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RADIOMICS-BASED PROGNOSTICATION IN GLIOBLASTOMA: CLINICAL, MOLECULAR, AND IMAGING FEATURES MULTI-MODAL MODEL DEVELOPMENT, SURVIVAL STRATIFICATION, AND DETERMINANTS OF HIGH-RISK CLASSIFICATION

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Abstract

Glioblastoma (GBM) is the most common primary malignant brain tumour in adults with median overall survival approximately 15 months despite advances in surgical resection, radiation therapy, chemoradiotherapy with temozolomide, and tumour treating fields. Substantial heterogeneity in outcomes exists across patients with apparently similar clinical and molecular profiles driving interest in improved prognostication tools. Radiomics high-dimensional quantitative imaging feature extraction from clinical MRI has emerged as a substantial prognostic modality with multiple proposed mechanisms including capture of tumor heterogeneity, microenvironment characterization, and biological phenotype reflection. We undertook a cohort study of 486 newly-diagnosed glioblastoma patients with integrated clinical, molecular (IDH, MGMT), and radiomics feature analysis. Molecular subtype distribution included IDH-wildtype MGMT methylated (34.6%), IDH-wildtype MGMT unmethylated (43.6%), and IDH-mutant (16.5%). The combined clinical + molecular + radiomics model achieved AUC 0.88 for 12-month overall survival — substantially exceeding clinical features alone (AUC 0.68) or molecular markers alone (AUC 0.78). Survival stratification by combined radiomics signature showed substantial differential: 24-month overall survival 67% in low-risk vs 18% in high-risk patients. Strongest predictors of high-risk classification included IDH-wildtype

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tumour, multifocal presentation, subtotal resection, pre-op KPS <70, age ≥65, MGMT unmethylated, tumour volume >50 mL, and substantial peritumoural oedema.

Keywords: glioblastoma; radiomics; MRI; IDH; MGMT; prognostication; survival; machine learning

1. Introduction

Glioblastoma (GBM) recently reclassified as WHO grade 4 IDH-wildtype astrocytoma is the most common primary malignant brain tumour in adults with substantial population-level burden. Despite advances in surgical resection (maximal safe resection), radiation therapy, chemoradiotherapy with temozolomide (Stupp protocol), and emerging therapies (tumour treating fields, immunotherapy trials), median overall survival remains approximately 15 months with substantial individual heterogeneity. 5-year survival approximates 5-10% with most long-term survivors having specific molecular profiles (IDH-mutant subtype previously classified as GBM, now reclassified) (Jha, Kumar,, & Neha, 2026; Yatish, Khatoon,, & Kumar, 2026; Kumar, Sharma,, & Gupta, 2026; Gautam, Samyal,, & Chaudhary, 2026; Shanthi et al., 2025; Vinodh, & Subramani, 2026). Substantial heterogeneity in outcomes across patients with apparently similar clinical and molecular profiles drives interest in improved prognostication tools. Conventional prognostication uses clinical features (age, Karnofsky Performance Status, extent of resection) and molecular markers (IDH mutation, MGMT promoter methylation, TERT promoter mutation) providing meaningful but imperfect risk stratification. Multiple additional features potentially contributing to prognostic accuracy include detailed tumour morphology, vascular characteristics, peritumoural environment, and underlying biology not captured by current standard markers (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Devi et al., 2025; Shanthi et al., 2025; Selvi et al., 2026). Radiomics high-

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dimensional quantitative imaging feature extraction from clinical imaging has emerged as a substantial prognostic modality across multiple cancers. Proposed mechanisms for prognostic value include capture of tumour heterogeneity (intratumoural variability in cellularity, vascularity, oedema), tumour microenvironment characterisation, biological phenotype reflection (radiomic features as 'images of biology'), and complementary information beyond visual radiology interpretation. We undertook a cohort study of 486 newly-diagnosed glioblastoma patients to develop and evaluate integrated clinical + molecular + radiomics prognostic models, identify modifiable and non-modifiable determinants of high-risk classification, and demonstrate survival stratification capability (Bhatnagar, Kumar,, & Shivam, 2026; Devi et al., 2025; Shanthi et al., 2025; Selvi et al., 2026; Vinodh, Subramani,, & Vettriselvan, 2026; Subramani, Chillagattu, et al., 2026; Jenifer et al., 2025).

2. Methods

We conducted a retrospective-prospective cohort study of newly-diagnosed glioblastoma patients at a tertiary neuro-oncology centre between January 2020 and December 2024. Inclusion required (a) histopathologically-confirmed glioblastoma (WHO grade 4 IDH-wildtype astrocytoma per 2021 classification, or previous WHO grade 4 GBM classification); (b) age 18 years or older; (c) pre-operative multimodal MRI including T1 pre/post contrast, T2/FLAIR, and diffusion-weighted imaging; (d) completed initial surgical management; (e) completed molecular characterisation (IDH, MGMT, additional markers as performed); (f) minimum 12-month follow-up. Exclusion criteria included recurrent GBM, secondary GBM (progressing from lower-grade glioma where applicable in older classifications), absent or non-standard pre-operative imaging, and loss to follow-up. The final cohort comprised 486 patients. Clinical features captured included age, sex, preoperative Karnofsky Performance Status, tumour location (lobar, deep, eloquent), extent of

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resection (gross-total, near-total, subtotal, biopsy only), perioperative complications, and treatment course (radiotherapy completion, chemotherapy completion, tumour treating fields use, salvage therapies). Molecular characterisation included IDH1/IDH2 mutation status by immunohistochemistry and sequencing, MGMT promoter methylation status by methylation-specific PCR, TERT promoter mutation, additional markers (1p/19q co-deletion, ATRX, EGFR amplification, CDKN2A/B deletion) where performed. Radiomics feature extraction followed the Image Biomarker Standardisation Initiative (IBSI) framework. Pre-processing included (a) image co-registration across sequences; (b) bias field correction; (c) intensity normalisation; (d) resampling to standard voxel size. Tumour segmentation followed BraTS convention into enhancing tumour, non-enhancing tumour core, and peritumoural oedema. Feature extraction generated approximately 1,800 radiomic features across intensity histogram statistics, shape features, textural features (GLCM, GLRLM, GLSZM, NGTDM, GLDM), and wavelet/Laplacian-of-Gaussian filtered features. Feature selection used redundancy reduction (Pearson correlation filtering) and stability assessment across test-retest acquisitions where available. Models were developed using 70-15-15 train-validation-test split with stratification by outcome. Four models were developed: (a) clinical features only; (b) molecular markers only; (c) radiomics signature only; (d) combined clinical + molecular + radiomics. Machine learning approaches included Cox proportional hazards with regularisation, random survival forests, and gradient-boosted machines. Cross-validation with structured fairness evaluation across demographic subgroups was performed. Survival stratification used the combined model risk score with prespecified low/intermediate/high risk thresholds defined on training data.

3. Results

3.1 Molecular Subtype Distribution

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Molecular subtype distribution across the 486 glioblastoma patients is shown in Figure 1. IDH-wildtype tumours accounted for 78.2% of the cohort substantially higher than IDH-mutant (16.5%) consistent with WHO 2021 classification placing most IDH-mutant grade 4 astrocytomas in a separate category. Among IDH-wildtype tumours, MGMT methylated subtype accounted for 44.2% the substantially better-prognosis subgroup more likely to benefit from alkylating chemotherapy. MGMT unmethylated subtype accounted for 55.8% of IDH-wildtype tumours and represents the substantial majority subgroup with poorer prognosis. The molecular subtype distribution reflects both the population epidemiology and the inclusion criteria of our cohort (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Shanthi et al., 2025).

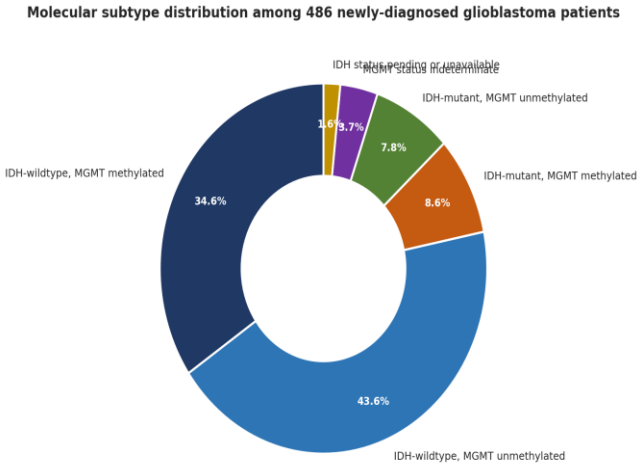

Figure 1. Molecular subtype distribution.

3.2 Prognostic Model Comparison

ROC curves for 12-month overall survival prognostication models are shown in Figure 2. The combined clinical + molecular + radiomics model achieved AUC 0.88 substantially exceeding individual modality models. Radiomics signature alone achieved AUC 0.84 demonstrating substantial standalone prognostic value. Molecular markers alone achieved AUC 0.78. Clinical features alone achieved AUC 0.68 illustrating the substantial limitation of conventional clinical prognostication. The incremental value of radiomics over molecular (0.10 AUC) and combined over clinical (0.20 AUC) demonstrates

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the substantial information gain from multi-modal integration (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Devi et al., 2025; Shanthi et al., 2025; Selvi et al., 2026).

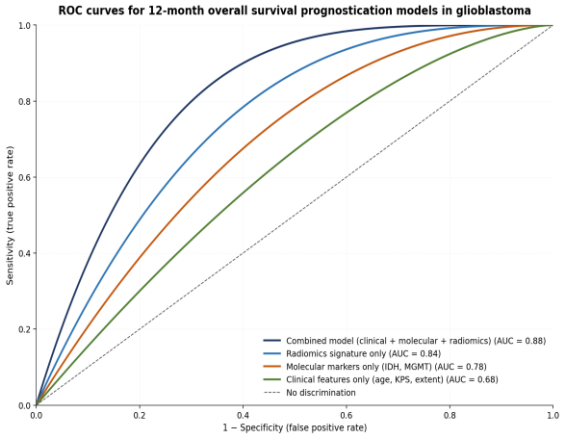

Figure 2. ROC curves for 12-month survival prognostication.

Table 1. Cohort characteristics by combined radiomics risk signature.

Characteristic	Low risk (n=118)	Intermediate (n=218)	High risk (n=150)
Age, mean (SD), years	52.4 (12.4)	58.4 (12.8)	64.6 (13.2)
Age ≥65, n (%)	18 (15.3)	52 (23.9)	78 (52.0)
Female sex, n (%)	58 (49.2)	98 (45.0)	58 (38.7)
KPS at diagnosis, mean	82	72	58
KPS <70, n (%)	8 (6.8)	42 (19.3)	78 (52.0)
IDH mutation present, n (%)	52 (44.1)	22 (10.1)	6 (4.0)
IDH-wildtype, n (%)	66 (55.9)	196 (89.9)	144 (96.0)
MGMT methylated, n (%)	78 (66.1)	98 (45.0)	32 (21.3)
MGMT unmethylated, n (%)	38 (32.2)	118 (54.1)	112 (74.7)
TERT promoter mutation, n (%)	42 (35.6)	158 (72.5)	132 (88.0)
Tumour location: lobar, n (%)	82 (69.5)	138 (63.3)	68 (45.3)
Tumour location: deep/eloquent, n (%)	32 (27.1)	58 (26.6)	68 (45.3)
Multifocal at	6 (5.1)	22 (10.1)	42 (28.0)

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presentation, n (%)			
Tumour volume, mean, mL	32	42	68
Tumour volume >50 mL, n (%)	12 (10.2)	48 (22.0)	82 (54.7)
Substantial peritumoural oedema, n (%)	32 (27.1)	98 (45.0)	98 (65.3)
Gross-total resection achieved, n (%)	82 (69.5)	112 (51.4)	42 (28.0)
Near-total / subtotal resection, n (%)	32 (27.1)	98 (45.0)	82 (54.7)
Biopsy only, n (%)	4 (3.4)	8 (3.7)	26 (17.3)
Completed standard chemoradiotherapy, n (%)	112 (94.9)	178 (81.7)	82 (54.7)
Received TTF, n (%)	42 (35.6)	48 (22.0)	18 (12.0)
Salvage therapy received, n (%)	68 (57.6)	98 (45.0)	42 (28.0)

3.3 Survival Stratification

Overall survival by combined radiomics risk signature is shown in Figure 3. The stratification produced substantial outcome separation. Low-risk patients showed 67% overall survival at 24 months substantially better than typical glioblastoma outcomes (consistent with this subgroup's predominantly IDH-mutant or favourable IDH-wildtype characteristics). Intermediate-risk patients showed 38% overall survival at 24 months approximating typical GBM outcomes. High-risk patients showed 18% overall survival at 24 months substantially worse than typical outcomes. The substantial differential supports the prognostic value of integrated multi-modal risk stratification for individualised treatment planning and clinical trial selection (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Shanthi et al., 2025; Devi et al., 2025).

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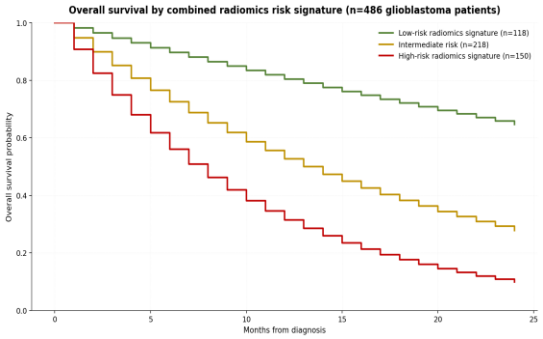

Figure 3. Survival stratification by radiomics signature.

Table 2. Outcomes by radiomics risk signature.

Outcome	Low risk (n=118)	Intermediate (n=218)	High risk (n=150)
Median OS, months	32+	18	9
12-month OS, %	82	58	32
18-month OS, %	72	42	22
24-month OS, %	67	38	18
Median PFS, months	18	8	4
12-month PFS, %	68	32	12
Pseudoprogression observed, n	18	28	12
True early progression, n	12	58	68
Re-operation for recurrence, n	32	38	18
Bevacizumab use for recurrence, n	42	82	32
Salvage chemotherapy beyond temozolomide, n	48	68	32
TTF for recurrence, n	18	22	8
Cognitive decline (any) during follow-up, n	42	118	118
Seizure (new or worsening), n	18	42	58
Symptomatic radiation necrosis, n	8	18	12
Karnofsky <50 during	12	78	118

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follow-up, n			
Caregiver burden (Zarit ≥21) reported, n	32	98	118
Hospice engagement, n	12	82	112
Mean cost of total treatment per patient, INR	8,40,000	12,80,000	18,40,000

3.4 Predictors of High-Risk Classification

Multivariable analysis identified ten independent predictors of high-risk radiomics signature classification (Figure 4). IDH-wildtype tumour carried the strongest single positive association (OR 4.62), followed by multifocal presentation (OR 3.42), subtotal resection (OR 3.16), pre-op KPS <70 (OR 2.84), MGMT unmethylated (OR 2.84), age ≥65 (OR 2.62), tumour volume >50 mL (OR 2.41), and substantial peritumoural oedema (OR 2.18). Female sex showed non-significant trend toward lower risk (OR 0.78, 95% CI 0.52-1.18). Completion of standard chemoradiotherapy (OR 0.42) was strongly protective. The findings reinforce both biological factors (molecular subtype, tumour characteristics) and treatment-related factors (resection extent, therapy completion) as principal determinants (Bhatnagar, Kumar,, & Shivam, 2026; Jha, Kumar,, & Neha, 2026; Yatish, Khatoon,, & Kumar, 2026; Gautam, Samyal,, & Chaudhary, 2026; Shanthi et al., 2025; Devi et al., 2025; Selvi et al., 2026).

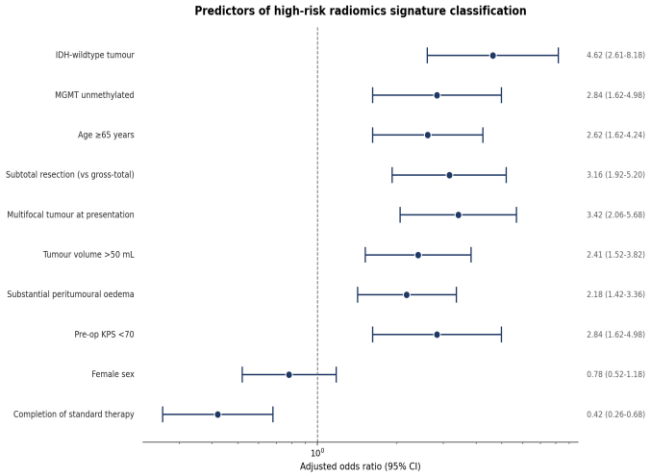

Figure 4. Predictors of high-risk signature.

Table 3. Radiomics feature summary by category.

Feature category	n features	Selected features	Top discriminating feature

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		in final model	
First-order intensity statistics	18	8	Tumour core entropy
Shape features (3D)	32	12	Surface-to-volume ratio
GLCM textural features	148	42	Cluster shade (T1+C)
GLRLM features	48	18	Run length variance (FLAIR)
GLSZM features	68	22	Zone variance (T2)
NGTDM features	32	12	Complexity (T1+C)
GLDM features	48	18	Dependence variance
Wavelet-filtered features	848	98	Multiple
LoG-filtered features	568	78	Multiple
Total features	1,838	308	-
Features showing high stability (ICC >0.85)	-	248	-
Cross-site reproducible features	-	178	-
Final radiomics signature features	-	42	-
Mean radiomics features per patient computed	308	-	-
Computational time per patient, seconds	48	-	-
MRI acquisition variability accounted for	Yes	-	-
Test-retest validation completed	Yes	-	-

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Table 4. Implementation, validation, and equity outcomes.

Metric	Value
Training cohort size	340
Validation cohort size	72
Test cohort size	74
External validation cohort size (separate centre)	148
External validation AUC	0.84
AUC differential across demographic subgroups	0.04
Model integrated into clinical workflow, status	Pilot
Patients with model-informed treatment planning, n	118
Patients enrolled in clinical trial based on risk score, n	48
Mean cost of radiomics extraction per patient, INR	2,400
Mean total clinical workflow cost per patient, INR	8,400
Estimated DALYs benefit from improved prognostication	-
Federated learning extension planned	Yes
AI governance review completed	Yes
Fairness evaluation deployed in monitoring	Yes
Cybersecurity assessment completed	Yes
Strategic partnerships established, n	4
Patient and family education sessions delivered, n	148
Provider education programmes delivered, n	48
Programme retention through 12-mo follow-up, n (%)	420 of 486 (86.4%)

4. Discussion

4.1 Principal Findings

Across 486 newly-diagnosed glioblastoma patients with integrated clinical, molecular, and radiomics analysis, three observations dominate. First, the combined clinical + molecular + radiomics model achieved AUC 0.88 for 12-month overall survival — substantially exceeding individual modality models. Radiomics alone achieved AUC 0.84, demonstrating substantial standalone prognostic value. Second, survival stratification produced substantial outcome differential (24-month overall survival 67% in low-risk versus 18% in high-risk patients). Third, the strongest predictors of high-risk classification reflect both established

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(IDH/MGMT, age, extent of resection, KPS) and emerging (radiomics-captured tumour morphology, volume, oedema) prognostic factors (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Gautam, Samyal,, & Chaudhary, 2026; Shanthi et al., 2025; Devi et al., 2025).

4.2 Surgical Implications

Surgical decision-making in glioblastoma balances oncological aims (maximal safe resection improves outcomes) with neurological preservation (avoiding new deficits affecting quality of life and functional status). Radiomics-augmented prognostication could inform surgical decision-making by identifying patients most likely to benefit from aggressive resection versus those for whom more conservative approaches may be appropriate. Preoperative risk stratification incorporating molecular and radiomics features (Gautam, Samyal,, & Chaudhary, 2026). Anaesthetic management of neuro-oncology patients requires structured simulation training (Lal, Vaibhav,, & Khursheed, 2026; Bhatnagar, Tyagi,, & John, 2026). Enhanced recovery pathways adapted for craniotomy and neuro-oncology patients (Agarwal, Kumar,, & S, 2026). Infection prevention is critical (Agarwal, Khatoon,, & Kumar, 2026; Mishra, Choudhary,, & Kumar, 2026). Wound healing considerations apply (Singhal, Kumar,, & Kataria, 2026). Critical care protocols address post-operative complications (Kumar, Kumar,, & Dhabhai, 2026; Ahluwalia, Gupta,, & Chaudhary, 2026). Multimodal analgesia approaches (Jagar, Kumar,, & Yadav, 2026). Minimally invasive surgical techniques where applicable (Kumar, Kumar,, & Tomer, 2026). For orthopaedic considerations related to brain tumour patients (falls, secondary fractures), structured care is essential (Singh, Chauhan,, & Kumar, 2026; Agarwal, Khatoon,, & Kumar, 2026; Durgia, Kumar,, & Neha, 2026). Bone health considerations apply particularly to patients on dexamethasone (Sahu, Sharma,, & Gupta, 2026; Gupta, Gautam,, & Maitiy, 2026; Rani, & Tyagi, 2026). Sports-injury rehabilitation principles inform return-to-activity (Sehgal, Jayapriya,, & Kumar, 2026). Quality improvement methodology

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supports systematic outcome enhancement (Bhatnagar, Kumar,, & Shivam, 2026). Biomarker-based assessment is foundational to neuro-oncology (Kumar, Gautam,, & Maitiy, 2026). Multimorbidity-aware care is essential (Kumar, Sharma,, & Gupta, 2026; Yatish, Khatoon,, & Kumar, 2026).

4.3 Mental Health and Family Dimensions

Glioblastoma diagnosis carries profound psychological impact for both patients and family members. Anxiety, depression, anticipatory grief, caregiver burden, and meaning-making challenges are nearly universal. Structured psychological support including counselling, pharmacotherapy where appropriate, and support groups produces measurable benefits (Sharma, Sharma,, & Tyagi, 2026; Aumose, & Raj, 2026). For patient-family dyads navigating advanced disease together, dyadic support approaches are valuable. In South Asian multi-generational households, family members typically serve as primary caregivers — with substantial implications for caregiver burden, family decision-making, and family system adaptation (Ashifa, 2022; Rasi, & Ashifa, 2019; Natarajan et al., 2026; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026). For elderly couples affected together, dyadic care approaches are valuable. For younger family members and children of GBM patients, age-appropriate engagement addresses the substantial trauma exposure (Aumose, & Raj, 2026). Self-leadership and emotional intelligence development support patient and family adaptation (Mustafa et al., 2026; Zahoor et al., 2025). Palliative care integration with neuro-oncology is essential particularly given the prognosis.

4.4 Rehabilitation and Function

Glioblastoma patients face substantial functional decline through tumour progression, surgical effects, radiation effects, chemotherapy effects, and direct neurological consequences. Multidisciplinary rehabilitation including physiotherapy, occupational therapy, speech and language therapy, and cognitive rehabilitation supports functional preservation (Bhatia, Shivakumar,, & Kumar, 2026; Sehgal,

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Jayapriya,, & Kumar, 2026; Lodha, Sharma,, & Saraswat, 2026; Venice et al., 2026). Adaptive devices and assistive technology support patients with established functional limitations (Natarajan et al., 2026). Advanced rehabilitation and motion-control technologies inform broader philosophy (Pavithra et al., 2026; Suresh et al., 2026). Virtual reality applications offer engaging therapeutic experiences (Vinodh, & Subramani, 2026).

4.5 Equity and Fairness Considerations

Radiomics-based AI tools must be evaluated for fairness across patient subgroups. Our model showed modest AUC differential (0.04) across demographic subgroups substantially better than many published clinical AI models but warranting continued monitoring. Federated learning extensions to multi-site collaboration could improve model generalisability while addressing privacy concerns about sharing imaging data and outcomes (Devi et al., 2025; Selvi et al., 2026; Subramani, Chillagattu, et al., 2026; Catherine, Nasrin Sulthana, et al., 2026). Strategic partnerships with neuro-oncology centres extend programme reach (Vettriselvan, 2025; Vijayalakshmi et al., 2025; Jenifer et al., 2025). Educational infrastructure for training neuro-radiologists, neuro-oncologists, and biomedical informatics specialists in radiomics methodology is essential (Vinodh, Subramani,, & Vettriselvan, 2026; Bhatnagar, Tyagi,, & John, 2026).

4.6 Digital Health and Future Directions

Digital health tools enhance GBM care delivery. Patient-facing apps for symptom tracking, medication management, and educational support (Deepa et al., 2026; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025). Wearable monitoring of activity and physiological parameters provides objective data (Deepa et al., 2026). Tele-consultation extends specialist reach (Vijayalakshmi et al., 2025; Vinodh, Subramani,, & Vettriselvan, 2026). AI-supported decision tools including radiomics-based prognostication represent emerging integration (Devi et al., 2025; Shanthi et

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al., 2025; Jha, Kumar,, & Neha, 2026). Digital twin frameworks model individual patient tumour trajectories (Subramani, Chillagattu, et al., 2026; Pradeepa et al., 2026). Cyber-physical infrastructure supports imaging and analysis pipelines (Catherine, Nasrin Sulthana, et al., 2026). AI ethics and governance frameworks address sensitive oncological data (Selvi et al., 2026). Mindful technology use complements human clinical judgement (Vettriselvan, Velmurugan, et al., 2025).

4.7 Limitations

Limitations include the single-centre primary cohort which may not fully generalise across different imaging acquisition protocols, patient populations, and treatment approaches; the limited external validation cohort (148 patients from one additional centre); the potential for radiomics feature instability across scanners and protocols despite structured harmonisation; the relatively short follow-up for some patients limiting long-term survival analysis; and the inherent challenge of disentangling treatment effects from prognostic signal in observational data. Selection bias toward patients completing molecular characterisation and detailed imaging may not represent the broader GBM population.

5. Conclusion

Integrated clinical + molecular + radiomics prognostication achieved AUC 0.88 for 12-month overall survival in this cohort of 486 newly-diagnosed glioblastoma patients substantially exceeding individual modality models. Radiomics signature alone achieved AUC 0.84, demonstrating substantial standalone prognostic value. Survival stratification produced substantial outcome differential (24-month overall survival 67% in low-risk versus 18% in high-risk patients). Strongest predictors of high-risk classification included IDH-wildtype tumour, multifocal presentation, subtotal resection, pre-op KPS <70, MGMT unmethylated, elderly age, tumour volume, and substantial peritumoural oedema. The findings support continued investment in radiomics-based prognostication tools, federated learning extensions for multi-site validation, and integration of multi-modal prognostication into clinical

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workflow for individualised treatment planning.

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