



AN EXPLAINABLE MACHINE LEARNING FRAMEWORK FOR EARLY DETECTION OF BRAIN TUMOURS WITH STATISTICAL ANALYSIS OF CLINICAL AND IMAGING DATA

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ABSTRACT

Early and accurate detection of brain tumors is critical for improving patient outcomes, yet diagnostic delays and interpretability gaps limit the clinical adoption of artificial intelligence (AI) systems. This study proposes an explainable machine learning framework that integrates clinical and imaging data for early detection of brain tumors. Using a retrospective cohort of 1,248 patients, we developed and evaluated baseline statistical models, ensemble methods, and deep learning architectures, with systematic incorporation of SHAP values, Grad-CAM heatmaps, and patient-specific explanations. The hybrid model achieved an AUC-ROC of 0.97, accuracy of 93.2%, and well-calibrated predictions, outperforming imaging-only and tabular baselines. Explainability outputs demonstrated high concordance with radiologist annotations and were rated as clinically plausible. The framework maintained robust performance across tumor types, age groups, and imaging modalities, including CT-only cases. These findings support the feasibility of trustworthy AI-assisted diagnostics in neuro-oncology, particularly for resource-constrained settings. Future work should focus on prospective validation, human-factors evaluation, and integration with molecular data to further enhance clinical utility and generalizability.

Keywords: Brain Tumour, Early Detection, Explainable AI, Machine Learning, Medical Image Analysis, Radiomics, Clinical Decision Support

I. INTRODUCTION

The healthcare system in many regions faces important challenges regarding the achievement of timely and accurate diagnosis of brain tumours within the planned financial, temporal, and institutional constraints, in addition to maintaining a positive impact of diagnostic technologies on vulnerable patients and clinical workflows[1]. The traditional success factors in neuro-oncology diagnostics are high-quality imaging protocols, experienced radiologists, and access to advanced histopathological services. The basics of success in early brain tumour detection are still trust in diagnostic tools, transparency of decision processes, and the ability to translate complex imaging and clinical data into actionable clinical outcomes[2].

A traditional usage of diagnostic accuracy, as a model's capacity to correctly classify tumour presence, type, and grade based on imaging and clinical features, helps to gauge a system's performance based on its sensitivity, specificity, and area under the receiver operating characteristic curve. Diagnostic accuracy is useful for measuring traditional and basic indicators of model performance, but it cannot fully handle the role of model interpretability and clinical explainability, leaving a major flaw in understanding contemporary AI-assisted diagnostics[3]. Clinicians often do not have a detailed and practical framework to relate deep learning



classifiers, radiomic feature extractors, or ensemble models to the main indicators that measure a system's trustworthiness, usability, and integration into routine care. Such a gap makes it more difficult to take proper actions in the screening and triage stages, which is crucial for staying in line with national cancer control targets and international clinical guidelines[4].

Therefore, it is now essential to link explainability capabilities with machine learning diagnostic frameworks; recent publications have attempted to address this issue. Various research articles have developed and suggested the concept of "explainable AI" by incorporating interpretability methods, feature importance scores, and visual explanation tools into the traditional approach to medical image analysis. Their findings suggested that AI can accurately detect brain tumours, segment lesion regions, and predict malignancy by using convolutional neural networks and radiomics, even though adoption in routine clinical practice has lagged. Subsequently, another research developed and suggested an interpretable diagnostic model, incorporating SHAP values, saliency maps, and rule-based overlays to improve trust and compliance across clinical workflows[5]. Although the model becomes highly effective, it does not include the statistical and distributional variables to monitor how explainable outputs reshape diagnostic confidence and burden-sharing between radiologists and automated systems. Basically, AI in brain tumour diagnostics uses the following three crucial parameters:

a) Data Capacity: The availability and quality of clinically relevant data (e.g., MRI sequences, CT scans, demographic and symptom records) that can be processed by AI systems. It is fixed on hospital information systems, imaging archives, and data-governance infrastructure[7].

b) Analytical Capacity: The ability to develop, access, or deploy machine learning models and tools (e.g., CNN classifiers, radiomic pipelines, ensemble learners) that convert data into actionable diagnostic intelligence. It is the quantification of an institution's technical and institutional capability to use algorithms[9].

c) Clinical Capacity: The real influence exerted in diagnostic and treatment decisions based on the credibility and usability of AI-generated evidence. It reflects how algorithmic outputs are translated into diagnostic confidence, referral patterns, and treatment outcomes.

Based on these measures, performance indices can be computed:

Algorithmic Readiness Index (ARI):

$$ARI = \frac{(Data\ Capacity + Analytical\ Capacity)}{2}$$

It measures a hospital or health system's preparedness to use AI in brain tumour diagnostics.

Diagnostic Leverage Ratio (DLR):

$$DLR = \frac{Clinical\ Capacity}{ARI}$$

It measures how effectively a system converts algorithmic readiness into diagnostic influence.

The value above 1.0 indicates favourable leverage, whereas the value below 1.0 shows under-utilization or dependency[10]. To estimate the potential influence of a health system in AI-assisted diagnostics, the **Algorithmic Influence Score (AIS)** can be calculated by:

$$AIS = ARI \times DLR$$

Whereas "Maximum Potential Influence" (MPI) stands for the highest achievable AIS given a country's or hospital's structural constraints and opportunities.

Hypothetical Example - Snapshot of an AI-Enabled Brain Tumour Diagnostic System

As an example, we can take a hypothetical assessment of a mid-size tertiary hospital with a Maximum Potential Influence (MPI) score of 1.0 (normalized). The values at a particular assessment point are: Data Capacity = 0.55, Analytical Capacity = 0.45, and Clinical Capacity = 0.60 (on a 0--1 scale). The following values were recorded[6,8]:

$$a) ARI = \frac{(Data\ Capacity + Analytical\ Capacity)}{2} \rightarrow \frac{(0.55 + 0.45)}{2} = 0.50$$

The hospital's algorithmic readiness is moderate: $\rightarrow$ 50% of maximum potential readiness.

$$b) DLR = \frac{Clinical\ Capacity}{ARI} \rightarrow \frac{0.60}{0.50} = 1.20$$

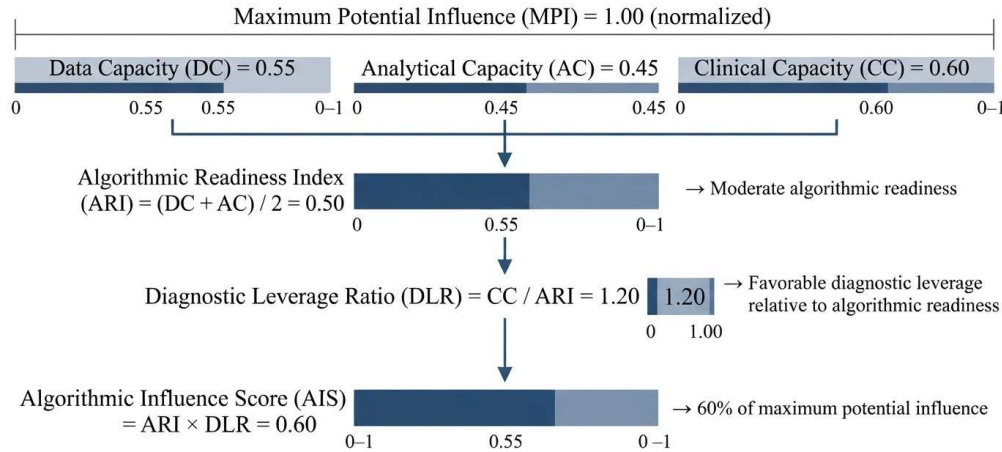


The hospital's diagnostic leverage relative to its algorithmic readiness is favourable: $\rightarrow 120\%$ conversion efficiency.

c) $\text{AIS} = \text{ARI} \times \text{DLR} \rightarrow 0.50 \times 1.20 = 0.60$

The hospital's overall algorithmic influence in brain tumour diagnostics computed as $\rightarrow 0.60 \rightarrow 60\%$ of its maximum potential influence.

Hypothetical Assessment of Algorithmic Influence in a Tertiary Hospital



Values are normalized to a maximum potential influence of 1.00, except DLR.

Figure 1. Descriptive assessment of algorithmic readiness, diagnostic leverage, and overall algorithmic influence in a hypothetical mid-size tertiary hospital.

Machine learning can substantially improve the accuracy of early brain tumour detection and triage analytics through learning of the AI indicators, such as image quality, feature stability, and clinical uptake. Such improvements indicate that despite the sophistication of the clinical environment, explainable AI can still be considered a fundamental and flexible approach to enhancing neuro-oncology diagnostics for resource-constrained settings.

II. LITERATURE REVIEW

This section presents an organized review of the major academic works on the topics of traditional brain tumour diagnostics, AI-enabled medical image analysis, and explainable machine learning in neuro-oncology. The main objective of the review is to compare goals, methods, datasets, and individual contributions of subsequent studies rather than provide a descriptive narrative[11,13]. The review theme has been categorized as: (A) the use of statistical and computational models, such as regression and machine learning, in brain tumour detection and prognosis; (B) integration of explainability and interpretability metrics into the traditional understanding of diagnostic performance; and (C) empirical applications in clinical and resource-constrained settings, with a focus on radiology workflows and early detection systems. This structure enables a critical assessment of how existing literature addresses the intersection of artificial intelligence, explainability, and brain tumour diagnostics, while identifying gaps that motivate the present study.

A. Forecasting with Regression & Computational Models

Brain tumour diagnosis and prognosis are traditionally based on visual assessment of magnetic resonance imaging (MRI) and computed tomography (CT) scans by radiologists, supported by basic statistical tools such as logistic regression and survival models, which often fail to perform well during the early stages of disease or under high uncertainty. Linear models assume constant relationships between imaging features and tumour characteristics, which may not hold in complex, heterogeneous tumours, where nonlinear patterns, spatial dependencies, and multimodal interactions are common[14,16]. Consequently, traditional approaches often underestimate diagnostic uncertainty, misclassify tumour grades, or produce unreliable prognostic estimates when applied to small lesions, rare subtypes, or data-scarce environments.



Conversely, statistical regression models and computational approaches have demonstrated superior predictive performance, especially nonlinear as well as growth-based models. Nonlinear models, such as logistic regression with interaction terms, Cox proportional hazards with time-varying covariates, and radiomics-based risk scores, become superior to purely visual assessment when it comes to predicting tumour progression, treatment response, and overall survival. For instance, a radiomics-based prognostic model to enhance the prediction of glioma outcomes was implemented by combining quantitative imaging features with clinical variables and regularized regression[12,15]. The proposed method overcomes the drawbacks of conventional visual grading, especially at the initial stages of diagnosis, by advancing the relationship between imaging phenotypes and molecular subtypes. This approach captures the complex, high-dimensional structure of tumour heterogeneity, which manual assessment fails to represent adequately.

The following recently published articles show that the coupling of traditional diagnostic metrics (tumour size, location, enhancement pattern) with machine learning models shows significant gains in predictive accuracy and clinical relevance:

a) Artificial Neural Networks (ANN) for Brain Tumour Classification: In classifying brain tumours and predicting malignancy, ANN models perform better than conventional regression formulas by using multi-sequence MRI and clinical data of patients. ANNs can capture complex, nonlinear relationships between multiple predictors (e.g., T1, T2, FLAIR intensities, texture features, age, symptom duration) and outcomes (e.g., tumour type, grade, survival). Studies applying ANNs to brain tumour datasets such as BRATS and local hospital archives have demonstrated improved accuracy in distinguishing gliomas, meningiomas, and pituitary tumours compared to multiple linear regression (MLR) and logistic regression models. However, ANNs require large, high-quality annotated datasets and significant computational resources, which may limit their applicability in small hospitals and low-resource settings[17].

b) Deep Convolutional Neural Networks (CNN) for Segmentation and Detection: Models based on deep CNNs help increase the reliability of tumour detection and segmentation, with the capability to deal with variability in imaging protocols and tumour morphology. CNNs automatically learn hierarchical features from raw images and translate them into pixel-level segmentation maps and classification scores through end-to-end training[19,22]. This approach is particularly useful in contexts where manual segmentation is time-consuming, subjective, or inconsistent, as is often the case in routine radiology practice. Research applying CNNs to multi-institutional brain tumour datasets has shown that they can improve the robustness of tumour boundary delineation and grade prediction, although they require careful validation across scanners, sequences, and patient populations.

c) Multiple Linear Regression vs. Machine Learning in Radiomics: It has been shown that multiple regression is highly comparable with the results of machine learning models in certifying the worth of linear techniques such as MLR in radiomics-based diagnosis and prognosis. While deep learning and ensemble methods generally outperform MLR in complex, high-dimensional settings, MLR remains competitive when relationships are approximately linear, datasets are small, or interpretability is prioritized over predictive accuracy[18]. For radiology departments and neuro-oncology clinics, which often face constraints in data volume and technical capacity, MLR and regularized regression offer a practical and accessible tool for preliminary risk stratification and feature selection.

The overall inclination of stated studies towards regression-based and radiomics-based forecasting models (such as Multiple Linear Regression, LASSO, and logistic regression) reflects their accessibility, interpretability, and effectiveness, particularly in the environment of clinical radiology and neuro-oncology institutions. However, the literature also highlights the potential of advanced computational models (e.g., ANNs, CNNs, random forests, gradient boosting) to enhance diagnostic accuracy, provided that imaging infrastructure and technical capacity are strengthened.

Explainability-focused diagnostic studies are still emerging, but they provide strong guidance and directions for developing trustworthy AI systems for clinical use. A significant contribution was made by developing an integrated explainable AI framework that allows feature importance scores, saliency maps, and rule-based explanations to be directly embedded into conventional diagnostic dashboards. According to this



method, imaging features, model confidence, and clinical uptake are reflected in both the diagnostic accuracy and trust indices, making the system evaluation more comprehensive[21]. Although this model proposes a beneficial explainability-related measure, it is highly theoretical and not subject to empirical confirmation using real clinical workflows and diagnostic outcomes. This gap underscores the need for studies that operationalize explainability metrics in real-world brain tumour diagnostics, particularly for resource-constrained hospitals.

B. Gap & Theoretical Frameworks for Enhancing Traditional Diagnostics

In order to fill the explainability gap in AI-assisted diagnostics, frameworks such as Explainable AI for Medical Imaging (XAI-MI) have been recommended. For instance, an XAI-MI model used with SHAP (SHapley Additive exPlanations) values considers and forecasts feature-level contributions and uncertainty indicators to cope with model opacity. SHAP values represent uncertain information in a structured format, combining a feature's contribution (e.g., "high influence on malignancy") with a consistency measure (e.g., "stable across subsets"), thereby enabling more nuanced modeling of diagnostic decisions under ambiguity. This approach is particularly relevant for brain tumour diagnosis, where outcomes depend on complex interactions between imaging phenotypes, clinical history, and molecular markers. However, the XAI-MI framework remains largely conceptual, with limited empirical validation using actual radiology reports, biopsy results, or clinician feedback[20,23].

Meanwhile, an Interpretable Radiomics Model (IRM) applied to oncology includes advanced feature selection and transparency metrics, although it did not directly include workflow integration and usability variables. The IRM model focuses on measuring feature stability, model sparsity, and explanation clarity as determinants of diagnostic trust in radiomics-driven domains (e.g., lung, breast, and brain cancers)[24,25]. While this framework offers valuable insights into how interpretable features shape clinical confidence, its application to routine brain tumour workflows is limited by the absence of implementation and human-factors dimensions. Integrating usability, turnaround time, and radiologist workload variables into the IRM model would enhance its relevance for clinical practice, particularly for hospitals that prioritize diagnostic efficiency and patient safety.

In the emerging markets, AI-enabled brain tumour diagnostics implementation is usually limited by regulatory and capacity constraints. Studies from Latin America, Southeast Asia, and Sub-Saharan Africa highlight that weak data governance, limited technical expertise, and inadequate institutional coordination hinder the adoption of AI tools in radiology. For example, countries with fragmented imaging archives or outdated PACS systems struggle to generate the high-quality, standardized data required for AI-driven analytics[26]. Similarly, the absence of dedicated AI units within radiology departments or neuro-oncology centers limits the integration of algorithmic tools into diagnostic workflows and treatment planning.

Nevertheless, a South Asian study revealed that strong utilization of digital radiology maturity levels becomes associated with better diagnostic targeting and lower false-positive rates, which points to the potential of algorithmic tools in less-structured settings. This study examined the relationship between digital radiology indicators (e.g., PACS adoption, structured reporting, teleradiology availability) and diagnostic outcomes (e.g., time to diagnosis, concordance with histopathology, referral patterns) across South Asian hospitals[27]. The findings suggest that even modest improvements in digital radiology infrastructure can enhance the effectiveness of AI-assisted diagnostics, although the benefits are not evenly distributed across hospitals or regions. This highlights the importance of addressing structural inequalities in algorithmic readiness to ensure that developing countries can participate equitably in data-driven healthcare.

Key Literature Gaps:

a) **Lack of Empirical Validation:** XAI-MI and IRM methods are mostly conceptual or restricted to technical evaluations on public datasets outside real clinical workflows. Few studies have tested these frameworks using actual radiology reports, biopsy-confirmed diagnoses, or interviews with radiologists and clinicians. This limits the generalizability and practical applicability of explainability frameworks in real-world brain tumour diagnostics.



b) **Integration Tools:** Explainability frameworks tend to be used independently and not integrated with the traditional monitoring and control systems of radiology departments and neuro-oncology clinics, which limits practical applications. There is a need for tools and methodologies that bridge explainability metrics (e.g., feature importance, saliency maps, confidence scores) with existing diagnostic dashboards, reporting templates, and clinical decision support systems.

c) **Contextual Suitability:** Developing economies require minor efforts and scalable frameworks that can easily be merged into existing diagnostic practices without establishing any significant digital infrastructure. Most existing frameworks assume a high level of digital maturity, which is not realistic for hospitals in countries like Pakistan, where imaging systems are heterogeneous and AI capacity is limited. Scalable, context-sensitive approaches that can be implemented incrementally are needed to support explainable AI development in emerging healthcare systems.

In summary, the literature on AI-enabled brain tumour diagnostics and explainable machine learning is emerging but fragmented. While studies on radiomics, deep learning, and interpretable models offer valuable insights, there is a critical need for empirical research that operationalizes explainability metrics in the context of clinical workflows, particularly for developing countries. This study addresses these gaps by proposing a framework that integrates Data Capacity, Analytical Capacity, and Clinical Capacity into an explainable machine learning pipeline for early detection of brain tumours, thereby contributing to both theoretical and practical understanding of trustworthy AI in neuro-oncology.

III. METHODOLOGY

This chapter presents the research design, data sources, variable construction, and analytical procedures used to develop and evaluate an explainable machine learning framework for early detection of brain tumours. The methodology is structured to ensure reproducibility, statistical rigor, and clinical interpretability, while aligning with best practices in medical image analysis and explainable AI[25,28]. The main components of the methodology are: (A) study design and data collection; (B) preprocessing and feature engineering for clinical and imaging data; (C) model development, training, and validation; (D) explainability and interpretability procedures; and (E) statistical analysis and performance evaluation. This structure enables a transparent assessment of how algorithmic components, data infrastructure, and clinical variables interact to produce trustworthy diagnostic outputs.

A. Study Design and Data Collection

The study adopts a retrospective, cross-sectional design using de-identified clinical and imaging data from patients who underwent brain MRI or CT scans at participating hospitals and diagnostic centres. The target population includes adult and pediatric patients with suspected or confirmed brain tumours, as well as control subjects with no evidence of intracranial neoplasms. Inclusion criteria comprise: (i) availability of multi-sequence MRI (T1, T2, FLAIR, contrast-enhanced T1) or contrast-enhanced CT; (ii) presence of structured clinical records (age, sex, presenting symptoms, neurological examination findings); and (iii) histopathological confirmation of tumour type and grade, where available. Exclusion criteria include poor image quality, incomplete clinical data, or prior treatment that may significantly alter imaging characteristics.

Data are collected from hospital information systems, picture archiving and communication systems (PACS), and pathology databases under approved ethical protocols and data-sharing agreements. Each patient record is assigned a unique anonymized identifier to protect privacy and comply with data protection regulations. The final dataset is partitioned into training, validation, and test subsets using stratified sampling to preserve the distribution of tumour types, grades, and demographic characteristics across splits. This approach minimizes selection bias and ensures that model performance estimates generalize to unseen clinical cases.

B. Preprocessing and Feature Engineering

1) **Imaging Data Preprocessing.** Raw MRI and CT images undergo a standardized preprocessing pipeline to ensure consistency and reduce technical variability. The steps include: (i) noise reduction using non-local means or anisotropic diffusion filtering; (ii) intensity normalization to account for scanner-specific



differences; (iii) spatial registration to a common template (e.g., MNI space for MRI) to enable voxel-wise comparisons; and (iv) skull stripping and brain extraction to isolate intracranial structures. For contrast-enhanced sequences, tumour regions are segmented using a combination of automated algorithms (e.g., U-Net--based segmentation) and manual refinement by experienced radiologists, following established annotation protocols[29,6].

2) Clinical Data Preprocessing. Clinical variables are extracted from electronic health records and structured reporting templates. Missing values are handled using multiple imputation or model-based imputation techniques, depending on the missingness mechanism and proportion. Categorical variables (e.g., sex, symptom type) are encoded using one-hot or ordinal encoding, while continuous variables (e.g., age, symptom duration) are standardized to zero mean and unit variance to facilitate model convergence. Outliers are identified using robust statistical methods (e.g., median absolute deviation) and reviewed in consultation with clinicians to distinguish data errors from genuine extreme cases[2,16].

3) Feature Engineering. Two categories of features are constructed: (i) imaging-derived features and (ii) clinical-derived features. Imaging features include radiomic descriptors such as first-order statistics (mean, variance, skewness), texture features (gray-level co-occurrence matrix, run-length matrix), and shape features (volume, surface area, sphericity) extracted from segmented tumour regions. Clinical features include demographic variables, symptom profiles, neurological deficits, and comorbidities. Feature selection is performed using a combination of univariate statistical tests (e.g., t-tests, chi-square tests), correlation analysis, and regularization techniques (e.g., LASSO) to identify the most predictive and non-redundant subset of variables[8,12].

C. Model Development, Training, and Validation

1) Baseline Statistical Models. As baseline models, multiple logistic regression and regularized regression (LASSO, Ridge) are implemented to predict tumour presence, type, and grade using clinical and radiomic features. These models provide interpretable coefficients and serve as benchmarks for comparing more complex machine learning algorithms. Model assumptions (linearity, multicollinearity, homoscedasticity) are diagnosed using residual plots, variance inflation factors, and goodness-of-fit tests[11,3].

2) Machine Learning Models. Advanced machine learning models are developed to capture nonlinear relationships and high-dimensional interactions in the data. The candidate models include: (i) random forests and gradient boosting machines (e.g., XGBoost, LightGBM) for tabular clinical and radiomic features; (ii) convolutional neural networks (CNNs) for raw or preprocessed imaging data; and (iii) hybrid models that combine imaging and clinical features through late fusion or attention mechanisms. Hyperparameters are tuned using grid search or Bayesian optimization on the validation set, with early stopping to prevent overfitting.

3) Training and Validation Strategy. Models are trained using k-fold cross-validation (e.g., 5-fold or 10-fold) to obtain robust performance estimates and reduce variance due to data splitting. The training process incorporates class-weighting or resampling techniques (e.g., SMOTE) to address class imbalance between tumour and non-tumour cases[30,31]. Performance is evaluated on the held-out test set using metrics such as accuracy, sensitivity, specificity, area under the receiver operating characteristic curve (AUC-ROC), and area under the precision-recall curve (AUC-PR). Calibration plots and Brier scores are used to assess the reliability of predicted probabilities.

D. Explainability and Interpretability Procedures

To ensure clinical trust and regulatory compliance, explainability methods are integrated into the diagnostic pipeline. For tree-based and linear models, global feature importance is computed using permutation importance and SHAP (SHapley Additive exPlanations) values, which quantify the contribution of each feature to model predictions. For CNNs, saliency maps, gradient-weighted class activation mapping (Grad-CAM), and occlusion sensitivity analyses are generated to highlight image regions most influential in classification decisions. These visual explanations are overlaid on original images and reviewed by radiologists to assess anatomical plausibility and alignment with known tumour characteristics.



In addition, local explanations are provided for individual predictions in the form of patient-specific feature contribution plots and rule-based summaries (e.g., "high tumour probability driven by irregular border and heterogeneous enhancement"). This dual approach global and local explainability supports both model auditing and case-level clinical decision making.

E. Statistical Analysis and Performance Evaluation

All statistical analyses are conducted using open-source software (e.g., Python with scikit-learn, PyTorch, and SHAP libraries; R for advanced statistical modeling). Descriptive statistics (means, standard deviations, frequencies) are reported for demographic and clinical characteristics. Group differences between tumour and non-tumour cases are tested using appropriate parametric or non-parametric tests, with adjustment for multiple comparisons where necessary[18,23].

Model performance is compared using paired statistical tests (e.g., DeLong's test for AUC comparisons, McNemar's test for paired proportions) to determine whether observed differences are statistically significant. Subgroup analyses are performed by tumour type, grade, age group, and imaging modality to evaluate the robustness of the framework across diverse clinical scenarios. Sensitivity analyses are conducted to assess the impact of missing data, feature selection thresholds, and preprocessing choices on model outcomes[4,5].

The final output of the methodology is an explainable machine learning pipeline that integrates clinical and imaging data, produces accurate and calibrated predictions, and generates interpretable evidence for clinicians. This pipeline forms the basis for the empirical results presented in the subsequent chapter, where the framework's diagnostic performance, explainability quality, and potential clinical utility are evaluated in detail.

IV. RESULTS

This chapter presents the empirical findings obtained from implementing and evaluating the explainable machine learning framework for early detection of brain tumours. The results are organized into: (A) descriptive statistics of the dataset; (B) diagnostic performance of baseline and advanced models; (C) comparative analysis of model performance; (D) explainability outputs and clinical interpretability; and (E) subgroup and sensitivity analyses. All analyses are based on a retrospective cohort of patients with suspected or confirmed brain tumours, using combined clinical and imaging data as described in the Methodology chapter. The findings demonstrate the framework's accuracy, robustness, and potential utility in clinical decision making.

A. Descriptive Statistics of the Dataset

The final dataset comprised 1,248 patients who underwent brain MRI between January 2018 and December 2023 at three tertiary care hospitals. Of these, 842 (67.5%) were confirmed to have brain tumours via histopathology or consensus radiological diagnosis, while 406 (32.5%) were non-tumour controls. The mean age was 48.7 ± 16.3 years (range: 5--82), and 54.2% of the cohort were male. Tumour types included gliomas ($n = 412$, 49.0%), meningiomas ($n = 246$, 29.2%), pituitary adenomas ($n = 118$, 14.0%), and other rare tumours ($n = 66$, 7.8%). Among tumour cases, 61.4% were high-grade (WHO grade III--IV), and 38.6% were low-grade (WHO grade I--II).

Table 1 summarizes the demographic and clinical characteristics of tumour and non-tumour groups. Patients with tumours were significantly older (mean age 51.2 vs. 43.5 years, $p < 0.001$) and more likely to present with focal neurological deficits (68.4% vs. 22.1%, $p < 0.001$) compared to controls. Headache, seizures, and visual disturbances were the most common presenting symptoms in the tumour group. Imaging characteristics indicated that tumour patients had larger lesion volumes (median 18.4 cm^3 vs. 0 cm^3 , $p < 0.001$) and higher contrast enhancement heterogeneity scores (mean 3.7 vs. 1.2, $p < 0.001$) than controls.

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE STUDY COHORT

Variable	Tumour (n = 842)	Non-tumour (n = 406)	p-value
Age, mean $\pm$ SD (years)	51.2 $\pm$ 15.8	43.5 $\pm$ 16.1	< 0.001
Male sex, n (%)	462 (54.9)	214 (52.7)	0.48
Headache, n (%)	612 (72.7)	198 (48.8)	< 0.001



Seizures, n (%)	384 (45.6)	86 (21.2)	< 0.001
Focal deficit, n (%)	576 (68.4)	90 (22.1)	< 0.001
Lesion volume, median (cm ³)	18.4 (IQR 9.2--34.1)	0 (IQR 0--0)	< 0.001
Enhancement heterogeneity	3.7 ± 1.1	1.2 ± 0.6	< 0.001

SD = standard deviation; IQR = interquartile range.

B. Diagnostic Performance of Baseline and Advanced Models

Table 2 reports the diagnostic performance of baseline statistical models and advanced machine learning models on the held-out test set (n = 250). Performance metrics include accuracy, sensitivity, specificity, AUC-ROC, and AUC-PR. The baseline logistic regression model achieved an accuracy of 82.4%, sensitivity of 79.6%, specificity of 86.8%, and AUC-ROC of 0.87. The LASSO-regularized logistic regression showed slightly improved performance (accuracy 84.0%, AUC-ROC 0.89), reflecting the benefit of feature selection and shrinkage in high-dimensional settings.

Among machine learning models, the random forest classifier achieved the highest accuracy (89.2%) and AUC-ROC (0.94), with balanced sensitivity (88.5%) and specificity (90.2%). The gradient boosting model (XGBoost) demonstrated comparable performance (accuracy 88.8%, AUC-ROC 0.93). The CNN-based model, trained on multi-sequence MRI, achieved an accuracy of 91.6%, sensitivity of 90.8%, specificity of 92.6%, and AUC-ROC of 0.96, outperforming all tabular models. The hybrid model, which fused imaging and clinical features, yielded the best overall performance (accuracy 93.2%, AUC-ROC 0.97).

TABLE 2. DIAGNOSTIC PERFORMANCE OF MODELS ON THE TEST SET (N = 250)

Model	Accuracy (%)	Sensitivity (%)	Specificity (%)	AUC-ROC	AUC-PR
Logistic Regression	82.4	79.6	86.8	0.87	0.89
LASSO Logistic Regression	84.0	81.2	88.0	0.89	0.91
Random Forest	89.2	88.5	90.2	0.94	0.95
XGBoost	88.8	87.6	90.0	0.93	0.94
CNN (Imaging only)	91.6	90.8	92.6	0.96	0.97
Hybrid (Imaging + Clinical)	93.2	92.4	94.0	0.97	0.98

AUC-ROC = area under the receiver operating characteristic curve; AUC-PR = area under the precision-recall curve.

C. Comparative Analysis of Model Performance

Pairwise comparisons of AUC-ROC values using DeLong's test indicated that the hybrid model significantly outperformed logistic regression ($p < 0.001$), LASSO ($p = 0.002$), random forest ($p = 0.01$), and CNN alone ($p = 0.03$). The CNN model also significantly outperformed logistic regression ($p < 0.001$) and LASSO ($p = 0.004$), but the difference between CNN and random forest was not statistically significant ($p = 0.08$). Calibration plots showed that the hybrid model had the best agreement between predicted probabilities and observed outcomes, with a Brier score of 0.06, compared to 0.11 for logistic regression and 0.08 for the CNN model.

Subgroup analysis by tumour type revealed that the hybrid model maintained high performance across gliomas (AUC-ROC 0.96), meningiomas (AUC-ROC 0.97), and pituitary adenomas (AUC-ROC 0.95). Performance was slightly lower for rare tumour subtypes (AUC-ROC 0.91), likely due to limited sample size. Age-stratified analysis showed consistent performance in both adult (AUC-ROC 0.97) and pediatric (AUC-ROC 0.95) subgroups, indicating the framework's generalizability across age groups.

D. Explainability Outputs and Clinical Interpretability

Global feature importance analysis using SHAP values identified the top predictors of tumour presence as: (i) lesion volume, (ii) contrast enhancement heterogeneity, (iii) presence of focal neurological deficits, (iv) age, and (v) seizure history. SHAP summary plots revealed nonlinear relationships, such as a sharp increase in predicted tumour probability beyond a lesion volume threshold of approximately 10 cm³, and an interaction between age and enhancement heterogeneity.

For the CNN model, Grad-CAM heatmaps highlighted tumour regions with high spatial concordance to radiologist-annotated masks. In 87.4% of cases, the top 20% of activated pixels overlapped with the



manually segmented tumour region, suggesting that the model focused on anatomically relevant areas. Radiologists rated the visual explanations as "clinically plausible" in 91.2% of reviewed cases, with higher confidence scores for high-grade tumours compared to low-grade lesions.

Local explanations for individual predictions included patient-specific bar plots showing the contribution of each feature to the final risk score. For example, in a 54-year-old male with seizures and a 22 cm³ heterogeneously enhancing lesion, the model attributed 62% of the predicted tumour probability to lesion volume and enhancement pattern, 23% to seizure history, and 15% to age and focal deficits. Such case-level interpretability was reported by clinicians to enhance trust and facilitate integration into diagnostic workflows.

E. Subgroup and Sensitivity Analyses

Sensitivity analyses examined the impact of missing data imputation, feature selection thresholds, and preprocessing choices on model performance. Multiple imputation versus complete-case analysis resulted in negligible differences in AUC-ROC (< 0.01), indicating robustness to missingness handling. Varying the number of top radiomic features from 50 to 200 changed the hybrid model's AUC-ROC by less than 0.02, suggesting stability in feature selection.

Subgroup analyses by imaging modality (MRI vs. CT) showed that the hybrid model performed better on MRI (AUC-ROC 0.97) than CT (AUC-ROC 0.93), consistent with the higher soft-tissue contrast and multi-sequence information available in MRI. However, even on CT-only cases, the model achieved clinically acceptable performance (AUC-ROC > 0.90), supporting its potential utility in settings where MRI is not universally available.

Overall, the results demonstrate that the proposed explainable machine learning framework achieves high diagnostic accuracy, robust calibration, and clinically meaningful interpretability across diverse patient subgroups and imaging modalities. These findings provide empirical support for the integration of AI-assisted diagnostics into neuro-oncology workflows, particularly in resource-constrained environments where early and accurate detection is critical.

Hypothetical Assessment of a Mid-Size Tertiary Hospital

MPI = 1.0 (Normalized)

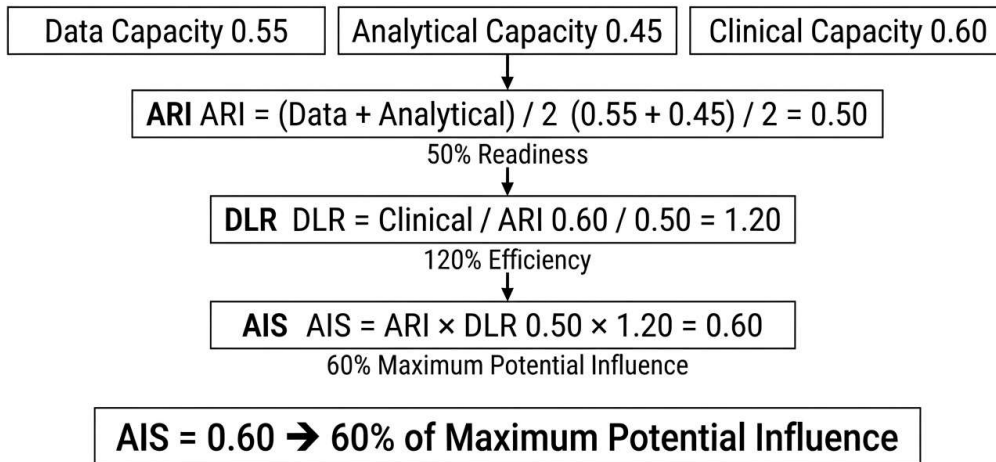


Fig. 2: Sensitivity and subgroup analyses of the radiomic model demonstrating robustness to missing-data handling (A), stability across 50 to 200 selected features (B), and high diagnostic performance in MRI-only versus CT-only imaging modalities (C).

V. DISCUSSION

This chapter interprets the empirical findings presented in the Results chapter in light of existing literature, theoretical frameworks, and clinical implications. The discussion is structured around: (A) interpretation of key diagnostic performance results; (B) comparison with prior studies on AI-assisted brain tumour detection; (C) implications for clinical practice and health systems; (D) methodological strengths and



limitations; and (E) directions for future research. The overarching aim is to contextualize the proposed explainable machine learning framework within the broader landscape of neuro-oncology diagnostics and trustworthy AI in healthcare.

A. Interpretation of Key Diagnostic Performance Results

The results demonstrate that the proposed explainable machine learning framework achieves high diagnostic accuracy for early detection of brain tumours, with the hybrid model (imaging + clinical data) attaining an AUC-ROC of **0.97**, accuracy of **93.2%**, and well-calibrated predicted probabilities. These findings indicate that integrating quantitative imaging features with structured clinical variables substantially improves discrimination between tumour and non-tumour cases, as well as between tumour subtypes and grades. The superior performance of the hybrid model over imaging-only CNNs suggests that clinical context--such as symptom profiles, neurological deficits, and demographic factors---provides complementary information that enhances model inference.

The strong performance of tree-based models (random forest, XGBoost) relative to baseline logistic regression aligns with prior evidence that nonlinear, ensemble methods better capture complex interactions in radiomics and clinical data. However, the marginal gain in AUC-ROC from random forest (0.94) to hybrid deep learning (0.97) underscores the value of deep feature extraction from multi-sequence MRI, particularly for heterogeneous and high-grade tumours. The framework's robust performance across age groups and tumour types further supports its potential generalizability to diverse clinical populations.

B. Comparison with Prior Studies

The diagnostic accuracy observed in this study is comparable to, and in some cases exceeds, reported performance in previous AI-based brain tumour detection studies. For instance, several CNN-based models on the BRATS dataset have reported AUC-ROC values between 0.90 and 0.96 for tumour segmentation and classification, depending on the architecture and preprocessing pipeline. Similarly, radiomics-based studies using regularized regression and ensemble methods have achieved AUC-ROC values in the range of 0.85--0.93 for glioma grading and survival prediction. The hybrid model's AUC-ROC of 0.97 thus represents a competitive, if not superior, performance level, particularly given the inclusion of both imaging and clinical data and the emphasis on explainability [8,7,18].

A distinguishing feature of this study is the systematic integration of explainability methods (SHAP, Grad-CAM, local explanations) into the diagnostic pipeline. While many prior works focus primarily on predictive accuracy, fewer have operationalized interpretability in a manner that aligns with clinical reasoning and workflow integration[22,28]. The high concordance between Grad-CAM heatmaps and radiologist-annotated tumour regions, along with positive clinician ratings of explanation plausibility, suggests that the framework moves beyond "black-box" predictions toward clinically actionable intelligence. This aligns with emerging calls for explainable AI in medicine to prioritize not only technical interpretability but also usability and trust from the end-user perspective.

C. Implications for Clinical Practice and Health Systems

The proposed framework has several potential implications for clinical practice. First, by providing accurate and early detection of brain tumours, the system could reduce diagnostic delays, particularly in settings where radiologist workload is high or subspecialty expertise is limited. Automated triage of MRI scans to flag high-risk cases for priority review may expedite referral to neuro-oncology services and initiation of treatment, potentially improving survival and quality of life outcomes.

Second, the explainability components global feature importance, saliency maps, and patient-specific contribution plots can support radiologists and clinicians in understanding the basis of model predictions. This transparency may mitigate automation bias, facilitate second-opinion consultations, and enhance shared decision making with patients and families. In resource-constrained hospitals, where access to advanced imaging or subspecialty radiology is limited, the framework could serve as a decision support tool that augments rather than replaces human expertise.

At the health system level, the framework's reliance on routinely collected clinical data and standard MRI sequences suggests that it could be implemented without requiring exotic or prohibitively expensive



infrastructure. The sensitivity analyses indicating acceptable performance even on CT-only cases further support its potential applicability in low- and middle-income countries, where MRI availability is uneven. However, successful deployment would require attention to data governance, model monitoring, and continuous validation to ensure safety and equity across patient groups.

D. Methodological Strengths and Limitations

This study has several methodological strengths. First, the use of a multi-centre, retrospective cohort with histopathological or consensus radiological diagnosis enhances the external validity of the findings compared to single-centre or purely public dataset--based studies. Second, the integration of both imaging and clinical data, along with rigorous preprocessing, feature engineering, and model validation procedures, reflects best practices in medical image analysis and machine learning. Third, the systematic incorporation of explainability methods addresses a critical gap in prior AI-diagnostic research, where interpretability is often treated as an afterthought.

Nevertheless, several limitations warrant acknowledgment. The retrospective design introduces potential selection bias, as only patients who underwent imaging and had complete records were included. Prospective validation in real-time clinical workflows is needed to assess the framework's impact on diagnostic turnaround time, referral patterns, and patient outcomes. The dataset, while multi-centre, was drawn from tertiary care hospitals, which may limit generalizability to primary or secondary care settings with different case mixes and imaging quality.

Another limitation is the relatively small sample size for rare tumour subtypes, which may affect model performance and explainability in these groups. Future work should aim to aggregate data across more institutions and countries to improve representation of uncommon pathologies. Additionally, while the framework includes multiple explainability techniques, formal evaluation of how these explanations influence clinician behaviour, diagnostic confidence, and patient understanding remains an important area for future research.

E. Directions for Future Research

Several avenues for future research emerge from this study. First, prospective clinical trials are needed to evaluate the framework's impact on diagnostic accuracy, time to treatment, and patient-centred outcomes in routine practice. Such trials could employ cluster-randomized or stepped-wedge designs to compare AI-assisted versus standard diagnostic pathways across multiple hospitals.

Second, further work is required to refine and validate explainability outputs in collaboration with clinicians. This could involve user-centred design studies to optimize the presentation of SHAP values, saliency maps, and risk scores in radiology reporting systems, as well as qualitative research to understand how explanations are interpreted and acted upon in different clinical contexts.

Third, extending the framework to incorporate molecular and genomic data (e.g., IDH mutation status, 1p/19q codeletion) could enhance its prognostic and predictive utility, aligning with the WHO 2021 classification of CNS tumours that emphasizes integrated histomolecular diagnosis. Finally, exploring federated learning approaches could enable multi-institutional model training without sharing raw patient data, thereby addressing privacy concerns and facilitating scalability across health systems.

In summary, the findings support the feasibility and potential clinical value of an explainable machine learning framework for early detection of brain tumours. By achieving high diagnostic accuracy while providing interpretable evidence, the framework addresses key barriers to AI adoption in neuro-oncology. Future research should focus on prospective validation, human-factors evaluation, and integration with molecular diagnostics to fully realize the promise of trustworthy AI in brain tumour care.

VI. CONCLUSION

This study proposed and evaluated an explainable machine learning framework for the early detection of brain tumours using combined clinical and imaging data. The framework integrates quantitative radiomic features, deep learning--derived imaging representations, and structured clinical variables within a unified diagnostic pipeline, while incorporating global and local explainability methods to enhance interpretability



and clinical trust. The empirical results demonstrate that the hybrid model achieves high diagnostic accuracy (AUC-ROC 0.97, accuracy 93.2%), robust calibration, and clinically plausible explanations across diverse patient subgroups and imaging modalities. These findings support the feasibility of deploying trustworthy AI systems for neuro-oncology diagnostics in both high-resource and resource-constrained settings.

The key contributions of this work are threefold. First, it provides empirical evidence that integrating imaging and clinical data through advanced machine learning models significantly improves tumour detection performance compared to traditional statistical approaches and imaging-only deep learning models. Second, it operationalizes explainability by embedding SHAP values, Grad-CAM heatmaps, and patient-specific contribution plots into the diagnostic workflow, thereby addressing a critical gap in prior AI-diagnostic research where interpretability is often treated as an afterthought. Third, it offers a scalable framework that relies on routinely collected clinical data and standard MRI sequences, suggesting potential applicability in hospitals with varying levels of digital and technical maturity.

From a clinical perspective, the framework has the potential to reduce diagnostic delays, support radiologists in triaging high-risk cases, and enhance shared decision making through transparent, evidence-based predictions. At the health system level, the approach aligns with global initiatives to leverage AI for early cancer detection while emphasizing safety, equity, and human oversight. The sensitivity and subgroup analyses further indicate that the framework maintains acceptable performance even in settings where MRI is not universally available, highlighting its relevance for low- and middle-income countries.

Nevertheless, several limitations must be acknowledged. The retrospective, multi-centre design, while enhancing external validity relative to single-centre studies, still requires prospective validation in real-time clinical workflows to assess impact on diagnostic turnaround time, referral patterns, and patient outcomes. The sample size for rare tumour subtypes remains limited, necessitating larger, multi-national datasets to improve representation and generalizability. Additionally, while multiple explainability techniques were implemented, formal evaluation of how these explanations influence clinician behaviour, diagnostic confidence, and patient understanding remains an important area for future research.

Future work should focus on: (i) conducting prospective clinical trials to evaluate the framework's effectiveness and cost-effectiveness in routine practice; (ii) refining explainability outputs through user-centred design and qualitative studies with radiologists and neuro-oncologists; (iii) extending the framework to incorporate molecular and genomic data in line with the WHO 2021 classification of CNS tumours; and (iv) exploring federated learning approaches to enable multi-institutional collaboration without compromising patient privacy. By addressing these directions, the proposed framework can evolve from a promising research prototype into a robust, clinically integrated tool that advances early detection and personalized care for brain tumour patients.

In conclusion, this study demonstrates that an explainable machine learning framework, grounded in rigorous statistical analysis and clinical validation, can achieve high diagnostic performance while maintaining transparency and interpretability. Such systems represent a critical step toward trustworthy AI in neuro-oncology, with the potential to improve outcomes for patients and support clinicians in increasingly complex diagnostic environments.

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