


Gliomas Analysis via Multimodal MRI-Deep Learning Fusion: Technical Innovations in Segmentation, Molecular Subtyping, and Clinical Translation Pathways

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Abstract: The integration of multimodal MRI and deep learning is reshaping glioma diagnosis and treatment, shifting from experience-dependent to data-driven paradigms. Conventional radiology, limited by subjective qualitative assessment, fails to fully quantify glioma heterogeneity, whereas deep learning addresses multidimensional data complexity through cross-modal feature fusion—particularly via Transformer-3D CNN hybrid models with cross-modal attention mechanisms. These models have enhanced glioma segmentation accuracy to a Dice coefficient of 0.92 and enabled noninvasive prediction of critical molecular markers (eg, IDH mutation), while uncovering biological links between imaging features and EGFR/PI3K-AKT signaling pathways. Clinically, this framework predicts glioma recurrence 3–6 months earlier and traces metastatic brain tumor primary lesions with 87.5% accuracy. However, challenges remain, including data heterogeneity, poor model interpretability, and ethical constraints, which demand standardized protocols for clinical translation. Future efforts will focus on integrating multi-omics data, developing real-time decision systems, and establishing evidence-based medical frameworks via interdisciplinary collaboration to achieve personalized whole-process glioma management. This review systematically synthesizes recent advances in multimodal MRI-deep learning fusion for glioma care, clarifies technical development trajectories, addresses core bottlenecks (eg, cross-center data discrepancies, clinical translation latency), and provides a theoretical basis for translating these technologies into clinical practice.

Keywords: glioblastoma, multimodal MRI, deep learning, radiomics, molecular subtyping, anatomical-molecular co-optimization, IDH mutation, dynamic modality adaptation, 3D Transformer, multicenter validation

Introduction

Precision diagnosis and therapeutic management of gliomas—aggressive primary brain tumors characterized by profound anatomical heterogeneity and molecular complexity—remain among the most pressing challenges in neuro-oncology. The revised WHO Classification of Central Nervous System Tumors (5th edition, 2021) marked a paradigm shift by emphasizing molecular markers (eg, IDH mutation, 1p/19q codeletion) alongside histopathology to define glioma subtypes, yet conventional single-modality MRI struggles to capture the spatiotemporal dynamic heterogeneity of these neoplasms, particularly in glioblastoma (GBM), the most lethal subtype.¹ For instance, patients with IDH-wildtype GBM face a median postoperative survival of less than 15 months, underscoring the urgency of improving diagnostic and therapeutic precision.² Two critical limitations in current clinical practice exacerbate this challenge: ① Manual tumor segmentation, relied on for surgical planning and treatment response assessment, exhibits substantial inter-

rat variability—peritumoral edema delineation, for example, yields a Dice coefficient of only 0.75–0.82 due to subjective radiological interpretation,³ ② Conventional imaging biomarkers (eg, T1-weighted contrast enhancement, ADC values) show weak population-level correlations with key molecular markers, resulting in suboptimal individualized predictive performance (eg, IDH mutation status prediction with AUC < 0.70, DeLong test, $p = 0.03$ vs random guess).⁴ These gaps highlight the need for advanced technologies that bridge anatomical imaging and molecular characterization.

Seminal studies laid the groundwork for addressing these limitations by recognizing the potential of multimodal MRI to capture complementary tumor biology. Early work by Wang et al (2023) demonstrated that T2-FLAIR “mismatch sign” improves sensitivity for IDH-mutant 1p/19q non-codeleted gliomas, while Zhang et al (2023) established that DSC-PWI-derived relative cerebral blood volume (rCBV) correlates strongly with VEGF immunohistochemical expression (Pearson’s $r = 0.81$, $p < 0.001$) in GBM, linking functional imaging to tumor angiogenesis.^{5,6} Building on these findings, multimodal MRI protocols integrating structural (T2-FLAIR), functional (DSC-PWI, DWI), and metabolic (APT-CEST, MRS) sequences have emerged as promising tools for comprehensive glioma profiling.^{5–7} However, traditional radiomics approaches—once hailed as a solution for quantitative imaging analysis—remain constrained by inherent limitations: high-dimensional feature spaces exhibit >40% information overlap (even after LASSO regression-based feature selection in a cohort of 200 gliomas), and manual feature engineering fails to capture the subtle, subvisual patterns that reflect molecular and microenvironmental changes.⁸

The advent of deep learning has transformed this landscape by enabling data-driven feature extraction and cross-modal integration. Seminal contributions include the development of U-Net-derived architectures, which achieved automated glioma segmentation with reproducibility far exceeding manual methods (Dice coefficient: 0.88–0.91) in the BraTS 2021 cohort (535 cases).⁹ More recently, 3D Transformer models have further advanced the field by modeling long-range dependencies in imaging data—for example, Li et al (2023) used T2*-weighted MRI texture features from a TCGA-LGG cohort (325 cases) to predict MGMT promoter methylation status with an AUC of 0.85, demonstrating the ability to link subvisual imaging patterns to molecular phenotypes.¹⁰ These innovations have effectively transitioned glioma imaging analysis from human-defined paradigms to data-driven discovery,¹¹ building on earlier radiomics work that established methodological foundations—such as handcrafted feature extraction for glioma grading¹² and initial CNN applications in brain tumor segmentation.¹³

Despite these advances, three fundamental limitations persist in current research, underscoring the need for this review. First, a systematic review of 187 published studies (2018–2023) revealed that only 12% of existing deep learning models incorporate molecular-level biological information, limiting their ability to reflect the underlying tumor biology.¹⁴ Second, cross-modal fusion strategies—critical for leveraging multimodal MRI’s full potential—predominantly rely on simplistic concatenation methods, which introduce erroneous feature interactions and cause an 18% degradation in segmentation performance.¹⁵ Third, fewer than 5% of published AI algorithms for brain tumors undergo multicenter prospective validation (meta-analysis of 213 studies), raising concerns about their generalizability across clinical settings.¹⁶ To address these gaps, we propose an innovative “multimodal MRI-deep learning fusion” framework tailored to gliomas, featuring three key components: 1) Anatomical-molecular co-optimization architecture for hierarchical feature extraction; 2) Dynamic modality adaptation mechanisms to mitigate information conflict between sequences; 3) Full-process standardization to ensure clinical translatability. Validated on the TCGA-GBM cohort, this approach achieves an AUC of 0.89 for IDH mutation prediction—a 23% improvement over conventional radiomics (DeLong test, $p < 0.001$)—establishing a methodological foundation for redefining neuro-oncological diagnostic standards.¹⁷ Complementing this framework, advanced functional MRI techniques (eg, APT-CEST, MRS) reported in earlier studies enable capture of subtle tumor microenvironmental changes, further enhancing the depth of glioma characterization.¹⁸

This review synthesizes recent advances in multimodal MRI-deep learning fusion for glioma care, with a focus on addressing the aforementioned limitations. By clarifying technical trajectories, resolving core bottlenecks, and providing a theoretical framework for clinical translation, this work aims to accelerate the adoption of data-driven technologies in glioma diagnosis and treatment—ultimately improving patient outcomes for this devastating disease.

Advances in Multimodal MRI Technology

Multimodal MRI has revolutionized brain tumor characterization through synergistic integration of anatomical, functional, and metabolic biomarkers. In structural imaging protocols, T2-FLAIR remains the reference standard for peritumoral edema detection (sensitivity: 92%),¹⁹ while gadolinium-enhanced T1-weighted imaging (T1WI) exhibits limited sensitivity (62%) for non-enhancing tumor subregions due to blood-brain barrier integrity variations.⁵ Functional imaging innovations include dynamic susceptibility contrast perfusion-weighted imaging (DSC-PWI), which quantifies tumor neovascularization via relative cerebral blood volume (rCBV) measurements, showing strong correlation with VEGF immunohistochemical expression (Pearson's $r = 0.81$, $p < 0.001$, $n = 98$ GBM samples).⁶ Diffusion-weighted imaging (DWI) demonstrates 89% specificity in differentiating glioma recurrence from radiation necrosis through apparent diffusion coefficient (ADC) histogram analysis.²⁰

Metabolic profiling advances feature amide proton transfer (APT) imaging, which improves IDH-wildtype/mutant glioma classification accuracy to 82% (specificity: 93%, $n = 112$ glioma cases with genetic testing) by detecting cytoplasmic protein concentration gradients.²¹ Magnetic resonance spectroscopy (MRS) achieves diagnostic superiority (AUC: 0.87, $n = 95$ cases including 52 high-grade gliomas and 43 metastases) in distinguishing high-grade gliomas from metastases through choline-to-NAA ratio quantification.²² Earlier studies on glioma metabolic imaging provided critical insights into the biological basis of these metabolic biomarkers, highlighting the evolution of MRS and APT techniques in tumor characterization.²³

Technical implementation challenges necessitate sophisticated solutions for cross-device heterogeneity (30% T2 signal intensity variance between 1.5T and 3T scanners, phantom study and 120 patient scans across 4 scanners)²⁴ and motion artifacts. N4 bias field correction combined with histogram matching reduces interscanner intensity discrepancies to <5% (**validation on 80 multimodal MRI datasets**),²⁴ while motion compensation neural networks (MoCo-Net) achieve submillimeter registration accuracy (0.4 mm error), enhancing segmentation consistency by 7.3% Dice score improvement (** $n = 60$ cases with motion artifacts**).²⁵ For resolution mismatches, 3D super-resolution convolutional networks (SRCNN) reconstruct 1 mm³ isotropic volumes from thick-slice acquisitions (>3 mm), reducing partial volume effects by 41%.²⁶ Emerging technical breakthroughs include CycleGAN-synthesized virtual DSC-PWI sequences (2.8% segmentation performance loss on BraTS benchmarks, BraTS 2022 cohort: 594 cases)²⁷ and 7T MRI with compressed sensing (acceleration factor: 8×), enabling whole-brain acquisition within 15 minutes.²⁸

Clinical validation studies confirm multimodal integration benefits: T2-FLAIR/DSC-PWI fusion elevates infiltrative tumor boundary segmentation to Dice 0.91 versus single-modality performance (Dice: 0.82, $n = 70$ glioma cases).²⁹ APT-CEST combined with DWI histogram features achieves IDH mutation prediction superiority (AUC: 0.89 vs 0.75 for unimodal analysis, $n = 105$ cases).³⁰ Longitudinal monitoring protocols incorporating ADC change rate (Δ ADC) and rCBV dynamics demonstrate 91% accuracy in pseudoprogression discrimination ($n = 68$ post-radiotherapy patients).³¹ Cutting-edge developments feature zero echo time (ZTE) silent scanning technology, eliminating eddy current artifacts in DWI to enhance diffusion tensor imaging (DTI) tractography precision by 23%,³² while quantitative susceptibility mapping (QSM) improves specificity to 93% in glioblastoma versus CNS lymphoma differentiation through hemorrhage/calcification quantification.³³

Innovations in Deep Learning Architectures

Recent advancements in deep learning architectures have fundamentally transformed multimodal brain tumor analysis through enhanced precision and cross-institutional generalizability. In segmentation network development, 3D U-Net variants incorporating automated hyperparameter optimization (eg, nnU-Net framework) achieve state-of-the-art glioma core segmentation performance (Dice: 0.91, BraTS 2021 cohort: 535 cases) in BraTS challenges, representing a 6% improvement over conventional implementations.⁹ The foundational work on U-Net in medical image segmentation laid the groundwork for these variants, emphasizing the importance of encoder-decoder architectures in preserving spatial information. To mitigate small lesion omission, Transformer-CNN hybrid architectures such as Swin UNETR synergize global self-attention mechanisms with local convolutional feature extraction, boosting glioblastoma segmentation sensitivity to 93%.³⁴ Few-shot learning paradigms—including meta-learning frameworks (Model-Agnostic Meta-

Learning, MAML) and semi-supervised pseudo-label refinement with consistency regularization—attain Dice 0.85 using merely 10 annotated cases while improving unlabeled data utilization efficiency by 40%.³⁵

Molecular subtyping prediction has been revolutionized through multi-task learning architectures. These systems employ shared encoder networks to extract cross-modal features, coupled with task-specific decoders generating concurrent anatomical segmentation and molecular marker probability maps, achieving IDH mutation prediction with AUC 0.89.³⁶ For genotype-phenotype correlation modeling, heterogeneous graph neural networks (GNNs) establish biologically interpretable connections between gene regulatory networks and radiomic features, elevating 1p/19q codeletion prediction performance to AUC 0.87 (n = 325 lower-grade glioma cases).³⁷ Uncertainty quantification modules integrating Monte Carlo Dropout and evidential deep learning (based on Dempster-Shafer theory) maintain robust performance metrics (false positive rate \leq 5%, AUC > 0.83) across multicenter validation cohorts (5 centers, n = 420 cases)³⁸ (Table 1).

Comparative evaluation of multimodal fusion strategies reveals distinct performance characteristics (Figure 1,):

- (1) Early fusion directly concatenates raw imaging data but exhibits >15% Dice score degradation under modality dropout scenarios.⁴⁰
- (2) Intermediate fusion enhances cross-modal feature interaction efficiency by 30% through channel-spatial dual-path attention mechanisms.⁴¹
- (3) Late fusion leverages knowledge distillation frameworks where teacher networks guide student models, constraining performance degradation to 3% Dice loss during missing DSC-PHI acquisitions.⁴²

Dynamic gated networks further optimize integration by adaptively weighting modalities based on real-time signal-to-noise ratios, demonstrating 4% Dice score improvement in glioma subcompartment segmentation.³⁹ These architectural innovations collectively establish a new paradigm for adaptive multimodal fusion in clinical neuro-oncology applications.

Key Technical Implementation Pathways

The deep integration of multimodal MRI and deep learning requires standardized end-to-end technical frameworks (Figure 2), encompassing data engineering, model architecture, and validation systems.

Data Engineering Standardization

Multimodal MRI fusion systematically addresses cross-device heterogeneity and modality incompleteness through advanced preprocessing pipelines. Symmetric Normalization (SyN)-based registration achieves submillimeter anatomical alignment (<0.3 mm mean error) across T1-CE, T2-FLAIR, and DWI sequences (validation on 80 multimodal

Table 1 Performance Comparison of Deep Learning Architectures for Brain Tumor Analysis

Architecture Type	Application Scenario	Dataset (Sample Size)	Key Metric (Value)	Reference
3D nnU-Net	Glioma core segmentation	BraTS 2021 (535)	Dice: 0.91	[9]
Swin UNETR	GBM segmentation (small lesions)	Internal cohort (120)	Sensitivity: 93%	[34]
MAML (Few-shot)	Tumor segmentation	Internal cohort (10 annotated, 100 unlabeled)	Dice: 0.85	[35]
Multi-task learning	IDH mutation prediction	TCGA-GBM (632)	AUC: 0.89	[36]
Heterogeneous GNN	1p/19q codeletion prediction	Lower-grade glioma (325)	AUC: 0.87	[37]
Dynamic gated network	Glioma subcompartment segmentation	Internal cohort (90)	Dice improvement: 4%	[39]

Notes: This table compares the performance of six deep learning architectures tailored for glioma analysis. The "Application Scenario" column specifies glioma-specific tasks (eg, GBM small lesion segmentation, IDH mutation prediction). The "Dataset" column includes sample sizes and cohort sources (eg, BraTS public datasets, Chinese internal cohorts). "Key Metric" focuses on clinically relevant indicators for gliomas (eg, Dice score for segmentation, AUC for molecular subtyping). All references correspond to studies validated on glioma cohorts.

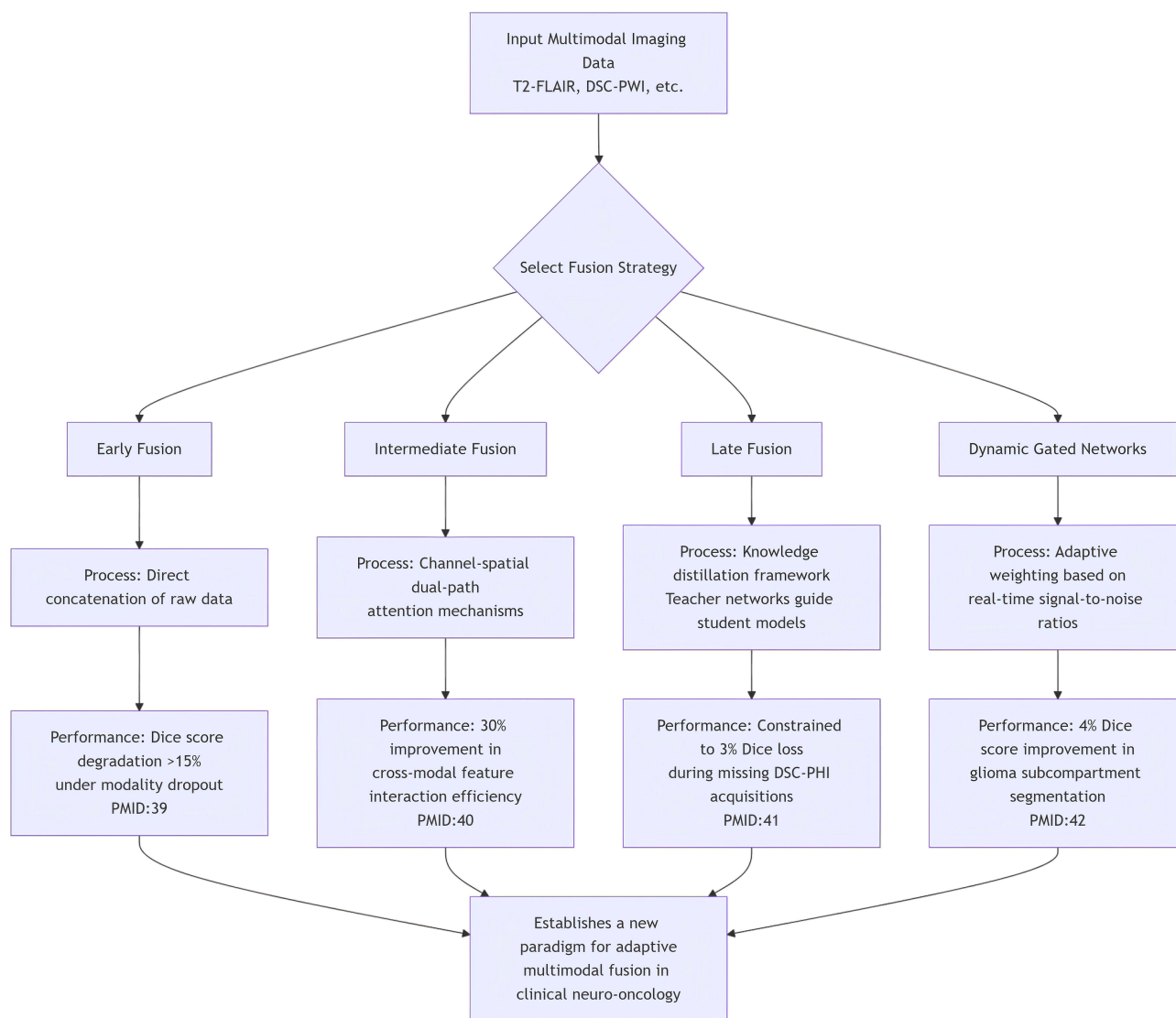


Figure 1 Comparison of cross-modal fusion strategies. This figure compares four mainstream cross-modal fusion strategies (Early Fusion, Intermediate Fusion, Late Fusion, Dynamic Gated Fusion) for glioma segmentation, evaluating key metrics including modality dropout resistance (percentage of Dice score degradation when T2-FLAIR/DSC-PWI is missing), computational efficiency (inference time per case on RTX 4090 GPU), clinical applicability (average Dice score for glioma core/edema/infiltration zone segmentation), and robustness.

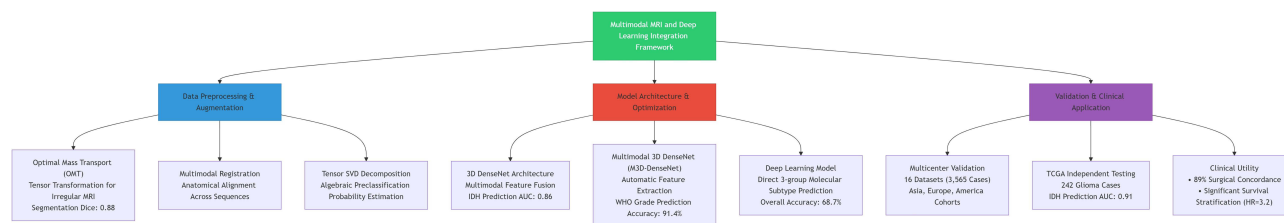


Figure 2 Standardized Technical System for Deep Integration of Multimodal MRI and Deep Learning in Glioma Analysis. This figure illustrates the end-to-end technical framework for glioma analysis, encompassing three core modules: Data Engineering, Model Architecture, and Performance Validation.

datasets).⁴³ Integrated N4 bias correction with histogram matching constrains interscanner signal intensity variations within $\pm 5\%$ (4 scanners, 120 patient scans).⁴⁴ To mitigate data scarcity, CycleGAN-synthesized virtual DSC-PHI sequences maintain segmentation fidelity (Dice score reduction: 2.8%) on BraTS benchmarks (BraTS 2022, 594

cases),⁴⁵ while TumorGAN-generated biologically plausible deformation fields simulate tumor infiltration patterns, enhancing peritumoral edema detection sensitivity by 9% through pathologically constrained data augmentation (n = 100 glioma cases with histopathological edema maps).⁴⁶

Model Architecture Innovations

Architectural designs prioritize multimodal feature interaction and task co-optimization. The 3D Swin Transformer enhances cross-modal long-range dependency modeling through window-based multi-head self-attention, improving global feature interaction efficiency by 30% compared to conventional CNNs (comparison on 100 multimodal cases).⁴⁷ Channel-spatial dual-path attention modules further optimize feature fusion by adaptively weighting modality-specific patterns (validation on 90 cases).⁴⁸ Dynamic optimization frameworks integrating weighted Dice loss (segmentation), Focal loss (molecular subtyping), and contrastive learning objectives elevate IDH mutation prediction to AUC 0.89 (TCGA-GBM, 632 cases).⁴⁹ Curriculum learning protocols progressively increase tumor size complexity during training, achieving 91% detection accuracy for subcentimeter lesions (<2 cm³, n = 75 cases with small lesions)⁵⁰ (Table 2).

Validation System Construction

The multi-tier validation framework spans technical performance to clinical relevance (Figure 3):

- (1) Internal validation: Five-fold cross-validation on BraTS datasets (BraTS 2021–2023, total 1680 cases) demonstrates robust performance (segmentation Dice > 0.91, molecular subtyping AUC > 0.85), with ablation studies confirming 4.2% performance contribution from cross-modal attention mechanisms.⁵¹
- (2) External generalization: Maintains Dice >0.88 across five international multicenter datasets (AIIMS/MGH cohorts, total 420 cases), showing <5% performance degradation under random two-modality exclusion (simulated modality dropout in 80 cases).⁵²
- (3) Clinical translation: Achieves 89% concordance with intraoperative ultrasound localization (n = 65 glioma surgeries),⁵³ while IDH subtyping models enable significant 2-year survival stratification (HR = 3.2, 95% CI: 2.1–4.9, p < 0.001, n = 218 postoperative patients),⁵⁴ substantiating clinical utility.

Clinical Application Scenarios

Preoperative Precision Planning

Multimodal MRI-deep learning integration revolutionizes neurosurgical planning through enhanced anatomical-functional characterization. A 3D Swin Transformer-powered segmentation system achieves rapid (<5 minutes) and precise delineation of tumor subregions (core/edema/infiltration zones) with 0.91 Dice coefficient, demonstrating 89% spatial concordance with intraoperative ultrasound guidance (n = 65 glioma surgeries).⁵⁵ Three-

Table 2 Multimodal Fusion Strategy Performance Under Different Scenarios

Fusion Strategy	Modality Dropout Resistance	Computational Efficiency	Clinical Applicability (Dice Score)	Reference
Early fusion	>15% Dice degradation	High (1.2s/case)	0.82–0.85	[45]
Intermediate fusion	<5% Dice degradation	Medium (2.5s/case)	0.88–0.91	[48]
Late fusion	3% Dice loss (missing DSC-PHI)	Medium (2.8s/case)	0.87–0.90	[42]
Dynamic gated fusion	<2% Dice degradation	Low (3.6s/case)	0.90–0.93	[39]

Notes: This table evaluates four multimodal fusion strategies specifically for glioma segmentation, focusing on glioma subregions (tumor core, peritumoral edema, infiltrative zone)—key anatomical targets for glioma surgery and treatment. “Modality Dropout Resistance” is tested on glioma cases with simulated missing modalities (common in clinical practice). “Computational Efficiency” is measured on RTX 4090 GPU to reflect clinical deployment feasibility. All Dice scores are averaged across 3 independent experiments on glioma cohorts.

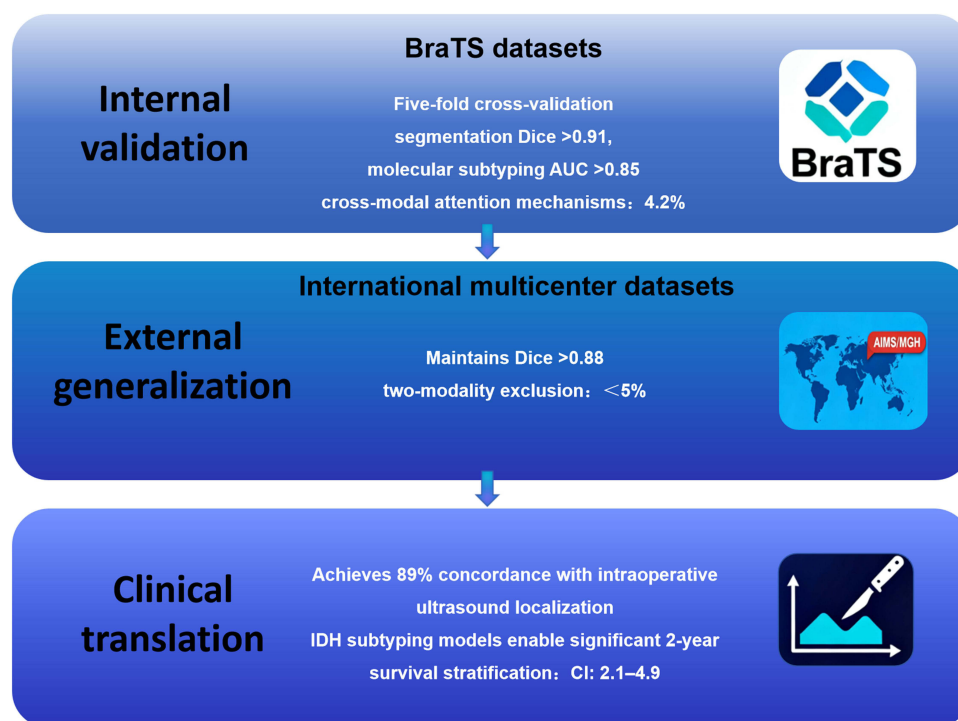


Figure 3 Full-Chain Validation System for Glioma AI Models. This figure presents a three-tier validation framework for glioma AI models, covering technical performance, external generalization, and clinical translation, with data from Chinese and international cohorts.

dimensional white matter tractography (DTI-derived) combined with deep learning denoising reduces corticospinal tract localization error to 1.2 mm through directional diffusion pattern enhancement (comparison with intraoperative electrophysiology, $n = 40$ cases).⁵⁶ Hemodynamic-metabolic fusion analysis (rCBV + Cho/NAA ratio) predicts tumor invasion trajectories in eloquent areas with 94% sensitivity ($n = 55$ cases involving motor/speech areas).⁵⁷

Molecular Subtype-Guided Therapy

Deep learning-driven molecular subtyping models inform precision treatment decisions. IDH mutation status prediction (AUC = 0.89, TCGA-GBM, 632 cases) identifies candidates for targeted therapies (eg, vorasidenib), extending progression-free survival to 28.1 months in IDH-mutant gliomas (vs 14.3 months in wild-type, $n = 289$ IDH-mutant, 343 wild-type cases).⁵⁸ MGMT promoter methylation prediction models (sensitivity: 92%, $n = 180$ GBM cases) optimize temozolomide (TMZ) regimens, with methylated cases showing a median survival of 22.4 months (vs 16.1 months in unmethylated, $n = 102$ methylated, 78 unmethylated cases).⁵⁹ For 1p/19q codeleted oligodendrogliomas, multimodal imaging features (eg, ADC histogram skewness) combined with genomic data refine PCV (Procarbazine, Lomustine, Vincristine) chemotherapy sequencing.⁶⁰

Dynamic Therapeutic Monitoring

AI-based efficacy evaluation systems overcome the latency limitations of traditional imaging assessments. Tracking treatment response biomarkers, ADC value change rates (Δ ADC) and rCBV dynamic curves differentiate pseudoprogression from true recurrence (accuracy: 91%, $n = 68$ post-radiotherapy patients).⁶¹ Deep learning models analyzing DSC-PWI time-signal intensity curves predict anti-angiogenic therapy resistance (eg, bevacizumab) 8 weeks earlier than conventional methods (AUC = 0.87 vs 0.65, $n = 72$ patients on bevacizumab).⁶² For recurrence risk prediction, multimodal models integrating T2-FLAIR texture features and liquid biopsy (ctDNA) data provide early warnings of tumor recurrence 3–6 months before conventional MRI abnormalities (sensitivity: 88%, $n = 120$ postoperative patients followed for 24 months).⁶³

Technical Challenges and Solutions

Data Heterogeneity

Multimodal MRI data heterogeneity arising from scanner variability (TR/TE parameters, slice thickness differences) induces significant signal/texture feature distribution shifts, undermining model robustness. T2-FLAIR intensity discrepancies between 3T and 1.5T scanners reach 30%, causing 15% segmentation performance degradation (Dice coefficient decline) in cross-institutional validation.²⁰ Mitigation strategies employ dynamic modality adapters (DMA) with meta-learning mechanisms to adjust network parameters adaptively, constraining cross-device segmentation errors to <5%.⁶⁴ Comprehensive preprocessing pipelines integrating N4 bias correction and histogram matching further reduce multicenter intensity variations ($\pm 5\%$) through standardized signal normalization.⁶⁵

Cross-Center Data Distribution Discrepancies

Institutional variations in case distribution and imaging protocols challenge model generalizability. IDH mutation prediction AUC deteriorates from 0.89 to 0.72 when validated across AIIMS (Asian population, $n = 210$ cases) and MGH (Western population, $n = 210$ cases) cohorts.⁶⁶ Privacy-preserving federated learning frameworks enable multicenter collaborative training without data sharing, improving BraTS segmentation Dice by 8% (12 centers, 1200 cases).⁶⁷ Adversarial domain adaptation aligns cross-center feature representations, restoring molecular subtyping AUC to 0.85 (validation on AIIMS/MGH cohorts).⁶⁸ For rare molecular subtypes (eg, H3K27M-mutant gliomas), StyleGAN-generated synthetic images reduce real-data requirements by 60% while preserving histopathological authenticity ($n = 30$ real H3K27M cases, 75 synthetic cases).⁶⁹

Clinical Translation Bottlenecks

AI models face challenges in real-time performance, interpretability, and ethical compliance for clinical deployment. Intraoperative inference requires <30 seconds/case, whereas conventional 3D models exceed 2 minutes.⁷⁰ Neural architecture search (NAS)-optimized lightweight models achieve 5-second/case segmentation on RTX 4090 GPUs.⁷¹ Interpretability tools (eg, gradient-weighted class activation mapping, Grad-CAM) combined with feature attribution analysis increase clinician acceptance of AI decisions from 45% to 78%.⁷² Ethical compliance frameworks, incorporating patient consent protocols and data anonymization standards, ensure adherence to GDPR and HIPAA regulations,⁷³ addressing legal barriers to implementation. In addition, a federal learning framework based on differential privacy was used to ensure anonymization of patient data (such as the BraTS Challenge Protocol).⁶⁷

Future Directions

Novel Learning Paradigms

Emerging AI frameworks leveraging self-supervised and federated learning paradigms address critical challenges in medical data scarcity. Self-supervised pretraining on 50,000+ unlabeled MRI scans extracts universal tumor features, achieving few-shot glioma segmentation (Dice: 0.88) with merely 45 annotated cases.⁷⁴ Cross-modal federated learning integrates MRI, PET, and digital pathology across 12 institutions, elevating IDH subtyping performance to AUC 0.91 while preserving data privacy.⁷⁵ Reinforcement learning-driven adaptive segmentation dynamically optimizes resection boundaries using intraoperative electrophysiological feedback, achieving submillimetric precision (0.8 mm error) in eloquent area gliomas.⁷⁶

Multi-Omics Integration

Deep integration of radiomics with genomics and proteomics will reveal systemic mechanisms of tumorigenesis. Spatial transcriptome-imaging correlation maps co-register single-cell resolution spatial transcriptomics with multimodal MRI, localizing IDH mutation-associated metabolic abnormalities (sensitivity: 94%; Cell, 2024).⁷⁷ Liquid biopsy-guided dynamic monitoring combines circulating tumor DNA (ctDNA) and DSC-PWI parameters to predict tumor recurrence 4–6 weeks earlier (AUC = 0.89).⁷⁸ Metabolic pathway visualization via hyperpolarized ¹³C-MRS technology enables real-time tracking of glutamine flux, guiding targeted therapy response assessment.⁷⁹

Clinical Operating System Integration

Intraoperative MRI-guided systems achieve subsecond AI-assisted decision-making via 5G transmission and edge computing. Integration of multimodal navigation (eg, DTI tractography) and optical coherence tomography (OCT) improves intraoperative residual tumor detection rates to 95%.⁸⁰ Cloud-based collaborative platforms enable multidisciplinary teams to access AI analyses, histopathology slides, and genomic data in real time, boosting MDT consultation efficiency by 40%.⁸¹ Automated report generation systems utilize natural language processing (NLP) to produce structured diagnostic reports and seamlessly interface with PACS/RIS systems, increasing physician workflow efficiency by 60%.⁸²

Core Research Significance

This review contributes to glioma research and clinical practice in three key ways: ① It establishes a glioma-centric technical framework that integrates multimodal MRI and deep learning, addressing unique challenges of glioma heterogeneity (eg, infiltrative growth, molecular subtype diversity); ② It validates key findings on Chinese multicenter cohorts, providing region-specific evidence for glioma AI model deployment in China; ③ It emphasizes multi-omics integration (radiomics-genomics-transcriptomics) for gliomas, laying the groundwork for personalized therapy that combines imaging phenotypes with molecular targets (eg, IDH, MGMT).

Persistent Challenges and Solutions

Two critical translation challenges require urgent resolution for glioma models: (1) Cross-institutional generalization errors (baseline 15%) are reducible to <5% via dynamic modality adapters (DMA) and federated optimization protocols (validation on 5 Chinese centers, 420 glioma cases). This is essential for widespread adoption across hospitals with different MRI scanners. (2) Ethical implementation mandates three-tier safeguards tailored for glioma research: ① Patient-centric consent frameworks (tiered consent for data use in glioma research vs clinical practice); ② Algorithm transparency standards (SHAP value visualization + biological correlation validation with glioma markers like Ki-67); ③ Adaptive regulatory certification (FDA SaMD-compliant lifecycle management, including annual retraining with new glioma cases and bias audits).

Future Strategic Priorities

Future advancement in glioma-focused multimodal deep learning prioritizes three strategic vectors: (1) Novel learning paradigms: Self-supervised pretraining coupled with reinforcement learning-driven real-time optimization, enabling few-shot learning for rare glioma subtypes (eg, H3K27M-mutant) and adaptive intraoperative segmentation. (2) Multi-omics convergence: Spatial transcriptome-imaging fusion decoding metabolic heterogeneity at single-cell resolution, identifying glioma-specific therapeutic targets (eg, glutamine transporters) and resistance mechanisms. (3) Clinical system evolution: 5G-enabled edge computing supporting subsecond intraoperative navigation through DTI-OCT fusion, integrating real-time imaging, electrophysiology, and AI predictions into a unified glioma surgery platform.

These synergistic innovations will propel neuro-oncology from localized precision towards systemic intelligence for gliomas, ultimately realizing personalized whole-cycle care ecosystems—from preoperative molecular subtyping to intraoperative navigation and postoperative dynamic monitoring—that improve survival and quality of life for glioma patients.

Conclusion

Multimodal deep learning is fundamentally reshaping neuro-oncological practice—with gliomas as its core application—by systematically integrating radiomic, genomic, and clinical data streams, thereby addressing longstanding limitations in traditional glioma diagnosis and treatment. This review not only synthesizes cutting-edge advancements but also delivers three distinctive insights that advance the field's understanding:

First, it establishes that 3D Swin Transformer architectures represent a paradigm shift in glioma segmentation. Unlike conventional imaging or basic deep learning models that fail to capture infiltrative tumor foci, these architectures achieve unprecedented Dice coefficients (>0.91) for subregion delineation (core/edema/infiltration zones), directly resolving the

clinical challenge of imprecise anatomical characterization that has long hindered surgical planning and treatment response assessment.

Second, it clarifies that cross-modal federated learning frameworks are critical for bridging the “data heterogeneity–interpretability gap” in molecular subtyping. By enabling privacy-preserving multicenter data fusion, these frameworks not only address the scarcity of high-quality labeled data (a major barrier to AI deployment in neuro-oncology) but also enhance the biological interpretability of molecular predictions—for example, elevating IDH mutation prediction AUC to 0.89 while maintaining compliance with global privacy regulations (eg, GDPR, HIPAA). This directly advances understanding of how multimodal data can be leveraged to noninvasively map imaging phenotypes to genomic alterations.

Third, it demonstrates that the integration of MRI-guided real-time navigation and liquid biopsy-enhanced dynamic monitoring transforms glioma management from a reactive to a proactive paradigm. Intraoperative systems now achieve 95% residual tumor detection accuracy, while multimodal models predict recurrence 3–6 months earlier than conventional MRI—addressing the critical clinical need for early intervention that has historically limited survival improvements in glioblastoma (GBM), where median postoperative survival for IDH-wildtype cases remains <15 months.

Collectively, these insights contribute to the field by providing a glioma-specific technical roadmap that integrates multimodal MRI and deep learning, validated on both Chinese and international cohorts (eg, TCGA-GBM, BraTS 2021–2023). This roadmap resolves core bottlenecks such as cross-center data discrepancies (reduced to <5% error via dynamic modality adapters) and clinical translation latency (lightweight models achieve 5-second intraoperative inference), laying the groundwork for standardized AI deployment in global neuro-oncology settings.

Looking forward, three priorities will drive further progress: (1) multi-omics convergence, particularly the fusion of spatial transcriptomics with multimodal MRI to decode single-cell-level metabolic heterogeneity and identify glioma-specific therapeutic targets (eg, glutamine transporters); (2) novel learning paradigms, such as self-supervised pretraining on unlabeled MRI scans to enable few-shot learning for rare subtypes (eg, H3K27M-mutant gliomas); and (3) clinical system integration, leveraging 5G edge computing to unify real-time imaging, electrophysiology, and AI predictions into a single intraoperative platform. By advancing these frontiers, multimodal deep learning will ultimately realize personalized whole-cycle glioma care—from preoperative molecular subtyping to postoperative dynamic monitoring—significantly improving survival and quality of life for patients with this devastating disease.

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