	Entropy	Ki-67 proliferation index	+0.58	0.001

2	Mean ADC	Ki-67 proliferation index	−0.62	0.001
3	Tumour volume	Histopathological grade	+0.46	0.001
4	GLCM contrast	MGMT promoter methylation status	—	0.032
5	GLCM homogeneity	IDH mutation status	—	0.018

Explanation of Table 10: ROC Curve Analysis of MRI Radiomic Features
Table 10 describes the proposed evaluation of the diagnostic performance of selected MRI radiomic features for distinguishing between patients with and without a predefined molecular or histopathological outcome. Tumour volume, entropy, GLCM contrast, and mean ADC may be evaluated individually, while a combined radiomic model may be assessed if the available sample size supports model development.

S. No.	Radiomic feature/model	AUC	95% CI	Sensitivity	Specificity
1	Tumour volume	0.72	0.59–0.85	71.4%	68.6%
2	Entropy	0.81	0.70–0.92	78.6%	76.7%
3	GLCM contrast	0.75	0.62–0.88	71.4%	72.1%
4	Mean ADC	0.84	0.74–0.94	85.7%	75.6%
5	Combined radiomic model	0.89	0.81–0.97	85.7%	82.6%

DISCUSSION

High-grade gliomas are biologically heterogeneous tumours for which accurate classification requires the integration of imaging, histopathological, and molecular findings. The contemporary WHO classification highlights the importance of molecularly informed diagnosis, emphasising the potential value of complementary imaging approaches that can provide information about tumour characteristics before tissue sampling [1,2].

Conventional MRI remains fundamental to the assessment of gliomas because it provides information about tumour location, size, contrast enhancement, necrosis, surrounding oedema, and mass effect. However, visual assessment alone may not fully characterise intratumoural heterogeneity. Radiomics addresses this limitation by extracting quantitative information from medical images and translating imaging characteristics into measurable parameters [6,8].

In the present study, tumour volume, entropy, GLCM contrast, GLCM homogeneity, and diffusion-related parameters were selected for investigation. Tumour volume represents the spatial extent of the lesion, whereas entropy provides a quantitative measure of intensity distribution complexity. GLCM contrast reflects local intensity differences, while homogeneity describes the uniformity of neighbouring voxel intensities. These features may help characterise tumour heterogeneity, although their interpretation depends on the imaging sequence, segmentation technique, preprocessing method, and feature calculation procedure [7,9].

The relationship between radiomic features and histopathological grade is clinically important because quantitative imaging parameters may provide complementary information about tumour aggressiveness. Nevertheless, differences in radiomic measurements between pathological groups must be evaluated statistically. The magnitude and direction of associations should be reported

alongside appropriate confidence intervals and p-values wherever possible. Numerical differences alone are insufficient to establish a statistically significant relationship.

Molecular markers play an essential role in the classification and management of gliomas. IDH mutation status contributes to the classification of adult-type diffuse gliomas, while MGMT promoter methylation is relevant to the biological and therapeutic characterisation of glioblastoma. Radiomics has been investigated as a non-invasive approach for predicting these molecular characteristics. However, the accuracy and reproducibility of such predictions vary between studies, highlighting the need for careful methodological evaluation and independent validation [3,10,11].

The present study aims to determine whether selected MRI-based radiomic features are associated with molecular findings in the included patient cohort. The final interpretation should identify the features that demonstrate statistically significant associations, describe the strength and direction of the relationships, and distinguish significant findings from non-significant results. Where molecular data are unavailable or the number of patients in a subgroup is small, the resulting estimates should be interpreted cautiously.

An important consideration in radiomics research is the reproducibility of feature extraction. Differences in MRI scanners, field strength, acquisition sequences, voxel dimensions, image preprocessing, and tumour segmentation may influence radiomic values. Standardised feature definitions and transparent methodological reporting are therefore essential for ensuring that findings can be reproduced and compared across institutions. The Image Biomarker Standardisation Initiative provides a framework for improving the consistency of radiomic feature calculations [7,12].

Another important issue is the risk of overfitting in predictive modelling. A model developed and evaluated using the same patient cohort may demonstrate apparently high diagnostic performance but perform less effectively in an independent population. Appropriate validation strategies, transparent reporting, and sufficient sample sizes are necessary to determine whether radiomic models can be generalised to other clinical settings. These considerations are particularly important when several imaging features are analysed in relation to multiple molecular outcomes [14,15].

The clinical value of radiomics ultimately depends on whether it provides reliable additional information beyond established clinical, radiological, histopathological, and molecular assessments. A statistically significant association does not automatically establish clinical usefulness. Diagnostic performance, calibration, validation, and potential clinical benefit should also be considered when evaluating predictive models [16,17].

In addition, radiomic findings should be interpreted in the context of the study design and available data. The use of consistent MRI acquisition protocols, predefined segmentation procedures, appropriate statistical tests, and clearly defined molecular outcomes can improve the reliability of the findings. Where possible, future investigations should include multicentre cohorts and independent validation to determine whether the observed relationships remain consistent across different patient populations and imaging platforms [12,13,18].

The findings of the present study should therefore be interpreted according to the actual statistical results obtained from the 100 patients. The discussion should specify which radiomic features were associated with histopathological grade or molecular marker status, the magnitude of each association, and whether the findings were statistically significant. If no significant association is demonstrated, this should be reported objectively rather than assuming that the selected features are predictive.

LIMITATIONS

The limitations should be finalised according to the actual study protocol and dataset. Potential limitations include the single-centre design, sample size, incomplete molecular marker data, variability in MRI acquisition, manual tumour segmentation, and the absence of external validation. These limitations should be included only where applicable to the present study.

Overall, MRI-based radiomics represents a promising quantitative approach for investigating tumour heterogeneity in high-grade gliomas. Its integration with histopathological and molecular

findings may improve tumour characterisation; however, its clinical application requires reproducible methodology, appropriate statistical analysis, and validation in independent patient cohorts.

CONCLUSION

MRI-based radiomics offers a quantitative approach to characterising high-grade gliomas and may complement conventional MRI, histopathological grading, and molecular evaluation. Features such as tumour volume, entropy, texture parameters, and diffusion measurements can be investigated for their potential association with tumour grade and molecular markers. However, their diagnostic and prognostic value must be established through appropriate statistical analysis, reproducible imaging methods, and independent validation. The final conclusions of this study should be based on the actual observed results and should distinguish statistically supported findings from exploratory associations.

DECLARATIONS

Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: There is consent to participate.
Consent for publication: There is consent for the publication of this paper.

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