Evaluating Pre-Trained Foundation Models for Glioblastoma Overall Survival Prediction

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ABSTRACT

Accurate glioblastoma (GBM) survival prediction from pre-treatment MRI is challenging due to
- limited labeled datasets
- Substantial inter-institu. variability

We investigated whether frozen, pre-trained medical imaging foundation models (FMs) provide transferable representations for overall survival prediction that generalize across institutions without retraining.

Models were developed on **UPENN-GBM** (n=611) and evaluated on three independent external cohorts:
- UCSF-PDGM (n=400)
- CFB-GBM (n=201)
- BraTS-TCGA-GBM (n=97).

Four pre-trained foundation models:
- BrainSegFounder
- VoCo
- BrainIAC
- SAM-Med3D

For feature extraction from T1, T1ce, T2, and T2-FLAIR MRI, which were combined with clinical variables in a DeepSurv model.

The foundation model ensemble achieved a C-index of 0.684 on the UPENN-GBM developing cohort and demonstrated consistent external performance with C-indices of 0.656 (UCSF-PDGM), 0.641 (BraTS-TCGA-GBM), and 0.608 (CFB-GBM). While imaging features did not significantly outperform a clinical-only model, they matched handcrafted radiomics on most cohorts without requiring tumor segmentation. Combining foundation model, radiomics, and clinical features further improved performance across all datasets.

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INTRODUCTION

Glioblastoma (**GBM**)
- The **most common, aggressive** primary malignant brain tumor
- Median overall survival of only 14–16 months despite standard treatment
- Accurate pre-treatment survival prediction is important for risk stratification, treatment planning, and clinical trial enrollment
- Survival prediction remains challenging because of the biological heterogeneity and the limited availability of large datasets
- **MRIs** provides complementary information about tumor morphology and biology and has been investigated for survival prediction
- Deep learning models **overfit** small datasets and generalize poorly across institutions because of variations in imaging protocols, scanners, and patient populations
- Recent **imaging foundation models** have demonstrated strong transferability across medical imaging tasks, but survival prediction is not usually on the scope

This work focuses on evaluating the ability of **pre-trained 3D imaging foundation models** to provide robust and transferable representations for GBM **overall survival prediction** across multiple institutions.

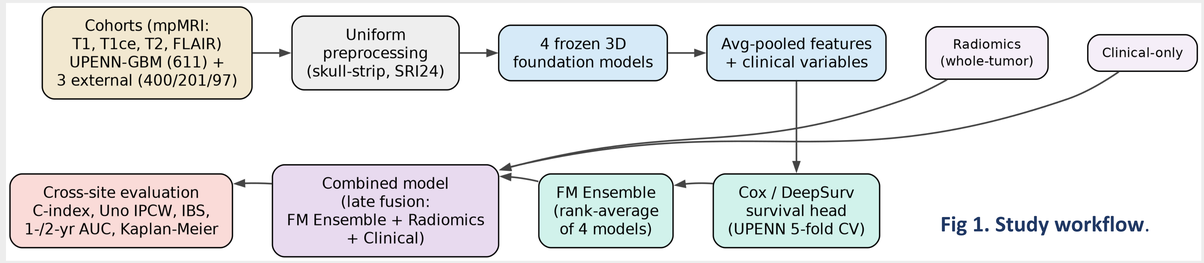


Fig 1. Study workflow.

METHODS AND MATERIALS

In this study we evaluate four state-of-the-art frozen 3D medical-imaging foundation models shown in **Table 1**, for GBM OS prediction from mpMRI.

Models are developed on **UPENN-GBM** (n=611) with five-fold cross-validation and evaluated on **three strictly held-out external cohorts** spanning three countries (**Table 2**).

We benchmark against a Clinical-Only model, a convolutional FM baseline (UniBrain), and a radiomics model, and we test whether late fusion improves prognostication.

Predictions use a Cox proportional-hazards head, and we jointly assess discrimination (C-index, year-1/year-2 ROC-AUC) and calibration (Integrated Brier Score), which we show can diverge **under cross-institutional domain shift**.

Table 1. Evaluated 3D foundational Models.

Model	Architecture	Pre-training data	Pre-training objective	Feat. dim
BrainSegFounder	3D Swin Transformer	~41k brain MRI (healthy + disease)	Two-stage self-supervised	768
VoCo	3D Swin Transformer	~160k CT/MRI (mostly CT)	Volume contrastive	768
BrainIAC	3D ViT (MAE)	~48k multi-sequence brain MRI	Masked autoencoding	768
SAM-Med3D	3D ViT (SAM)	~22k volumes / 143k masks	Promptable segmentation	384
UniBrain	ResNet-34 (CNN)	Brain MRI	Knowledge-enhanced pre-training	768
ResNet-34 (control)	ResNet-34 (CNN)	none (random init)	none (no pretraining)	768

Table 2. Datasets and patient characteristics.

Characteristic	UPENN-GBM ($n = 611$, train)	UCSF-PDGM ($n = 400$)	CFB-GBM ($n = 201$)	BraTS-TCGA-GBM ($n = 97$)
Country	USA	USA	France	USA (multi)
Age, median (range)	64 (19–88)	61 (17–94)	70 (25–85)	60 (19–85)
Male, n (%)	367 (60)	241 (60)	124 (62)	61 (63)
MGMT methylated	18%	70%	N/A	N/A
IDH mutated	2.6%	5.0%	N/A	N/A
OS, median (IQR)	403 (182–684)	369 (173–662)	336 (161–504)	384 (209–634)
Censoring	3.8%	42.2%	0%	8.2%

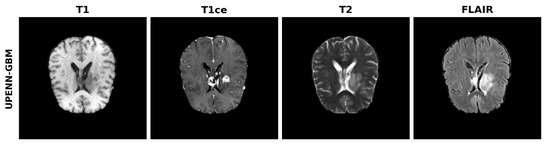


Fig 2. Sample image for UPENN-GBM.

RESULTS

Table 3. Per-model performance, C-index and 1-year/2-year AUC. UPENN-GBM is within-site 5-fold cv; the other cohorts are cross-site.

Model	UPENN-GBM (n=611)		UCSF-PDGM (n=400)		CFB-GBM (n=201)		BraTS-TCGA-GBM (n=97)	
	C-index	AUC (1y/2y)	C-index	AUC (1y/2y)	C-index	AUC (1y/2y)	C-index	AUC (1y/2y)
FM Ensemble	**0.684**	**0.758 / 0.752**	0.656	0.723 / 0.717	**0.608**	**0.679 / 0.652**	**0.641**	**0.686 / 0.703**
BrainIAC	0.650	0.719 / 0.703	0.652	0.723 / 0.709	0.595	0.666 / 0.649	0.616	0.662 / 0.659
SAM-Med3D	0.647	0.692 / 0.711	0.645	0.709 / 0.711	0.606	0.664 / 0.629	0.641	0.687 / 0.699
VoCo	0.635	0.693 / 0.699	0.640	0.697 / 0.699	0.597	0.668 / 0.644	0.639	0.685 / 0.685
BrainSegFounder	0.603	0.628 / 0.664	0.657	0.723 / 0.708	0.590	0.649 / 0.628	0.626	0.646 / 0.708
UniBrain	0.645	0.693 / 0.693	0.659	0.727 / 0.713	0.600	0.654 / 0.641	0.640	0.692 / 0.698
ResNet-34 (no pretrain)‡	0.630	0.672 / 0.688	0.627	0.681 / 0.661	0.568	0.628 / 0.603	0.613	0.646 / 0.631
Clinical-Only	0.650	0.709 / 0.708	0.659	0.727 / 0.717	0.606	0.666 / 0.643	0.634	0.687 / 0.693
FM+Rad+Clin (combined)§	**0.690**	**0.769 / 0.764**	**0.663**	**0.728 / 0.732**	**0.617**	**0.673 / 0.640**	**0.683**	**0.763 / 0.781**

Fig 3. Calibration (Brier score over time) for the Cox FM Ensemble (solid) and the combined FM+radiomics+clinical model (dashed).

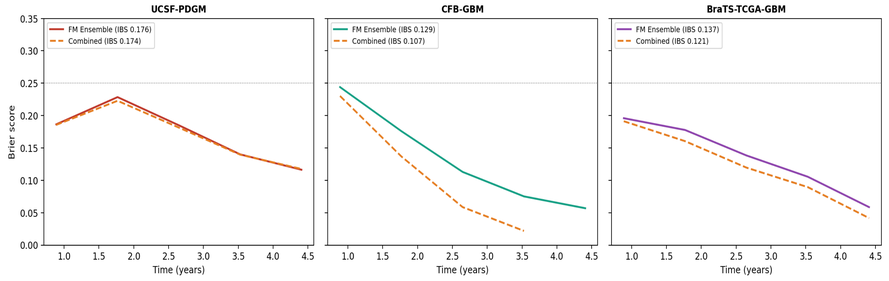
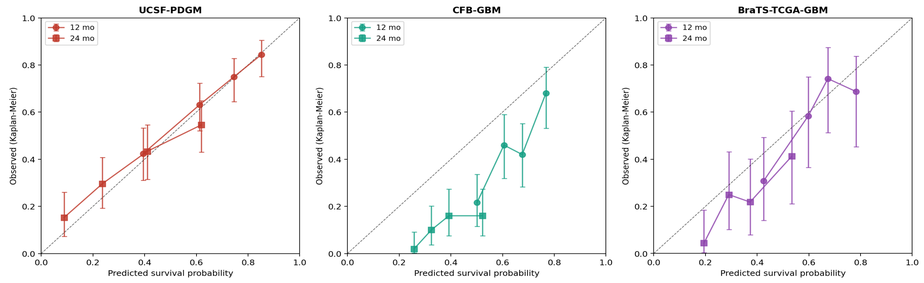


Fig 4. Calibration reliability diagrams for the Cox FM Ensemble (cross-site)



DISCUSSION

Frozen 3D medical imaging foundation models
- Demonstrated **robust** transferability for GBM survival prediction across multiple external cohorts without retraining.
- Foundation model ensemble **consistently provided the most stable performance** and maintained strong discrimination despite differences in acquisition protocols, institutions, and available clinical information, indicating that large-scale pre-training captures transferable prognostic imaging representations.
- Among the individual backbones, performance varied across cohorts, whereas ensembling multiple foundation models improved both robustness and calibration by leveraging complementary feature representations.
- The **ensemble also demonstrated stable calibration** across external datasets, supporting its potential for reliable individualized risk estimation under domain shift.

Although **imaging features did not significantly outperform routine clinical variables**, they achieved **comparable performance without requiring tumor segmentation** and remained applicable when molecular biomarkers were unavailable.

Several **limitations** should be acknowledged.
- The external cohorts lacked complete molecular information.
- The frozen feature representations remain difficult to interpret
- The current late-fusion strategy used a simple unweighted combination.
- Future work should investigate interpretable foundation model representations and learned multimodal fusion approaches.

Table 4. Single-view models vs. the combined late-fusion model. External rows are cross-site (UPenn→external); the UPENN-GBM row is within-site five-fold cross-validation.

Setting	FM Ensemble	Radiomics	Clinical	FM+Rad+Clin
UPENN-GBM	0.684	0.618	0.650	0.690
UCSF-PDGM	0.656	0.596	0.659	0.663
CFB-GBM	0.615	0.554	0.604	0.617
BraTS-TCGA-GBM	0.641	0.670	0.634	0.683