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ARTIFICIAL INTELLIGENCE IN NEUROIMAGING OF GLIOMAS:  
CURRENT APPLICATIONS, CLINICAL VALUE AND CHALLENGES

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# ARTIFICIAL INTELLIGENCE IN NEUROIMAGING OF GLIOMAS: CURRENT APPLICATIONS, CLINICAL VALUE AND CHALLENGES

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**ABSTRACT**

**Introduction and purpose:** Gliomas represent a heterogeneous group of primary central nervous system tumors that pose substantial diagnostic challenges and are associated with highly variable clinical outcomes. Magnetic resonance imaging (MRI) plays a central role in the evaluation of gliomas, however, conventional image interpretation provides limited insight into tumor biology and prognostic stratification. Recent methodological advances in artificial intelligence, including machine learning and deep learning techniques, have enabled more advanced analysis of complex neuroimaging data and the extraction of clinically relevant information. This review summarizes and critically analyzes current AI applications in glioma neuroimaging, focusing on image enhancement, tumor segmentation, grading and classification, molecular characterization, and outcome prediction.

**Methodology:** This narrative review synthesizes recent literature on AI-based neuroimaging analysis in glioma, focusing on machine learning and deep learning approaches applied to MRI and advanced imaging modalities, including diffusion MRI, sodium MRI, and multimodal imaging. Selected clinical contexts, such as pediatric gliomas and diffuse midline gliomas, are also discussed.

**Results:** Across multiple retrospective cohorts and benchmark datasets, AI-based methods have consistently achieved high diagnostic and predictive performance. These methods show potential to improve tumor characterization, noninvasive molecular assessment, and prognostic modeling, although clinical translation remains limited.

**Conclusions:** Artificial intelligence is increasingly recognized as a complementary approach to conventional neuro-oncological imaging. However, major challenges persist, including data heterogeneity, limited external and prospective validation, insufficient model interpretability, and difficulties in clinical workflow integration. Future research should emphasize standardized reporting, multi-center validation, and explainable AI to enable safe and clinically meaningful implementation.

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**KEYWORDS**

Artificial Intelligence, Glioma, Magnetic Resonance Imaging, Radiomics, Deep Learning, Neuro-Oncology

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**1. Introduction**

Gliomas constitute the most common primary malignant tumors of the central nervous system and remain a major cause of neurological morbidity and mortality worldwide (Brown et al., 2025; Ahangari et al., 2025). Despite advances in neurosurgery, radiotherapy, and systemic treatments, the prognosis of high-grade gliomas—particularly glioblastoma—remains poor, with median survival measured in months rather than years (Fares et al., 2025). One of the fundamental challenges in glioma management is the pronounced biological heterogeneity observed both between and within tumors, which underlies variable treatment responses and clinical outcomes (Wang et al., 2025; Fares et al., 2025). Magnetic resonance imaging (MRI) is the imaging modality of choice for the evaluation of suspected gliomas and plays a central role throughout the patient pathway, from initial diagnosis to treatment planning and longitudinal monitoring (Ahangari et al., 2025; Brown et al., 2025). Conventional MRI sequences, including T1-weighted, contrast-enhanced T1-weighted, T2-weighted, and fluid-attenuated inversion recovery (FLAIR) imaging, provide essential anatomical and pathological information. However, traditional radiological interpretation is largely qualitative and subject to interobserver variability, particularly in infiltrative or treatment-altered tumors (Wang et al., 2025). Moreover, conventional MRI has limited ability to capture tumor microstructure, metabolic activity, and molecular characteristics that are now recognized as critical determinants of prognosis and therapeutic decision-making (Fares et al., 2025; Ahangari et al., 2025). The evolving classification of gliomas, increasingly based on molecular and genetic features such as isocitrate dehydrogenase (IDH) mutation status, 1p/19q

codeletion, and transcriptomic subtypes, has further highlighted the limitations of standard imaging approaches (Wang et al., 2025; Fares et al., 2025). While tissue sampling remains the reference standard for molecular characterization, biopsy procedures are invasive, may be associated with complications, and can suffer from sampling bias due to intratumoral heterogeneity (Ahangari et al., 2025). Consequently, there is a growing interest in developing noninvasive imaging-based methods capable of providing biologically meaningful insights into tumor behavior and molecular status (Brown et al., 2025; Wang et al., 2025). Artificial intelligence (AI), encompassing machine learning (ML) and deep learning (DL) techniques, has rapidly emerged as a promising approach to address these challenges. By leveraging the high-dimensional nature of neuroimaging data, AI algorithms can identify complex spatial and textural patterns that are imperceptible to the human eye and integrate information across multiple imaging modalities (Brown et al., 2025; Fares et al., 2025). Convolutional neural networks, radiomics-based ML models, and hybrid frameworks combining imaging with clinical and molecular data have demonstrated impressive performance in retrospective studies, particularly in tasks such as tumor segmentation, grading, and molecular status prediction (Pourmahboubi et al., 2025; Ilani et al., 2025; Wang et al., 2025). Beyond task-specific models, recent developments in representation learning and foundation models aim to create generalizable imaging embeddings that can be reused across multiple clinical tasks, potentially reducing the need for large task-specific datasets (Barba et al., 2025). Similarly, advances in modality-agnostic learning seek to address real-world challenges such as missing imaging sequences and heterogeneous acquisition protocols, which often limit the generalizability of AI models trained on curated research datasets (Lteif et al., 2025). Despite encouraging methodological results, the implementation of AI-based tools in routine clinical workflows remains constrained by heterogeneous data sources, insufficient external validation and challenges related to model interpretability. Many published studies rely on retrospective single-center datasets, lack external validation, or do not adequately address issues of interpretability, robustness, and clinical integration (Brown et al., 2025; Wang et al., 2025; Ahangari et al., 2025). As a result, there is a critical need for comprehensive reviews that not only summarize current methodological advances but also critically appraise their clinical relevance and readiness for implementation. The aim of this review is to provide an in-depth overview of contemporary AI applications in glioma neuroimaging, with a focus on clinically relevant tasks, methodological innovations, and persistent challenges. By synthesizing evidence across imaging modalities, tumor subtypes, and patient populations, this review seeks to clarify the current state of the field and outline future directions toward clinically meaningful AI-assisted neuro-oncology.

## 2. Methodology

This review was designed as a narrative synthesis of the current literature on artificial intelligence applications in glioma neuroimaging. A structured literature search was conducted using PubMed and related biomedical databases to identify peer-reviewed articles focusing on the use of machine learning and deep learning techniques in the analysis of neuroimaging data from glioma patients. Inclusion criteria comprised original research articles and review papers that applied AI-based methods to neuroimaging modalities relevant to glioma assessment, including conventional MRI, advanced MRI techniques such as diffusion-weighted and perfusion imaging, computed tomography (CT), positron emission tomography (PET), and multinuclear MRI (Raymond et al., 2025; Bilgin et al., 2025; Gallotti et al., 2025). Studies were required to clearly describe their AI methodology, imaging data sources, and clinical objectives. Articles focusing exclusively on non-imaging data or lacking sufficient methodological detail were excluded. Given the substantial heterogeneity across studies in terms of imaging protocols, AI architectures, datasets, and evaluation metrics, a quantitative meta-analysis was not feasible. Instead, a qualitative narrative synthesis was performed, grouping studies according to their primary clinical task, such as image enhancement, tumor segmentation, grading and classification, molecular characterization, or prognostic modeling (Wang et al., 2025; Brown et al., 2025). Special attention was given to studies addressing real-world clinical challenges, including limited data availability, missing imaging modalities, and external validation across independent cohorts (Lteif et al., 2025; Barba et al., 2025).

### 3. Results

#### 3.1. Image Quality Enhancement in Glioma Neuroimaging

Advanced neuroimaging techniques provide valuable insights into tumor microstructure, metabolism, and physiology; however, their clinical utility is often constrained by technical limitations. In particular, specialized MRI modalities such as sodium imaging, diffusion-based techniques, or spectroscopic imaging suffer from reduced spatial resolution, low signal-to-noise ratio (SNR), prolonged acquisition times, and limited availability in routine clinical settings (Raymond et al., 2025; Fares et al., 2025). These constraints have historically restricted their use to research environments and small patient cohorts, limiting their translational impact. Recent advances in artificial intelligence, especially deep generative models, have introduced novel strategies for overcoming these technical barriers. Generative adversarial networks (GANs) have demonstrated strong performance in image super-resolution, denoising, and cross-modality synthesis across multiple neuroimaging applications (Raymond et al., 2025; Wang et al., 2025). In the context of glioma imaging, GAN-based frameworks have been applied to enhance image quality while preserving biologically meaningful signal characteristics, an essential requirement for maintaining clinical validity. A notable example is the ATHENA framework, which was developed to generate high-resolution synthetic sodium MRI images at 3T (Raymond et al., 2025). Sodium neuroimaging offers unique insights into cellular viability and metabolic homeostasis, as altered sodium concentrations are associated with tumor proliferation, necrosis, and membrane integrity. However, native sodium MRI is hampered by intrinsically low SNR and coarse spatial resolution, discouraging its routine clinical use (Raymond et al., 2025). The ATHENA model leveraged anatomically constrained GANs trained on large proton MRI datasets to generate synthetic sodium images with significantly improved SNR while maintaining consistency with native sodium measurements. Importantly, the synthetic sodium signal demonstrated strong linear correlations with native sodium values across contrast-enhancing, T2-hyperintense, and necrotic tumor regions (Raymond et al., 2025). These findings suggest that AI-enhanced image synthesis can preserve quantitative fidelity while substantially improving image quality. Beyond image-level metrics, ATHENA-derived synthetic sodium images showed stronger correlations with tissue-level sodium-proton exchanger (NHE1) expression assessed through image-guided biopsies compared with native sodium MRI (Raymond et al., 2025). This observation is clinically significant, as it indicates that AI-based enhancement may strengthen the association between imaging biomarkers and underlying tumor biology rather than merely improving visual appearance. Such biologically grounded validation represents an important step toward clinical translation of AI-enhanced imaging techniques. From a broader perspective, AI-driven image enhancement may enable wider adoption of advanced metabolic and functional imaging techniques without requiring specialized hardware or extended acquisition protocols. Similar strategies are increasingly being explored for diffusion-weighted imaging, perfusion imaging, and low-field MRI systems, where AI-based denoising and super-resolution techniques can mitigate technical limitations inherent to the acquisition process (Fares et al., 2025; Wang et al., 2025). By improving image quality and harmonizing data across scanners and acquisition protocols, AI-driven enhancement may serve as a foundational step toward robust downstream analysis and multicenter clinical deployment.

#### 3.2. Representation Learning and Patient-Level Embeddings

While early AI applications in neuro-oncology primarily focused on task-specific models—such as segmentation or classification networks—recent efforts have shifted toward more generalizable approaches based on representation learning (Barba et al., 2025). Representation learning aims to extract compact, informative feature representations from high-dimensional imaging data that can be reused across multiple clinical tasks, thereby reducing dependence on large labeled datasets and task-specific model training. The DUNE framework exemplifies this paradigm shift in neuroimaging AI. DUNE introduces a neuroimaging-oriented workflow that transforms full-sized brain MRI scans into standardized patient-level embeddings using an integrated preprocessing pipeline and a UNet-based autoencoder architecture (Barba et al., 2025). By training the model on a large and heterogeneous dataset comprising both morphologically normal brains and pathological scans from glioma patients, DUNE learns to encode complex anatomical and pathological patterns into compact numerical representations. These embeddings were subsequently used as inputs for conventional machine learning algorithms to predict a wide range of clinical variables, including volumetric measures, cardiovascular disease risk, neurodegenerative diagnoses, and glioma-specific outcomes (Barba et al., 2025). In glioma cohorts, DUNE-derived embeddings demonstrated robust predictive performance for IDH mutation status and overall survival, achieving results comparable to or exceeding those of previously published task-specific deep learning models. A key strength of the DUNE approach lies in its demonstrated generalizability across independent cohorts and disease domains. Embeddings trained on heterogeneous datasets generalized successfully to external cohorts, including glioma, Alzheimer's disease, and schizophrenia populations, suggesting that the learned representations capture fundamental aspects of brain structure and pathology rather than disease-specific artifacts (Barba et al., 2025). This capacity for cross-disease generalization is particularly

attractive for neuro-oncology, where data scarcity and heterogeneity frequently limit model robustness. The clinical significance of representation learning approaches lies in their flexibility and scalability. Instead of developing separate AI models for each diagnostic or prognostic task, a single embedding framework can support multiple downstream applications using relatively simple machine learning algorithms. This approach aligns with emerging concepts of foundation models and large-scale pretrained architectures, which aim to generalize across institutions, scanners, and imaging protocols (Barba et al., 2025; Wang et al., 2025). Nevertheless, important challenges remain. While embeddings capture complex imaging patterns, their abstract and high-dimensional nature makes it difficult to directly relate specific features to recognizable anatomical or pathological characteristics. This lack of transparency complicates clinical interpretation and may hinder adoption by clinicians who require explainable decision support (Brown et al., 2025; Ahangari et al., 2025). Addressing this limitation will require the development of explainable AI techniques capable of linking learned representations to clinically meaningful imaging phenotypes and biological processes. Table 1.1 summarizes representative studies applying artificial intelligence for image quality enhancement and patient-level representation learning in glioma neuroimaging.

### **3.3. Importance of Accurate AI-Based Tumor Segmentation and Classification**

Tumor segmentation is a critical step in glioma imaging, underpinning numerous downstream applications including volumetric assessment, surgical and radiotherapy planning, radiomics analysis, and longitudinal response evaluation (Pourmahboubi et al., 2025; Wang et al., 2025). Manual segmentation performed by expert neuroradiologists is time-consuming and subject to substantial interobserver variability, particularly in cases with infiltrative tumor margins, non-enhancing components, or post-treatment changes such as pseudoprogression and radiation necrosis (Brown et al., 2025). Artificial intelligence has demonstrated substantial promise in automating glioma segmentation with high accuracy and reproducibility. Convolutional neural networks (CNNs), particularly encoder–decoder architectures such as U-Net, have become the dominant approach in this domain due to their ability to capture both local image details and global contextual information (Pourmahboubi et al., 2025; Ilani et al., 2025). These models enable precise delineation of tumor subregions, including contrast-enhancing tumor, non-enhancing tumor core, and peritumoral edema, which are clinically relevant for treatment planning and prognosis.

### **3.4. Deep Learning Architectures and Transfer Learning**

Numerous studies have reported high segmentation performance using U-Net-based architectures, with Dice similarity coefficients frequently exceeding 0.90 on public benchmark datasets such as the Brain Tumor Segmentation (BraTS) Challenge (Pourmahboubi et al., 2025; Ilani et al., 2025). Performance has been further enhanced through the use of transfer learning, whereby networks pretrained on large natural image datasets or medical imaging repositories are fine-tuned on glioma-specific segmentation tasks. VGG19-powered U-Net architectures represent a prominent example of this strategy. These hybrid models leverage pretrained convolutional backbones to improve feature extraction efficiency and generalization, achieving Dice coefficients above 0.96 and strong performance across multiple evaluation metrics, including precision, recall, and intersection-over-union (Pourmahboubi et al., 2025). Transfer learning is particularly advantageous in neuro-oncology, where labeled datasets are often limited in size and diversity. Cross-dataset validation studies have demonstrated that well-designed segmentation models can maintain robust performance across external cohorts, suggesting potential readiness for real-world clinical deployment (Ilani et al., 2025). However, it is important to note that many reported results are still derived from curated datasets with standardized imaging protocols, which may not fully reflect the heterogeneity encountered in routine clinical practice (Brown et al., 2025; Wang et al., 2025).

### **3.5. Modality-Agnostic and Robust Segmentation Frameworks**

A major limitation of many AI-based segmentation models is their reliance on complete multimodal MRI inputs. In clinical reality, imaging protocols often vary due to patient condition, scanner availability, institutional preferences, or time constraints, resulting in missing or incomplete sequences (Lteif et al., 2025). Models trained on fixed multimodal inputs may therefore perform poorly when deployed in heterogeneous clinical environments. To address this challenge, modality-agnostic segmentation frameworks have been proposed. Anatomy-guided approaches that incorporate structural priors during training have shown improved robustness under missing-modality conditions. The Region ModalMix (RMM) augmentation strategy represents a notable example, integrating anatomical context into the training process to enhance segmentation performance when one or more input modalities are absent (Lteif et al., 2025). When evaluated on the BraTS

dataset, modality-agnostic models using RMM achieved significant improvements in segmentation accuracy compared with baseline models trained on single-modality inputs, as measured by Dice similarity coefficient and Hausdorff distance (Lteif et al., 2025). Importantly, external validation on heterogeneous post-operative glioma datasets demonstrated sustained performance despite distribution shifts, highlighting improved generalizability. These developments are particularly relevant for clinical translation, as they explicitly address real-world imaging variability. By reducing dependence on rigid imaging protocols, modality-agnostic AI systems may facilitate broader adoption across institutions with differing resources, scanner types, and acquisition practices (Lteif et al., 2025; Wang et al., 2025).

**Table 1.** Image quality enhancement and patient-level representation learning in glioma neuroimaging

First Author (Year)	Study Type	Imaging Modality	AI Methodology	Clinical Task	Key Findings / Performance
Barba et al. (2025)	Original research	MRI (multi-cohort)	UNet-based autoencoder, representation learning	Patient-level embedding, molecular prediction, survival	Generalizable embeddings predicted IDH status (AUROC $\approx$ 0.92) and survival (C-index $\approx$ 0.61), matching task-specific models
Raymond et al. (2025)	Original research	Sodium MRI + proton MRI	GAN (ATHENA), super-resolution synthesis	Image enhancement, metabolic imaging	Synthetic sodium MRI showed higher SNR and stronger correlation with NHE1 expression than native sodium MRI
Brown et al. (2025)	Narrative review	MRI, omics data	ML, DL, radiomics	Glioblastoma screening and classification	Reported accuracies $>$ 90%; highlighted lack of standardization and external validation
Ahangari et al. (2025)	Systematic review	MRI, histopathology	CNNs, multimodal AI	Glioblastoma diagnosis and grading	AI improves diagnostic precision; interpretability and clinical integration

### 3.6. Clinical Implications and Limitations of Automated Segmentation

From a clinical perspective, automated tumor segmentation has the potential to streamline radiological workflows, reduce clinician burden, and enable more consistent quantitative assessment of tumor burden (Brown et al., 2025). Integration of AI-based segmentation into radiology workstations and surgical planning platforms could support precision treatment strategies, particularly in high-volume clinical settings. However, several limitations must be considered. Segmentation performance may degrade in cases with atypical tumor morphology, extensive treatment-related changes, or rare tumor subtypes that are underrepresented in training datasets (Wang et al., 2025). Furthermore, most segmentation models are trained and evaluated on retrospective datasets, and prospective validation in routine clinical environments remains limited. Regulatory approval and integration into existing clinical infrastructure also represent nontrivial hurdles. Models must demonstrate consistent performance, robustness, and safety across diverse patient populations before they can be adopted in clinical practice (Brown et al., 2025; Ahangari et al., 2025).

### 3.7. Clinical Importance of Automated Grading

Accurate grading of gliomas is a cornerstone of neuro-oncological decision-making, influencing surgical strategy, adjuvant therapy selection, and prognosis estimation (Ahangari et al., 2025). Traditionally, tumor grading relies on histopathological examination, supported by radiological assessment. However, imaging-based grading using conventional MRI remains challenging, particularly when radiological features overlap between low-grade gliomas (LGG) and high-grade gliomas (HGG) or when treatment-related changes obscure tumor boundaries (Brown et al., 2025). Artificial intelligence has been increasingly explored as a means to improve noninvasive glioma grading by leveraging quantitative imaging features that capture subtle textural, spatial, and intensity-based patterns (Wang et al., 2025). Both radiomics-based machine learning models and deep learning approaches have demonstrated the ability to distinguish LGG from HGG with high accuracy, often outperforming conventional radiological interpretation.

### 3.8. MRI-Based AI Models for Glioma Grading

Most AI-based grading studies utilize multiparametric MRI data, including T1-weighted, contrast-enhanced T1-weighted, T2-weighted, and FLAIR sequences (Brown et al., 2025; Wang et al., 2025). Radiomics-based approaches extract handcrafted features related to tumor shape, texture, and intensity distribution, which are then used as inputs for classical machine learning classifiers such as support vector machines, random forests, and gradient boosting algorithms. Several studies have reported area under the receiver operating characteristic curve (AUC) values exceeding 0.90 for MRI-based differentiation of LGG and HGG, highlighting the diagnostic potential of AI-assisted grading (Wang et al., 2025). Deep learning models further enhance grading performance by learning hierarchical features directly from image data, eliminating the need for manual feature engineering (Ilani et al., 2025). Advanced MRI techniques, including diffusion-weighted imaging and perfusion imaging, provide surrogate markers of cellular density, vascularity, and tumor infiltration. Integration of these modalities into AI frameworks has been shown to improve grading accuracy and robustness across diverse patient cohorts (Fares et al., 2025). Key studies addressing automated tumor segmentation, grading, and classification using artificial intelligence are summarized in Table 2.

**Table 2.** Automated tumor segmentation, grading, and classification

First Author (Year)	Study Type	Imaging Modality	AI Methodology	Clinical Task	Key Findings / Performance
Wang et al. (2025)	Review article	Multiparametric MRI	Radiomics, DL-enhanced pipelines	Tumor characterization Prognosis	Radiomics predicts molecular markers and outcomes; reproducibility and generalizability are key limitations
Fares et al. (2025)	Review article	MRI, diffusion MRI	ML, DL, radiomics	GBM heterogeneity prognosis	Imaging-based biomarkers capture tumoral heterogeneity and support personalized therapy
Lteif et al. (2025)	Original research	MRI (BraTS, external datasets)	Modality-agnostic DL, Region ModalMix	Tumor segmentation	Robust segmentation under missing-modality conditions; improved Dice and HD95
Şerban et al. (2025)	Review article	MRI, molecular data	ML, computational psychiatry	Neuropsychiatric manifestation	Tumor-associated psychiatric syndrom recon

### 3.9. CT-Based Machine Learning for Glioma Grading

While MRI remains the imaging modality of choice for glioma evaluation, computed tomography (CT) is often the first-line imaging technique in acute clinical settings and is more widely available in resource-limited environments (Bilgin et al., 2025). Historically, CT has been considered insufficient for detailed glioma characterization due to limited soft-tissue contrast. However, recent studies have challenged this assumption by demonstrating that machine learning algorithms can extract diagnostically relevant information from routinely acquired CT images. Proof-of-concept studies using radiomics and classical machine learning classifiers, such as Naive Bayes models, have shown that CT-derived features can differentiate low-grade from high-grade gliomas with AUC values exceeding 0.90 (Bilgin et al., 2025). These findings suggest that CT-based AI models may complement MRI-based approaches, particularly in emergency settings where rapid decision-making is required. The clinical implications of CT-based AI grading are substantial. Such models may accelerate diagnostic workflows, reduce delays to definitive imaging or biopsy, and improve access to advanced diagnostic support in regions with limited MRI availability (Bilgin et al., 2025; Brown et al., 2025).

### 3.10. Classification Beyond Grading

Beyond binary grading, AI models have been applied to more nuanced classification tasks, including differentiation of gliomas from other intracranial tumors such as meningiomas and pituitary adenomas. Deep learning architectures employing hybrid segmentation–classification pipelines and transfer learning strategies have demonstrated high accuracy in multi-class tumor classification tasks (Ilani et al., 2025). These classification frameworks may support early diagnosis and treatment planning, particularly in cases where imaging findings are ambiguous or atypical. However, as with grading models, external validation and prospective clinical evaluation remain limited, underscoring the need for cautious interpretation of reported performance metrics (Brown et al., 2025).

### 3.11. Radiomics as a Bridge Between Imaging and Tumor Biology

Radiomics represents a paradigm shift in medical imaging analysis, enabling extraction of large numbers of quantitative features that describe tumor phenotype in a reproducible and objective manner (Wang et al., 2025). In glioma imaging, radiomic features have been shown to correlate with histopathological characteristics, molecular alterations, and clinical outcomes, positioning radiomics as a bridge between imaging and tumor biology. Radiomic pipelines typically involve image preprocessing, tumor segmentation, feature extraction, feature selection, and model construction. Integration of deep learning techniques has enhanced multiple stages of this workflow, improving robustness, reducing manual intervention, and enabling analysis of complex tumor habitats (Wang et al., 2025; Fares et al., 2025).

### 3.12. Radiogenomics and Molecular Subtype Prediction

One of the most impactful applications of AI in glioma neuroimaging is noninvasive prediction of molecular tumor characteristics. Molecular markers such as IDH mutation status and glioblastoma transcriptional subtypes carry significant prognostic and therapeutic implications (Fares et al., 2025; Wang et al., 2025). AI-based radiogenomic models have demonstrated promising performance in predicting these features directly from imaging data. Advanced diffusion MRI techniques, including diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI), provide microstructural information that enhances molecular prediction. Radiomic features derived from these modalities have been successfully used to predict mesenchymal glioblastoma subtypes, which are associated with poorer prognosis and treatment resistance (Gallotti et al., 2025).

### 3.13. Transfer Learning Across Preclinical and Clinical Domains

An innovative approach to overcoming limited clinical datasets involves transfer learning between preclinical and clinical imaging domains. Studies leveraging xenograft-derived imaging data have demonstrated that machine learning models trained on preclinical datasets can generalize to human patient cohorts when appropriately designed (Gallotti et al., 2025). Radiomic models trained on diffusion MRI data from glioblastoma xenografts achieved high accuracy in predicting mesenchymal subtype when validated in independent patient cohorts, suggesting that certain imaging biomarkers capture fundamental biological processes that transcend experimental context (Gallotti et al., 2025). While promising, such approaches require careful biological validation to ensure clinical reliability.

### 3.14. Integration of Multimodal Imaging in AI-Based Glioma Analysis

A critical advantage of artificial intelligence over conventional imaging analysis lies in its ability to integrate heterogeneous data sources into unified predictive models. Contemporary glioma imaging increasingly relies on multimodal approaches that combine structural MRI with advanced techniques such as diffusion-weighted imaging, perfusion imaging, magnetic resonance spectroscopy, sodium MRI, and positron emission tomography (PET) (Fares et al., 2025; Wang et al., 2025). Each modality captures distinct aspects of tumor biology, including cellular density, vascular permeability, metabolic activity, and ionic homeostasis. AI-based multimodal fusion frameworks have demonstrated superior performance compared with single-modality models across multiple clinical tasks. By jointly analyzing complementary imaging features, these systems can better characterize intratumoral heterogeneity and improve robustness in the presence of noisy or incomplete data (Ahangari et al., 2025; Fares et al., 2025). For example, integrating diffusion-derived metrics with conventional anatomical imaging enhances sensitivity to infiltrative tumor components that may not be visually apparent on standard MRI sequences. Radiomics pipelines benefit particularly from multimodal integration, as feature sets derived from different imaging modalities capture nonredundant biological information. Machine learning classifiers trained on multimodal radiomic features have shown improved accuracy for tumor grading, molecular subtype prediction, and survival estimation compared with unimodal approaches (Wang et al., 2025). Importantly, these gains appear most pronounced in intermediate or ambiguous cases, where conventional imaging interpretation is challenging and prone to interobserver variability. Despite these advantages, multimodal AI systems introduce additional methodological and logistical complexity. Differences in spatial resolution, image registration accuracy, and acquisition protocols complicate data integration and model training (Brown et al., 2025). Moreover, missing imaging modalities remain a common challenge in real-world clinical workflows. Modality-agnostic and representation learning approaches discussed earlier represent promising strategies to mitigate these limitations by enabling flexible integration of available data while preserving predictive performance (Lteif et al., 2025; Barba et al., 2025).

### 3.15. Specialized Clinical Contexts

#### 3.15.1. Diffuse Midline Glioma

Diffuse midline glioma (DMG) is a rare, highly aggressive tumor that predominantly affects pediatric patients and is associated with a dismal prognosis. Owing to its deep midline location and infiltrative growth pattern, surgical resection is often not feasible, and diagnosis frequently relies on imaging characteristics supplemented by limited tissue sampling (Haddadi Avval et al., 2025). Consequently, advanced neuroimaging and noninvasive diagnostic tools are of particular importance in this disease entity. Artificial intelligence has recently been explored as a means to extract clinically meaningful information from MRI data in DMG. AI applications in this context have focused on tumor classification, segmentation, radiogenomic inference, and survival prediction, employing a wide range of algorithms from traditional machine learning to deep neural networks (Haddadi Avval et al., 2025). Radiomics-based approaches have been particularly valuable in identifying subtle imaging patterns associated with molecular alterations and clinical outcomes. Advanced MRI techniques, including diffusion-weighted imaging, perfusion-weighted imaging, magnetic resonance spectroscopy, and PET, have been integrated into AI frameworks to enhance tumor characterization. These modalities provide complementary information on cellularity, vascularity, metabolism, and molecular composition, which is especially valuable in DMG, where tissue access is limited (Haddadi Avval et al., 2025). Despite encouraging preliminary results, progress in this area is constrained by the rarity of the disease and the lack of large, publicly available, multi-institutional datasets. Addressing these limitations will require coordinated international collaboration and standardized data-sharing initiatives.

#### 3.15.2. Pediatric Gliomas

Pediatric gliomas represent a heterogeneous group of tumors with biological and clinical characteristics that differ substantially from adult gliomas. Developmental variability, age-specific tumor biology, and long-term treatment-related sequelae pose unique challenges for diagnosis and management (Dalboni da Rocha et al., 2025). Artificial intelligence has demonstrated significant potential to improve pediatric neuroimaging by enhancing image quality, accelerating acquisition, and supporting diagnostic and prognostic decision-making. AI-based tools have been applied to pediatric glioma imaging for tumor segmentation, classification, and outcome prediction. Convolutional neural networks have achieved high accuracy in tumor delineation, facilitating volumetric assessment and longitudinal monitoring (Dalboni da Rocha et al., 2025). Radiomics and deep learning models have also been explored for tumor characterization and risk stratification, although the limited availability of pediatric datasets remains a major bottleneck. Ethical considerations are particularly

salient in pediatric AI applications. The use of AI in vulnerable populations necessitates careful attention to data privacy, informed consent, and algorithmic bias. Moreover, the need for explainable and transparent AI models is amplified in pediatric settings, where clinical decisions may have lifelong implications (Dalboni da Rocha et al., 2025). Future research should prioritize the development of interpretable models trained on diverse, multi-institutional pediatric datasets to ensure equitable and clinically responsible deployment.

### **3.15.3. Neuropsychiatric Manifestations and Emerging AI Applications**

Gliomas frequently give rise to neuropsychiatric symptoms that may precede radiological detection or confound differential diagnosis with primary psychiatric disorders. These manifestations reflect complex interactions between tumor biology, metabolic reprogramming, neuroimmune activation, neurotransmitter dysregulation, and large-scale neural network disruption (Şerban et al., 2025). Despite their clinical relevance, tumor-associated neuropsychiatric syndromes remain underrecognized and are often misdiagnosed. Emerging AI-based approaches offer new opportunities to investigate these phenomena. Lesion-network mapping, computational psychiatry models, and AI-driven predictive frameworks may enable earlier detection of tumor-related neuropsychiatric dysfunction and facilitate mechanistically informed interventions (Şerban et al., 2025). Integration of neuroimaging data with molecular biomarkers and clinical phenotyping may ultimately redefine psychiatric symptoms as integral components of tumor biology rather than secondary complications. Although this area remains largely exploratory, it highlights the broader potential of AI to expand the scope of neuro-oncological imaging beyond traditional diagnostic endpoints. Incorporating functional and behavioral dimensions of disease into AI models may improve holistic patient assessment and contribute to more personalized therapeutic strategies (Şerban et al., 2025).

### **3.15.4. Role of AI in Precise Neuro-Oncology**

The ultimate promise of AI in glioma neuroimaging lies in its contribution to precision neuro-oncology. By enabling noninvasive characterization of tumor biology, AI-based imaging biomarkers may support individualized treatment strategies, reduce reliance on invasive diagnostic procedures, and facilitate adaptive therapy planning (Ahangari et al., 2025; Fares et al., 2025). Integration of AI-derived imaging biomarkers with molecular and clinical data may enable refined risk stratification and treatment selection. For example, noninvasive prediction of molecular subtypes could inform surgical aggressiveness, radiotherapy planning, or enrollment in targeted therapy trials (Wang et al., 2025). Similarly, AI-based longitudinal monitoring of imaging changes may enable earlier detection of progression or treatment resistance, supporting more timely clinical interventions. However, realizing this vision requires a shift from retrospective proof-of-concept studies toward clinically integrated decision-support systems evaluated in prospective trials. Demonstrating tangible benefits in patient outcomes, quality of life, and healthcare efficiency will be critical to justify widespread clinical adoption (Brown et al., 2025). As summarized in Table 3, AI-based radiomics and molecular prediction approaches extend beyond conventional imaging tasks, addressing tumor biology, rare glioma subtypes, and clinically challenging contexts.

**Table 3.** AI-based radiomics and molecular prediction addressing tumor biology, rare glioma subtypes, and clinically challenging contexts.

First Author (Year)	Study Type	Imaging Modality	AI Methodology	Clinical Task	Key Findings / Performance
Ilani et al. (2025)	Original research	T1-weighted MRI	CNNs, transfer learning	Tumor classification	High accuracy (>98%) in multi-class brain tumor classification
Pourmahboubi et al. (2025)	Original research	MRI	U-Net with transfer learning	Tumor segmentation	Improved Dice coefficient (>0.96) with pretrained encoders
Bilgin et al. (2025)	Original research	CT	Radiomics + ML	Glioma grading (LGG vs. HGG)	CT-based models achieved AUC $\approx$ 0.90, comparable to MRI-based studies
Gallotti et al. (2025)	Original research	DTI, NODDI	Radiomics + XGBoost, transfer learning	Molecular subtype prediction	Mesenchymal GBM predicted with AUROC $\approx$ 0.93 using diffusion MRI features
Haddadi Avval et al. (2025)	Narrative review	MRI, PET	ML, DL, radiomics	Diffuse midline glioma	AI supports classification, segmentation, and prognosis; limited by data scarcity

## 4. Discussion

### 4.1. Model Interpretability and Explainability in Glioma Neuroimaging

Model interpretability remains a central concern in the clinical deployment of AI-based neuroimaging tools. While deep learning models frequently achieve high predictive accuracy, their decision-making processes are often opaque, limiting clinician trust and complicating regulatory approval (Brown et al., 2025; Ahangari et al., 2025). In neuro-oncology, where diagnostic and therapeutic decisions have profound implications for patient outcomes, explainability is particularly critical. Several interpretability techniques have been applied to glioma imaging models, including saliency maps, gradient-based attribution methods, and feature importance analyses in radiomics-based machine learning models (Wang et al., 2025). These techniques aim to identify image regions or features that contribute most strongly to model predictions. In segmentation tasks, interpretability is often implicit, as outputs correspond directly to spatial tumor delineations. However, in classification and prognostic models, linking predictions to biologically meaningful imaging features remains substantially more challenging (Brown et al., 2025). Radiomics-based approaches offer a degree of inherent interpretability, as handcrafted features can often be associated with tumor morphology, texture, or spatial heterogeneity. For instance, features capturing edge sharpness or intensity variance may reflect infiltrative growth patterns or necrotic components (Wang et al., 2025). Nevertheless, the biological interpretation of many radiomic features remains indirect and requires careful validation. Representation learning frameworks introduce additional challenges, as learned embeddings are highly abstract and multidimensional. Although such embeddings demonstrate strong predictive performance across tasks, their lack of transparency complicates clinical interpretation and acceptance (Barba et al., 2025). Future research should prioritize hybrid approaches that combine the flexibility of deep learning with interpretable representations, enabling clinicians to contextualize AI-driven predictions within established radiological and biological frameworks.

### 4.2. Generalizability, Bias, and Data Quality Considerations

Generalizability remains one of the most significant barriers to clinical translation of AI-based glioma neuroimaging tools. Many published models are trained on retrospective, single-center datasets that do not adequately reflect the diversity of imaging protocols, scanner hardware, and patient populations encountered in routine clinical practice (Brown et al., 2025; Wang et al., 2025). As a result, model performance often degrades when applied to external cohorts. Bias may be introduced at multiple stages of the AI pipeline, including data acquisition, annotation, feature selection, and evaluation. Selection bias can arise when training datasets overrepresent specific tumor grades, molecular subtypes, or demographic groups. Annotation bias may result from interobserver variability in manual segmentations or histopathological labeling (Ahangari et al., 2025). Such biases can lead to systematic performance disparities across patient subgroups. Advanced preprocessing and harmonization techniques may partially mitigate data heterogeneity, but they cannot fully compensate for fundamental differences in acquisition protocols and institutional practices (Wang et al., 2025). Consequently, multi-institutional collaborations and data-sharing initiatives are essential to develop robust, generalizable models. Prospective validation across diverse clinical environments represents a critical step toward safe and equitable AI deployment (Brown et al., 2025).

### 4.3. Prognostication and Outcome Prediction

Beyond diagnosis and classification, AI-based neuroimaging models have been increasingly applied to prognostic tasks, including survival prediction and treatment response assessment. Imaging-derived features capturing tumor heterogeneity, infiltration patterns, and microenvironmental characteristics have been shown to correlate with overall survival and progression-free survival (Fares et al., 2025; Wang et al., 2025). Representation learning frameworks, such as patient-level embeddings derived from autoencoders, further expand prognostic modeling capabilities. By capturing global imaging patterns, these embeddings enable survival prediction using relatively simple machine learning algorithms, offering a flexible and scalable approach to outcome modeling (Barba et al., 2025). Such approaches may be particularly valuable in heterogeneous clinical settings, where task-specific models struggle to generalize. Nevertheless, prognostic AI models face significant methodological challenges, including censoring, treatment heterogeneity, and confounding clinical variables. Imaging-based predictions must therefore be interpreted within the broader clinical context, and prospective validation incorporating standardized endpoints is essential to establish true clinical utility (Ahangari et al., 2025; Brown et al., 2025).

#### 4.4. Challenges and Barriers to Clinical Translation

Despite substantial methodological progress, the clinical adoption of AI in glioma neuroimaging remains limited. One of the most significant barriers is data heterogeneity, encompassing variability in imaging protocols, scanner hardware, acquisition parameters, and patient populations (Wang et al., 2025). Many AI models demonstrate impressive performance on curated research datasets but fail to maintain accuracy when applied to real-world clinical data. Another major challenge is the lack of standardized reporting and validation practices. Inconsistent evaluation metrics, absence of external validation, and limited transparency in model development hinder meaningful comparison across studies (Brown et al., 2025). Although reporting guidelines and benchmark initiatives have improved methodological rigor, adherence remains inconsistent. Model interpretability further complicates translation. Deep learning models often function as “black boxes,” providing limited insight into the features driving their predictions. This opacity reduces clinician trust and complicates regulatory approval (Ahangari et al., 2025). While explainable AI techniques offer partial solutions, their clinical relevance and reliability require further validation. Finally, integration into clinical workflows presents practical challenges. Regulatory clearance, interoperability with existing radiology systems, clinician training, and post-deployment performance monitoring are essential components of safe implementation. Without addressing these factors, even technically robust AI tools are unlikely to achieve widespread clinical impact (Brown et al., 2025).

#### 4.5. Regulatory, Ethical, and Workflow Considerations

Beyond technical performance, successful clinical integration of AI-based neuroimaging tools requires careful consideration of regulatory, ethical, and workflow-related factors. Regulatory agencies increasingly demand evidence of safety, effectiveness, and clinical benefit, necessitating rigorous validation studies and transparent reporting of model behavior (Ahangari et al., 2025). Ethical considerations include data privacy, informed consent, and accountability for AI-assisted clinical decisions. In pediatric populations and rare tumor entities, these concerns are amplified due to increased vulnerability and limited data availability (Dalboni da Rocha et al., 2025; Haddadi Avval et al., 2025). Transparent communication of model limitations and uncertainty is essential to avoid inappropriate reliance on automated outputs. Workflow integration is often underestimated. AI tools must seamlessly interface with picture archiving and communication systems (PACS), radiology information systems, and electronic health records. Clinician education and post-deployment monitoring are critical to ensure appropriate use and sustained performance (Brown et al., 2025).

### 5. Conclusions

Artificial intelligence has emerged as a powerful adjunct to neuroimaging in the management of gliomas, enabling noninvasive diagnosis, molecular characterization, and prognostic assessment. Advances in deep learning, radiomics, representation learning, and multimodal integration have expanded the role of neuroimaging from qualitative interpretation toward quantitative, biologically informed analysis (Fares et al., 2025; Wang et al., 2025). Nevertheless, significant challenges remain in translating these advances into routine clinical practice. Addressing issues related to data heterogeneity, model interpretability, generalizability, and clinical integration will be essential to realize the full potential of AI-assisted neuro-oncology (Brown et al., 2025; Ahangari et al., 2025). With continued methodological refinement, rigorous prospective validation, and close collaboration between clinicians, data scientists, and regulatory bodies, AI-based neuroimaging may ultimately become an integral component of precision neuro-oncological care.

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