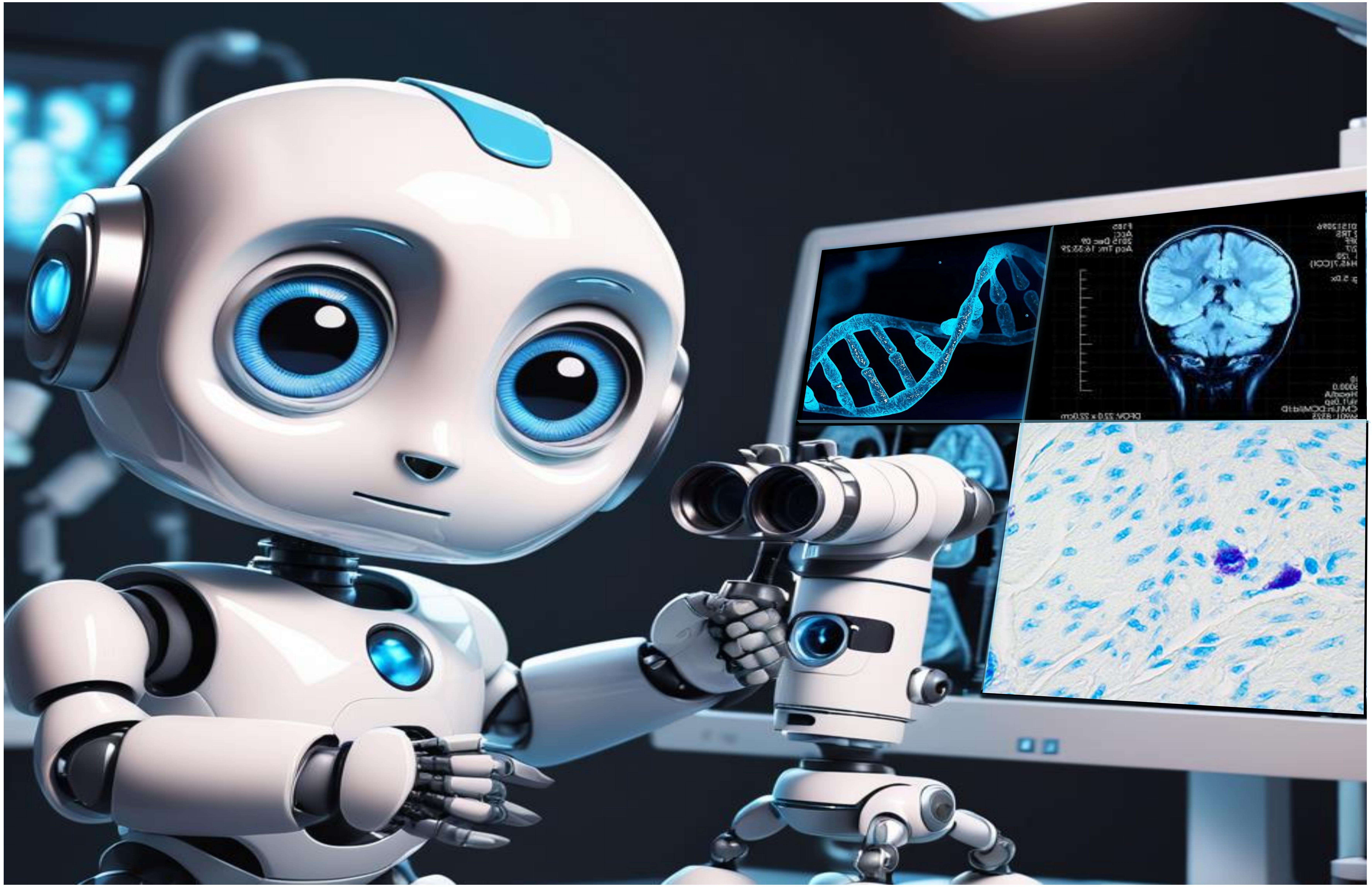
AI-based Multimodal Data Fusion in Oncology



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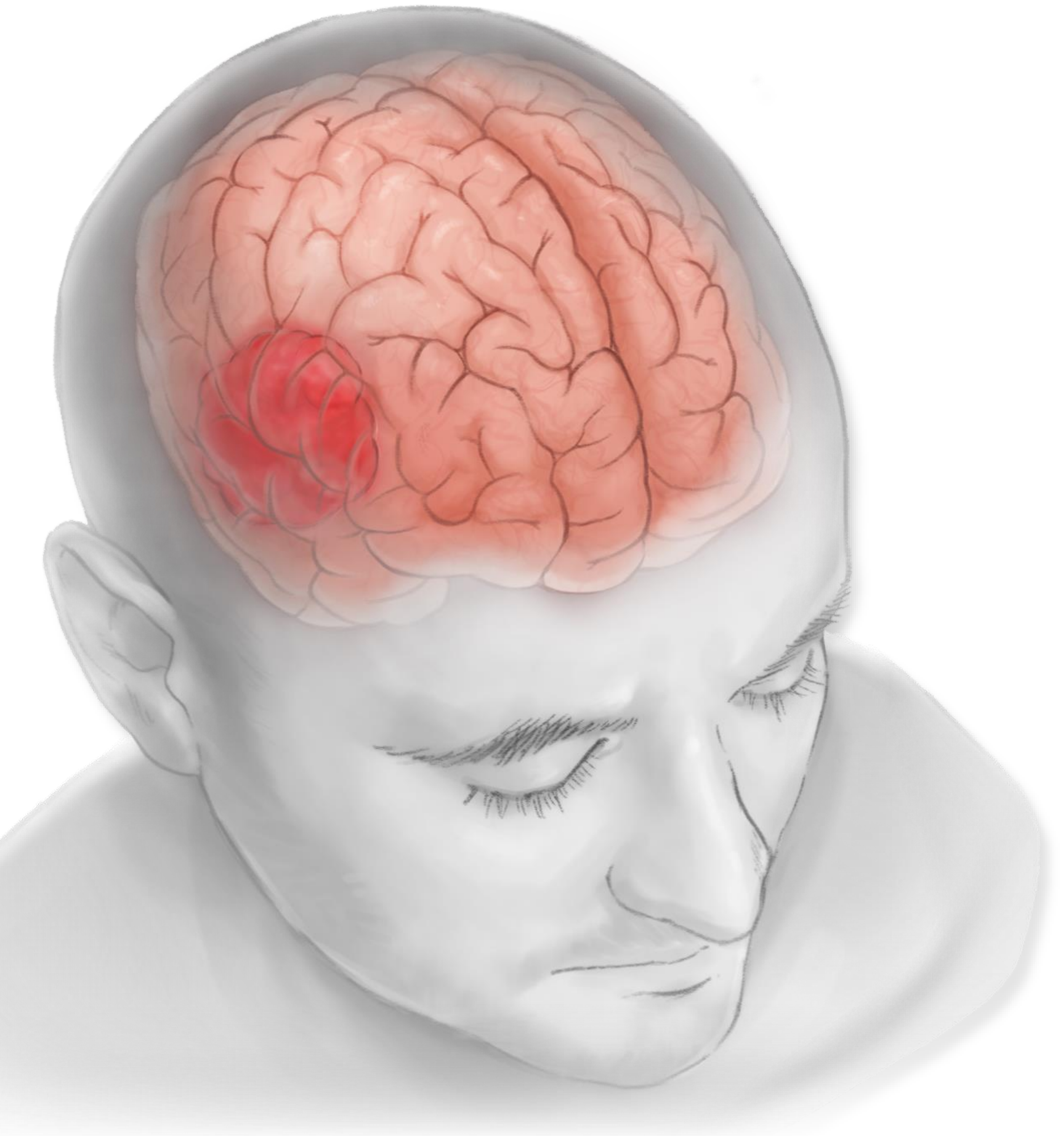
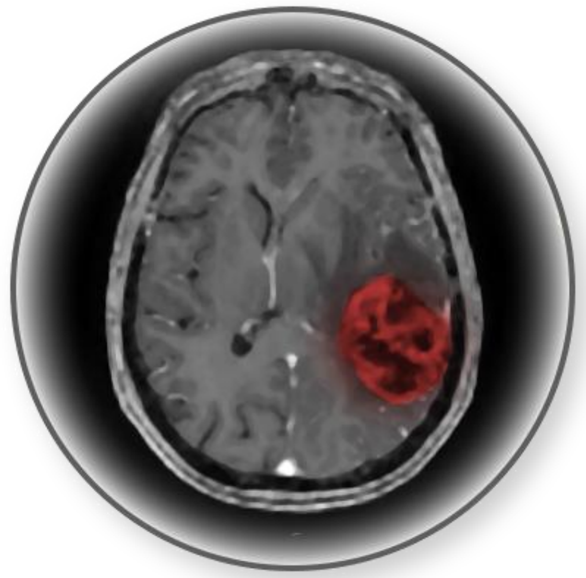
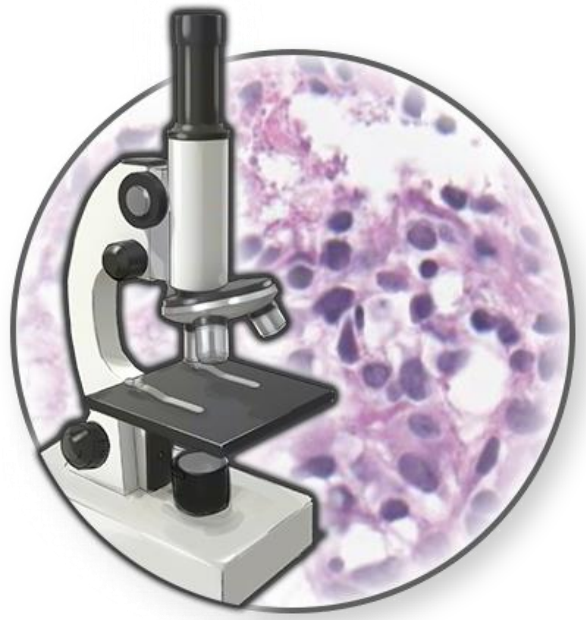
Motivation





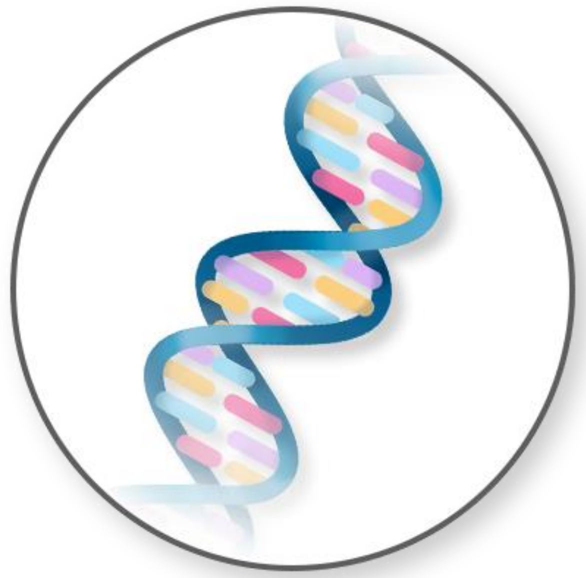
CLINICAL CONTEXT MATTERS

- Unimodal data are insufficient to capture patient-specific state
- Histology + IDH1 mutation status: glioma WHO grade
- Radiology data: macroscopic tumor representation and interaction with host further affect treatment and outcome



MANUAL ASSESSMENT IS CHALLENGING:

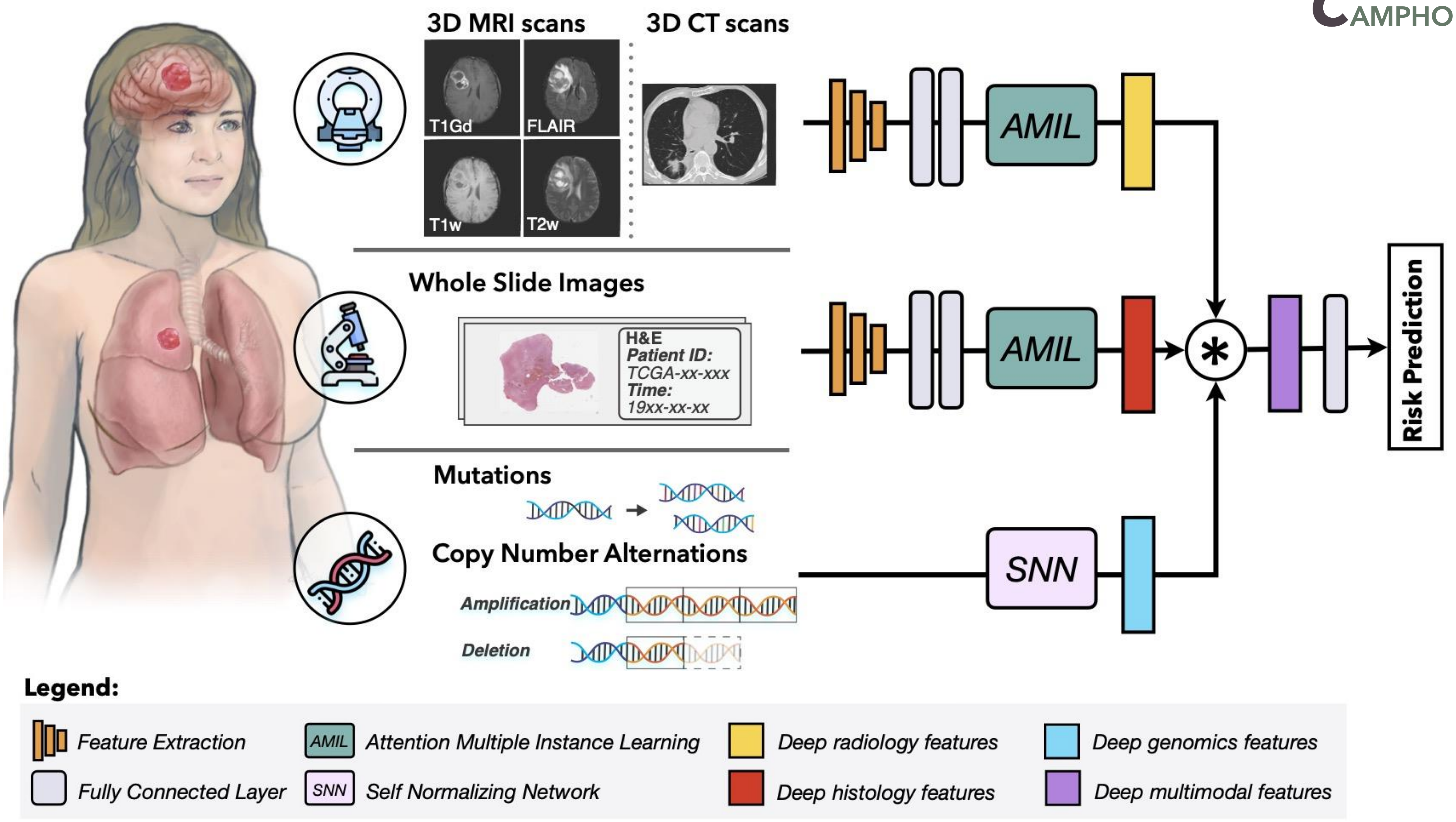
- The amount and complexity of medical data: challenging for experts to adequately assess patient state under the multimodal context
- Manual interpretations can be subjective + biased



NEED:

- Holistic framework for automated integration of multimodal data to enhance patient outcome prediction in oncology

CAncer Multimodal Prognosis from Histology, Omics & RAdiology

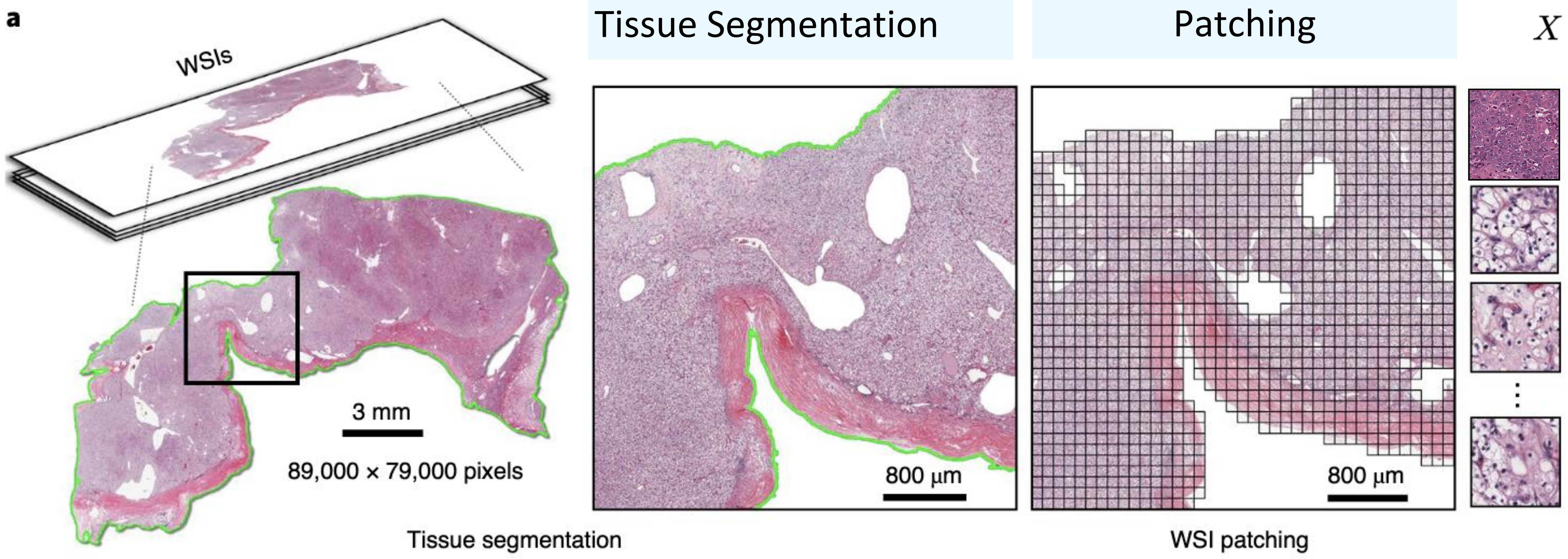


Histology Module

PREPROCESSING

Tissue Segmentation

Patching



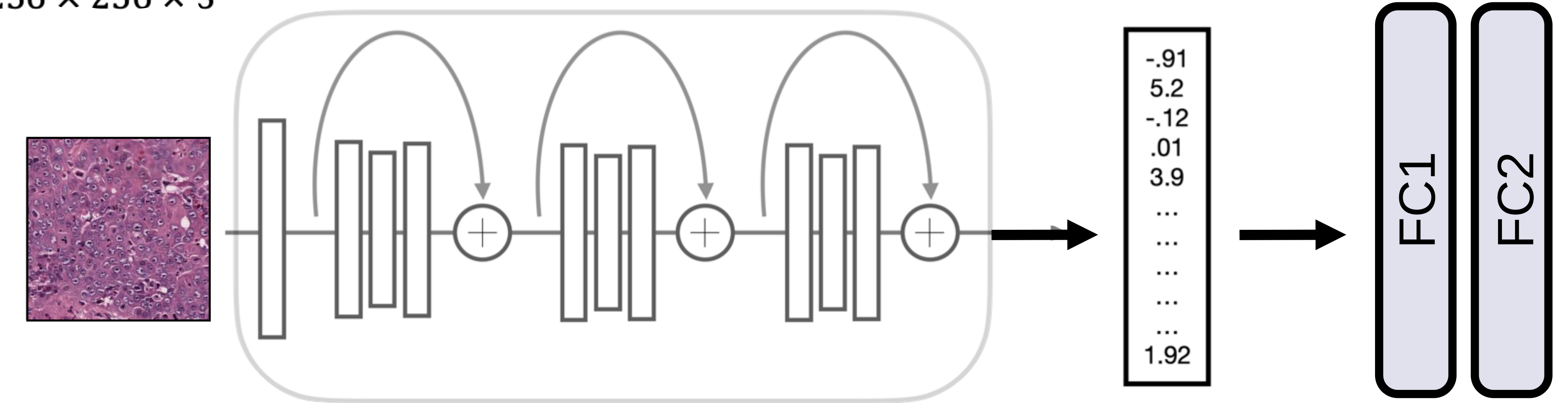
PATCH EMBEDDINGS

$X = \{\mathbf{x}_1, \mathbf{x}_2, \dots, \mathbf{x}_K\}$

Input $\mathbf{x}_k$: $256 \times 256 \times 3$

Feature extraction

Feature refining



Pretrained Encoder

$f(\cdot;\theta) : \mathbb{R}^{C\times H\times W} \rightarrow \mathbb{R}^{1024}$

Embedding $\mathbf{z}_k$: 1024

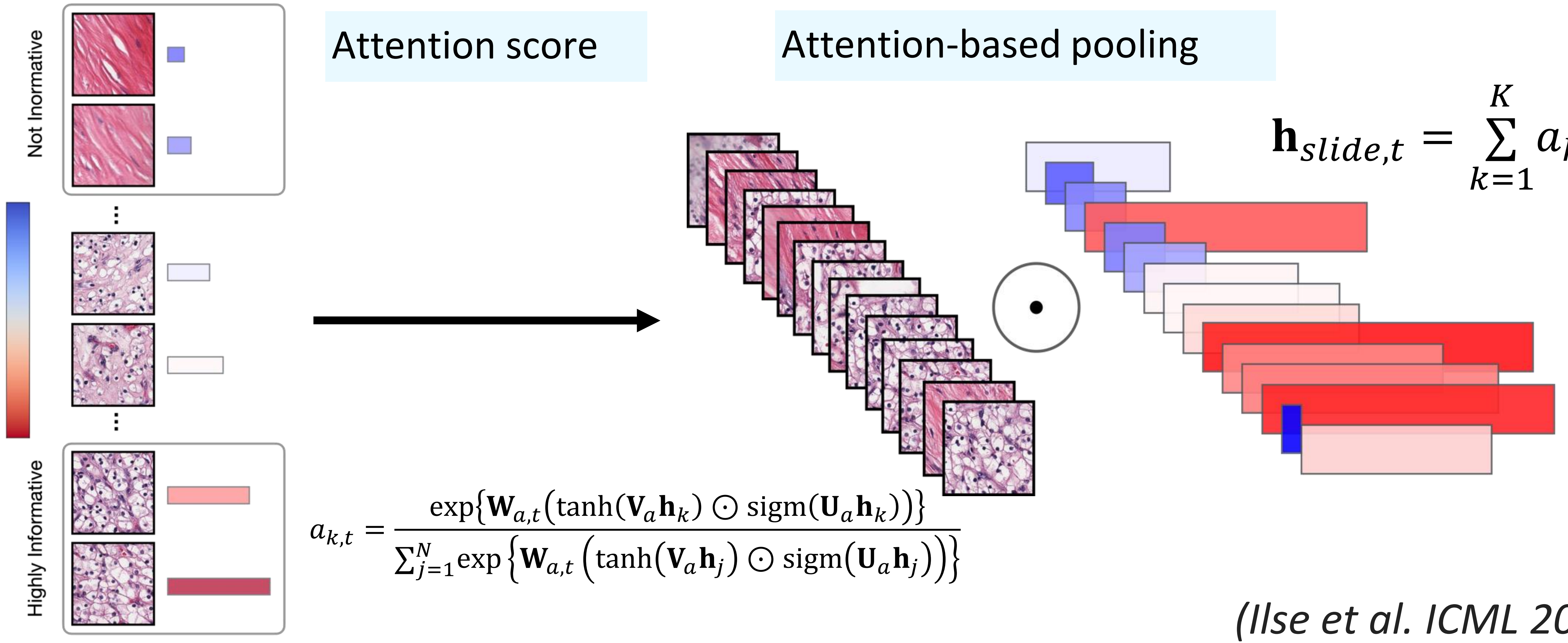
ATTENTION LEARNING

Attention score

Attention-based pooling

Patient Embedding

$$\mathbf{h}_{slide,t} = \sum_{k=1}^{K} a_{k,t}\mathbf{h}_k$$



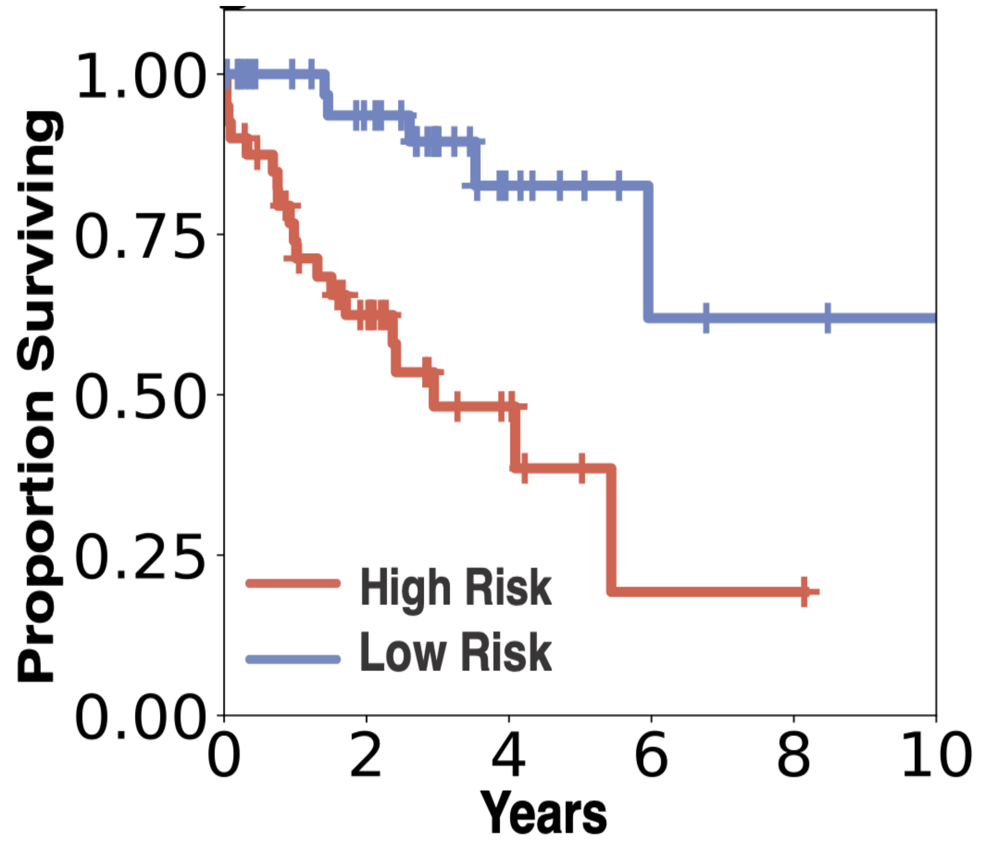
$$a_{k,t} = \frac{\exp\{\mathbf{W}_{a,t}(\tanh(\mathbf{V}_a\mathbf{h}_k) \odot \mathrm{sigm}(\mathbf{U}_a\mathbf{h}_k))\}}{\sum_{j=1}^{N}\exp\left\{\mathbf{W}_{a,t}\left(\tanh(\mathbf{V}_a\mathbf{h}_j) \odot \mathrm{sigm}(\mathbf{U}_a\mathbf{h}_j)\right)\right\}}$$

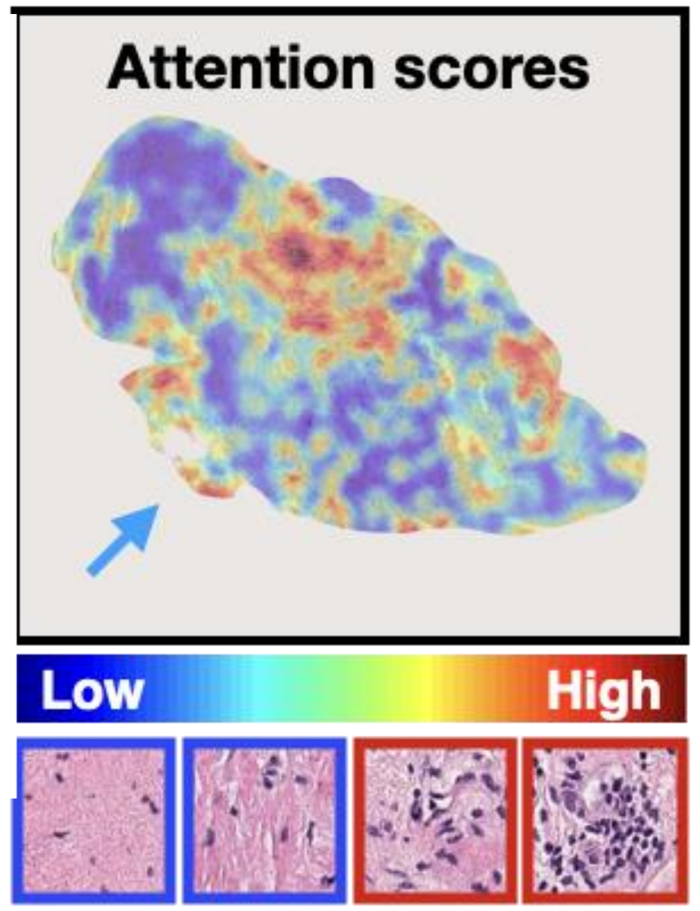
(Ilse et al. ICML 2018)

PREDICTIONS

Risk Prediction

Interpretability

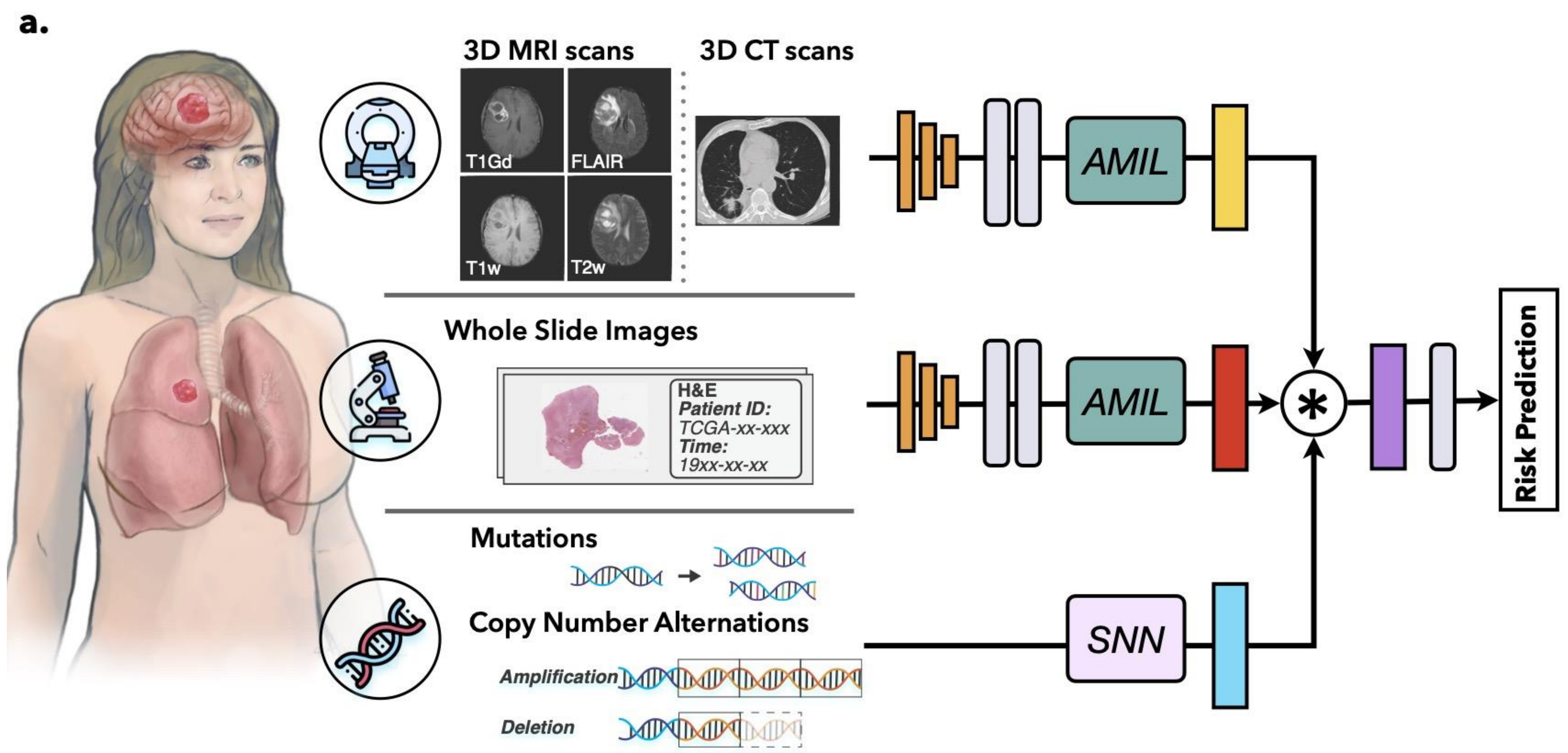


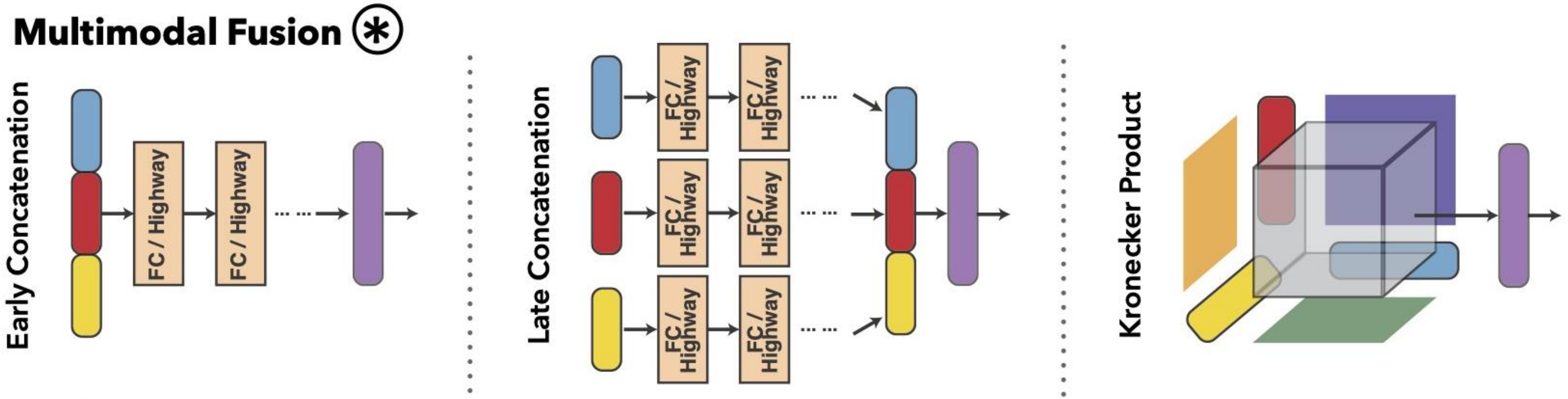


Radiology Module
PREPROCESSING
SLICE EMBEDDINGS
Registration + Skull Stripping
Axial Slicing
T1Gd
FLAIR
T1w
T2w
Feature extraction
Axial Concatenation
Feature refining
T1Gd
FLAIR
T1w
T2w
T1Gd
FLAIR
T1
T2
FC1
FC2
ATTENTION LEARNING
PREDICTIONS
Not Informative
Highly Informative
Attention score
Attention-based pooling
Patient Embedding
Risk Stratification
Interpretability
$\mathbf{h}_{slide,t} = \sum_{k=1}^{K} a_{k,t}\mathbf{h}_k$
$a_{k,t} = \frac{\exp\{\mathbf{W}_{a,t}(\tanh(\mathbf{V}_a\mathbf{h}_k) \odot \mathrm{sigm}(\mathbf{U}_a\mathbf{h}_k))\}}{\sum_{j=1}^{N}\exp\{\mathbf{W}_{a,t}(\tanh(\mathbf{V}_a\mathbf{h}_j) \odot \mathrm{sigm}(\mathbf{U}_a\mathbf{h}_j))\}}$
(Ilse et al. ICML 2018)
Proportion Surviving
1.00
0.75
0.50
0.25
0.00
0
2
4
6
8
10
Years
High Risk
Low Risk
Hight Attention
Low Attention

Fusion Module

a.





Study Design: Survival Prediction

Internal Cohorts

Internal NSCLC	
Radiology	817
Histology	1278
Genomics	1058
Radio+Histo+Omics	90

Internal Glioma	
Radiology	311
Histology	524
Genomics	803
Radio+Histo+Omics	220

The Cancer Genome Atlas

The Cancer Imaging Archive

NLST National Lung Screening Trial National Cancer Institute

CPTAC National Cancer Institute at the National Institutes of Health

BraTS

NSCLC Radiogenomics

REMBRANDT

External Cohorts

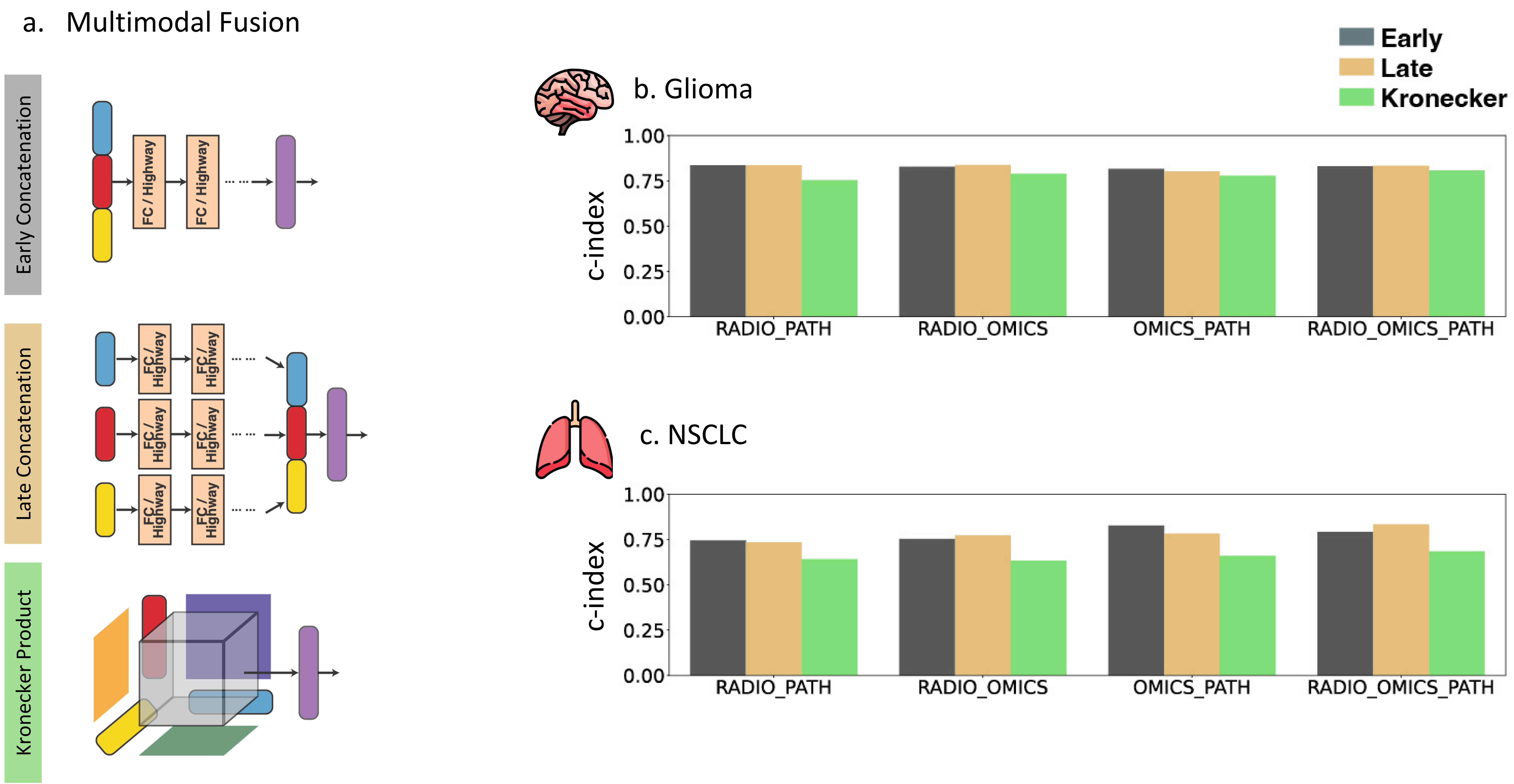
External Glioma		
DE	Radio+Histo+Omics	141
US	Histo+Omics	55

TRANSFER LEARNING:

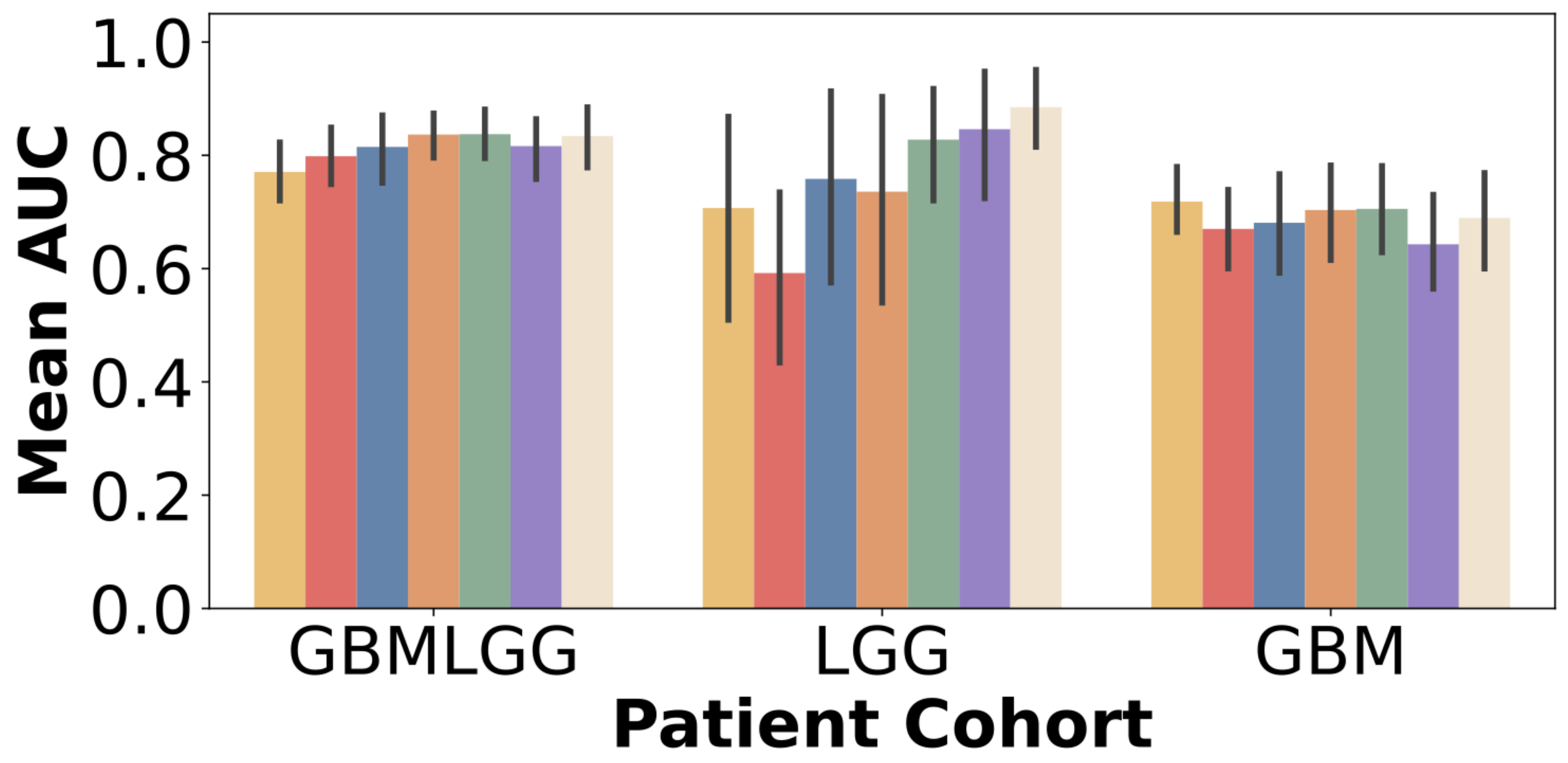
- Unimodal pre-training (5 fold cv)
- Multimodal fine-tuning (10 fold cv)

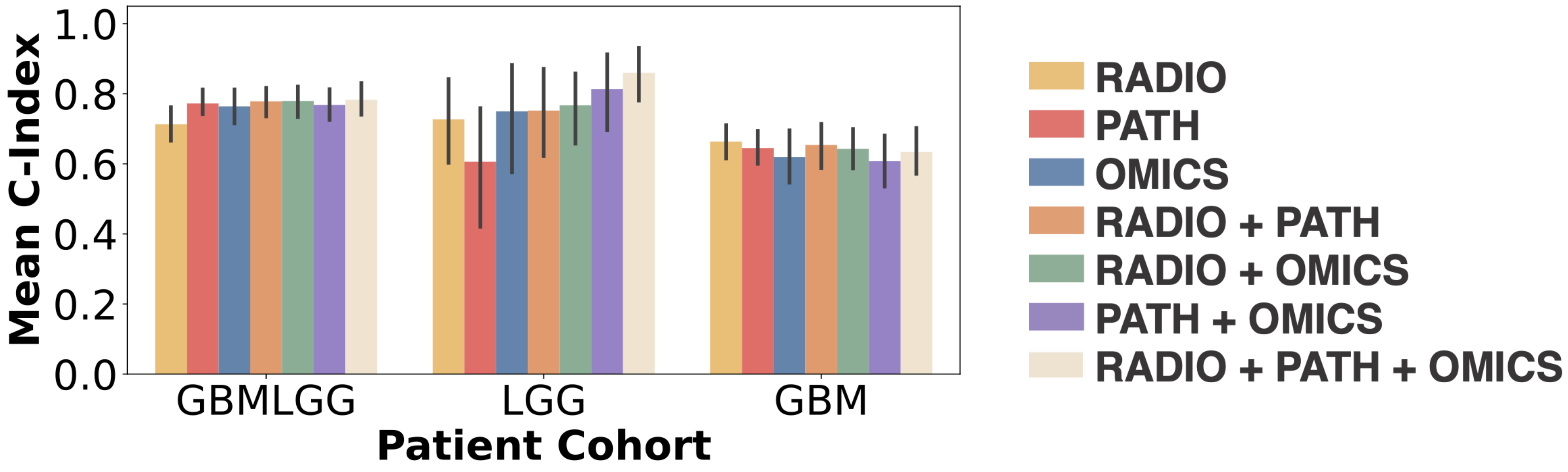
- Large data diversity:
  - population
  - scanners
  - biopsy and staining protocols,
  - noise, micron/pixel,
  - etc
- Generalization to external cohorts without domain-specific adaptations

Multimodal Data Fusion

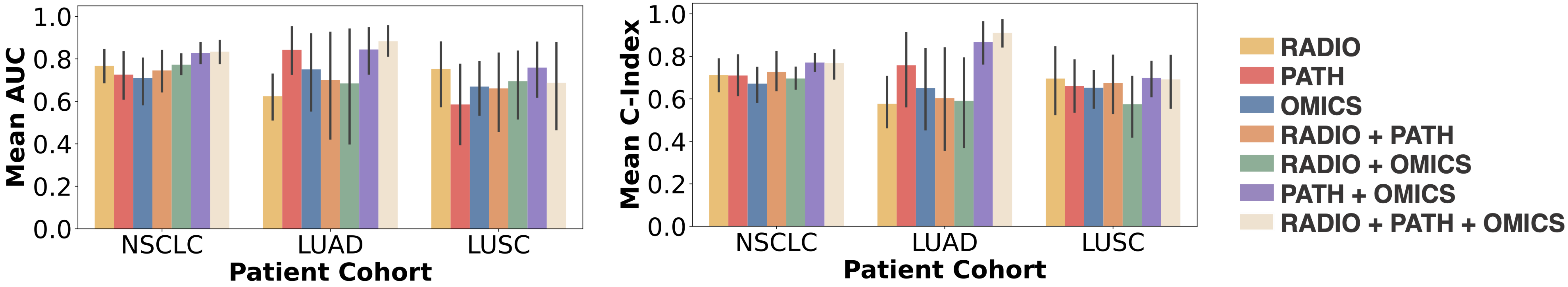


Performance on Internal Glioma Cohort





Performance on Internal Lung Cohort

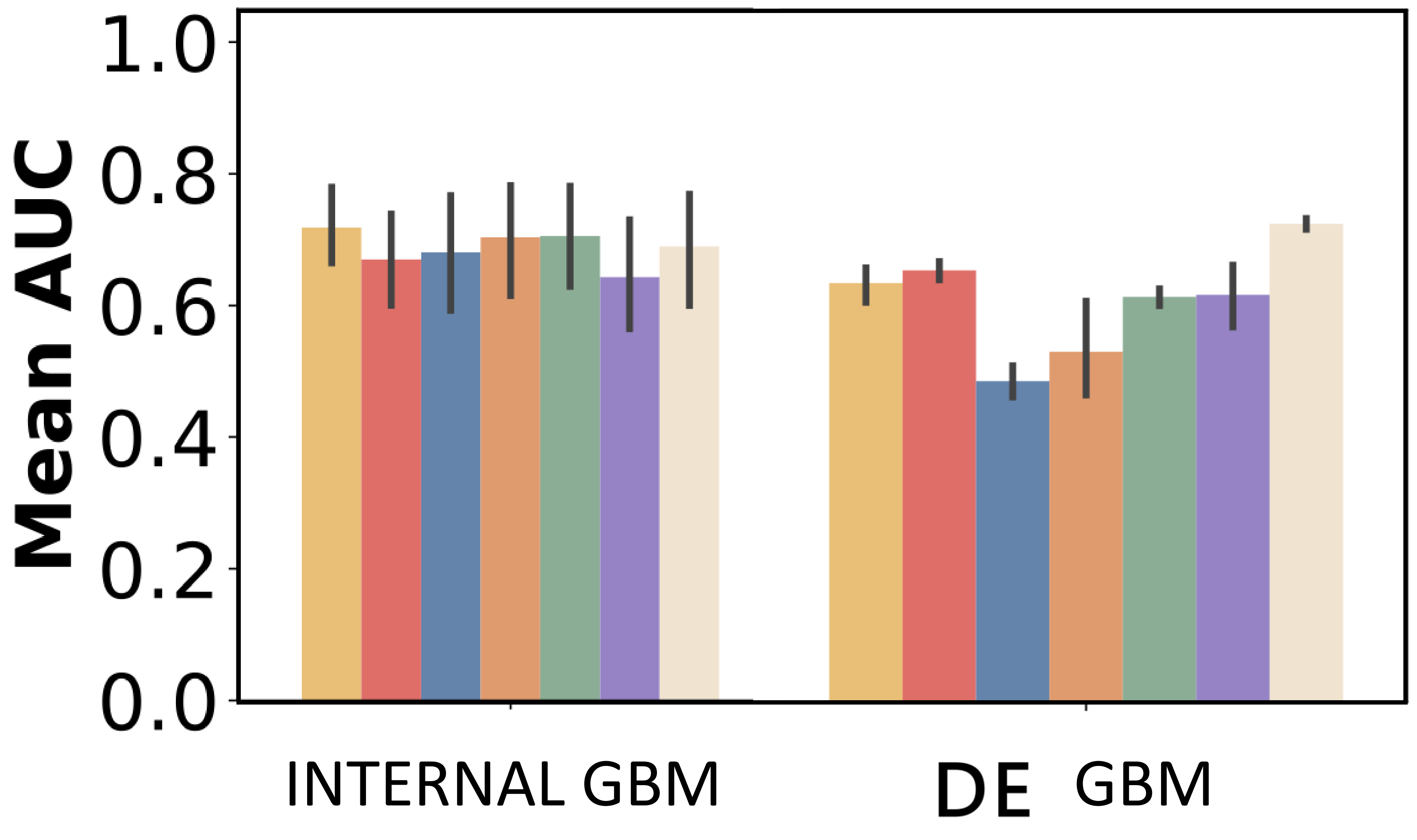


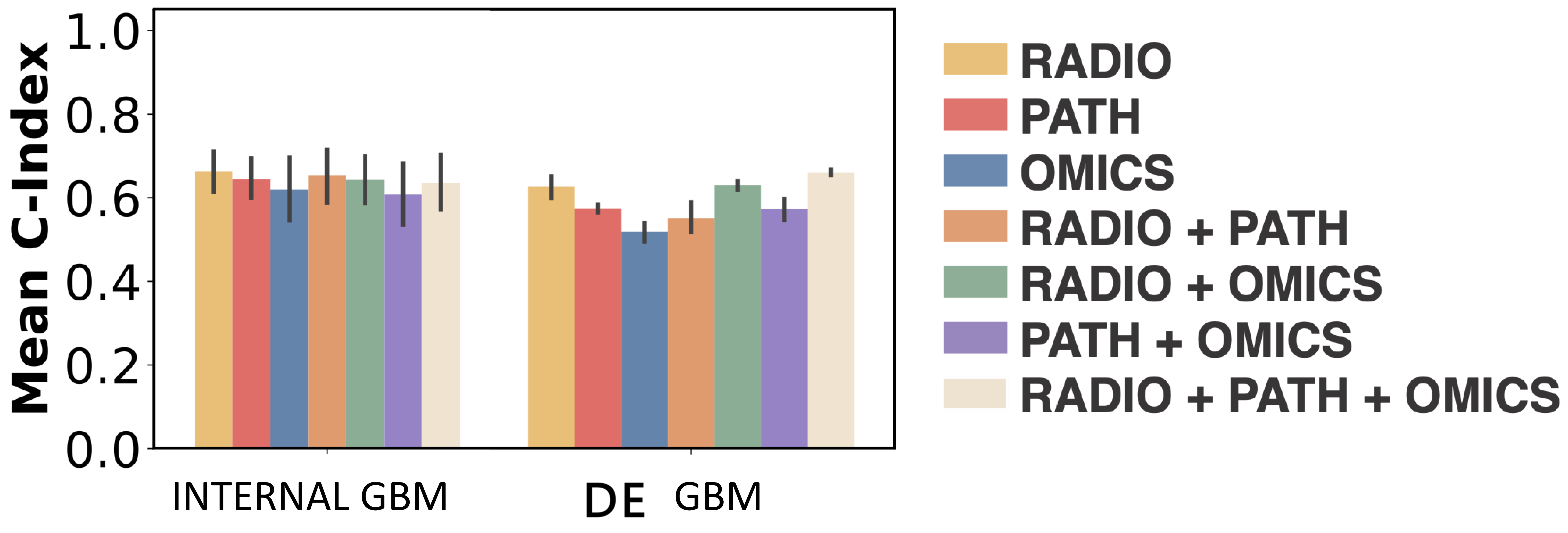
Generalization to External Cohort

DE

External GBM		
DE	Radio+Histo+Omics	141

Homogenous genomics profile:
- all : IDH1 wild type, 1p/19 non-codeleted
- 95% : HGF & BRAG deletion | TET2 amplification

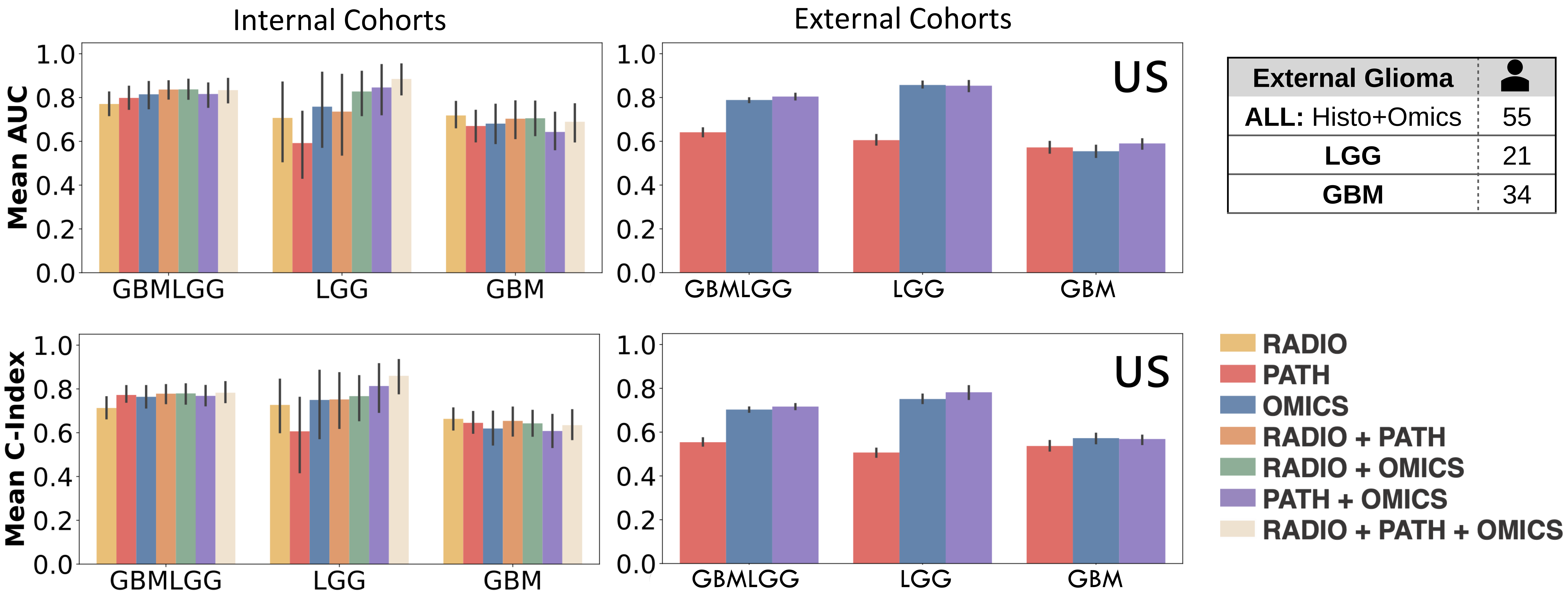




Multimodal fusion
- Outperforms both uni and bi-modal (AUC=0.73, c-index=0.66)
- Surpassed the performance of the internal cohort (↑ 3.6% AUC, ↑ 2.7% c-index)
- Improves performance and generalization by leveraging complementary and shared info in data

Generalization to External Cohort

US



External Glioma	
ALL: Histo+Omics	55
LGG	21
GBM	34

Multimodal fusion

- Outperforms uni-modal for GBMLGG (AUC=0.80,c-index=0.72), LGG (c-index=0.78), GBM (AUC=0.59)
- Surpassed the performance of the internal cohort for LGG (↑ 6.8% AUC, ↑ 4.3% c-index)
- Improves performance and generalization by leveraging complementary and shared info in data

Comparison with Clinical Baselines

Lung baseline

- clinical: tumor stage, patient age, gender, KRAS, and TP53 mutations

Models	NSCLC		LUAD		LUSC	
	AUC	c-index	AUC	c-index	AUC	c-index
Clinical	0.5322±0.15	0.5014±0.14	0.8174±0.21	0.7607±0.24	0.4239±0.26	0.3004±0.20
CAMPHORA	**0.8342±0.09**	**0.7684±0.11**	**0.8827±0.12**	**0.9108±0.10**	**0.6871±0.33**	**0.6914±0.21**

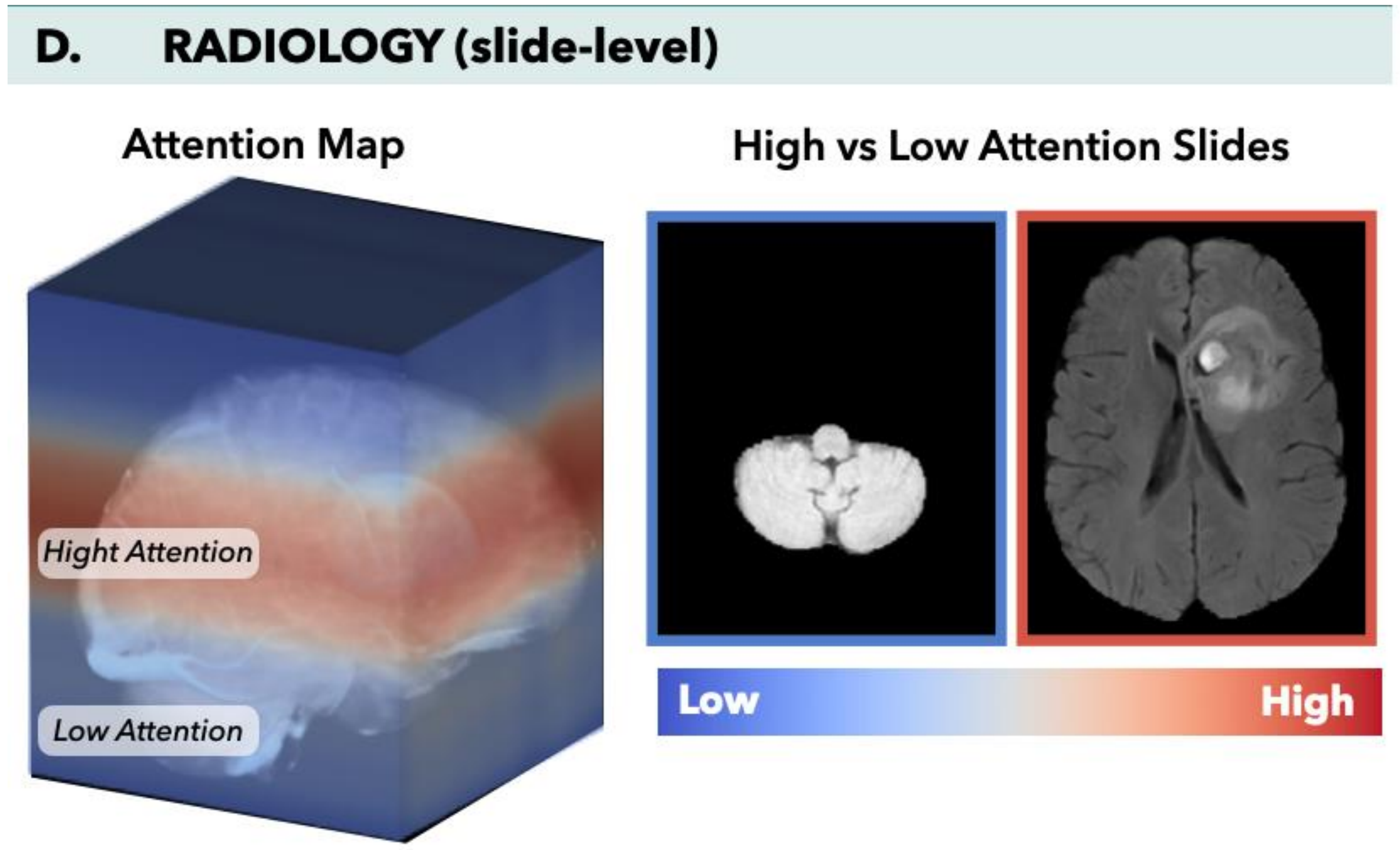
Glioma baseline

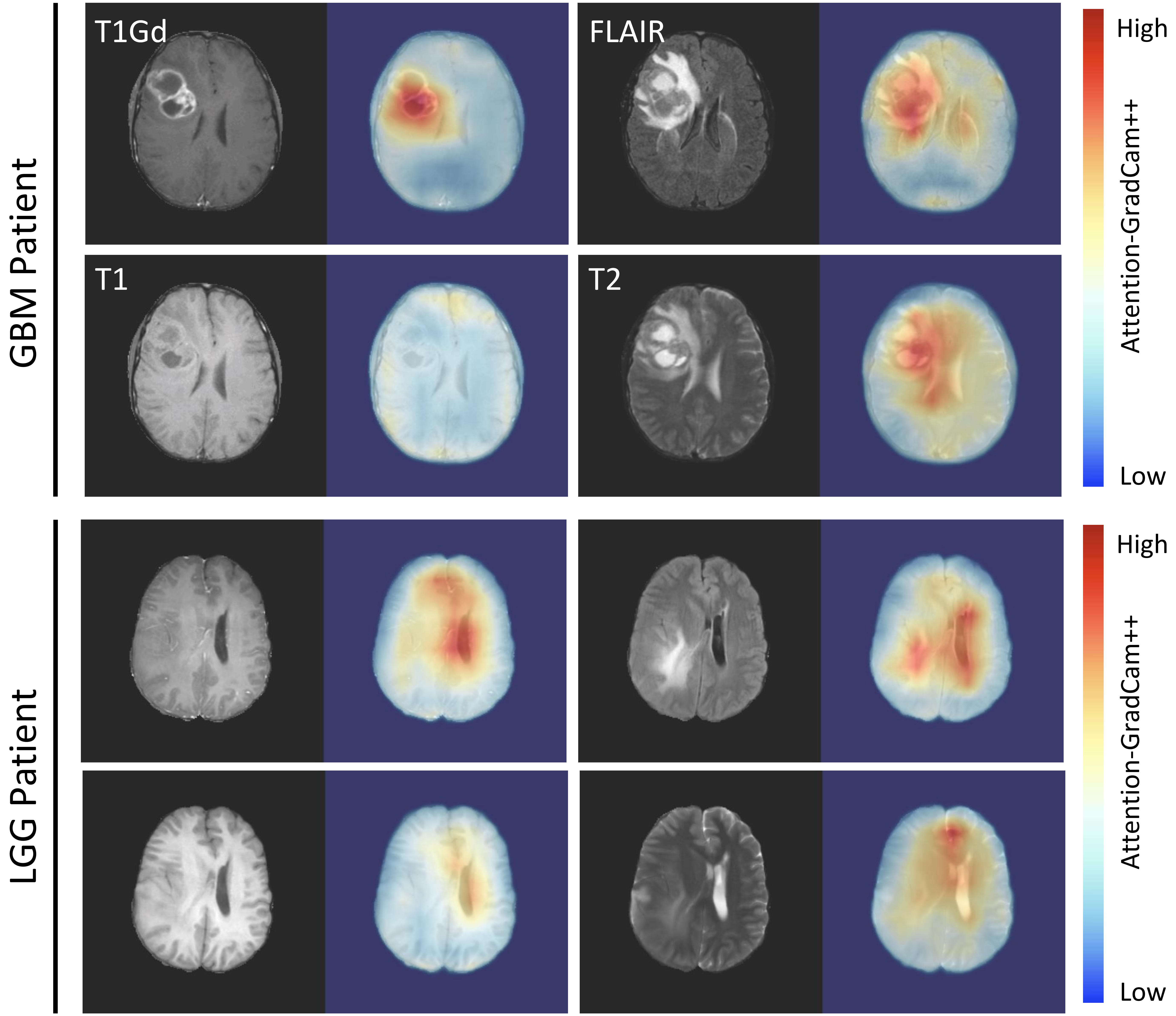
- clinical: tumor grade, patient age, gender, IDH1, 1p/19q status
- volume: of active tumor, edema, necrotic core

Models	GBMLGG		GBM		LGG		DE GBM	
	AUC	c-index	AUC	c-index	AUC	c-index	AUC	c-index
Clinical + Vol	0.5705±0.11	0.5978±0.09	0.5039±0.40	0.4280±0.36	0.5123±0.17	0.5079±0.13	0.6476±0.02	0.6457±0.01
CAMPHORA	**0.8342±0.09**	**0.7684±0.11**	**0.8827±0.12**	**0.9108±0.10**	**0.6871±0.33**	**0.6914±0.21**	**0.7257± 0.01**	**0.6612± 0.01**

Interpretability Histology

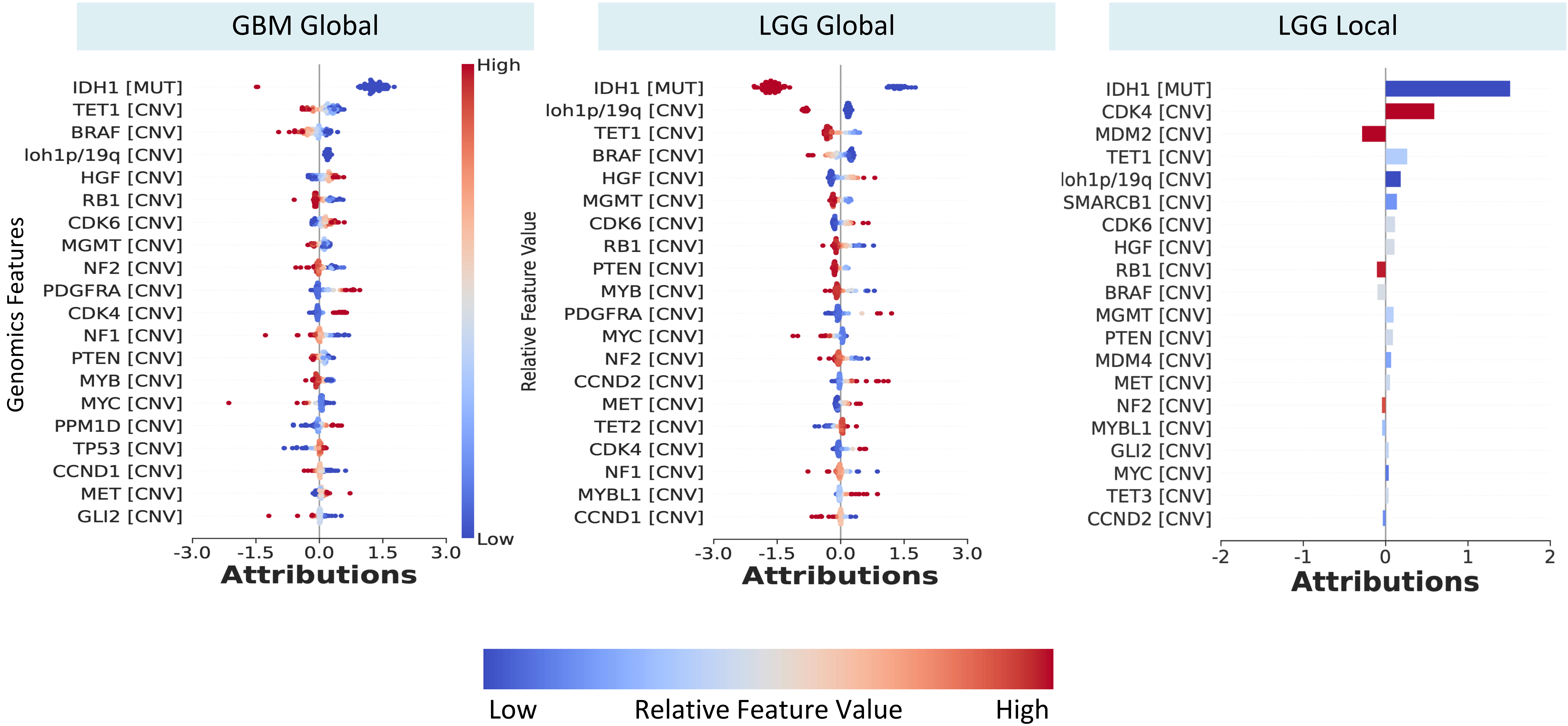
Interpretability Radiology





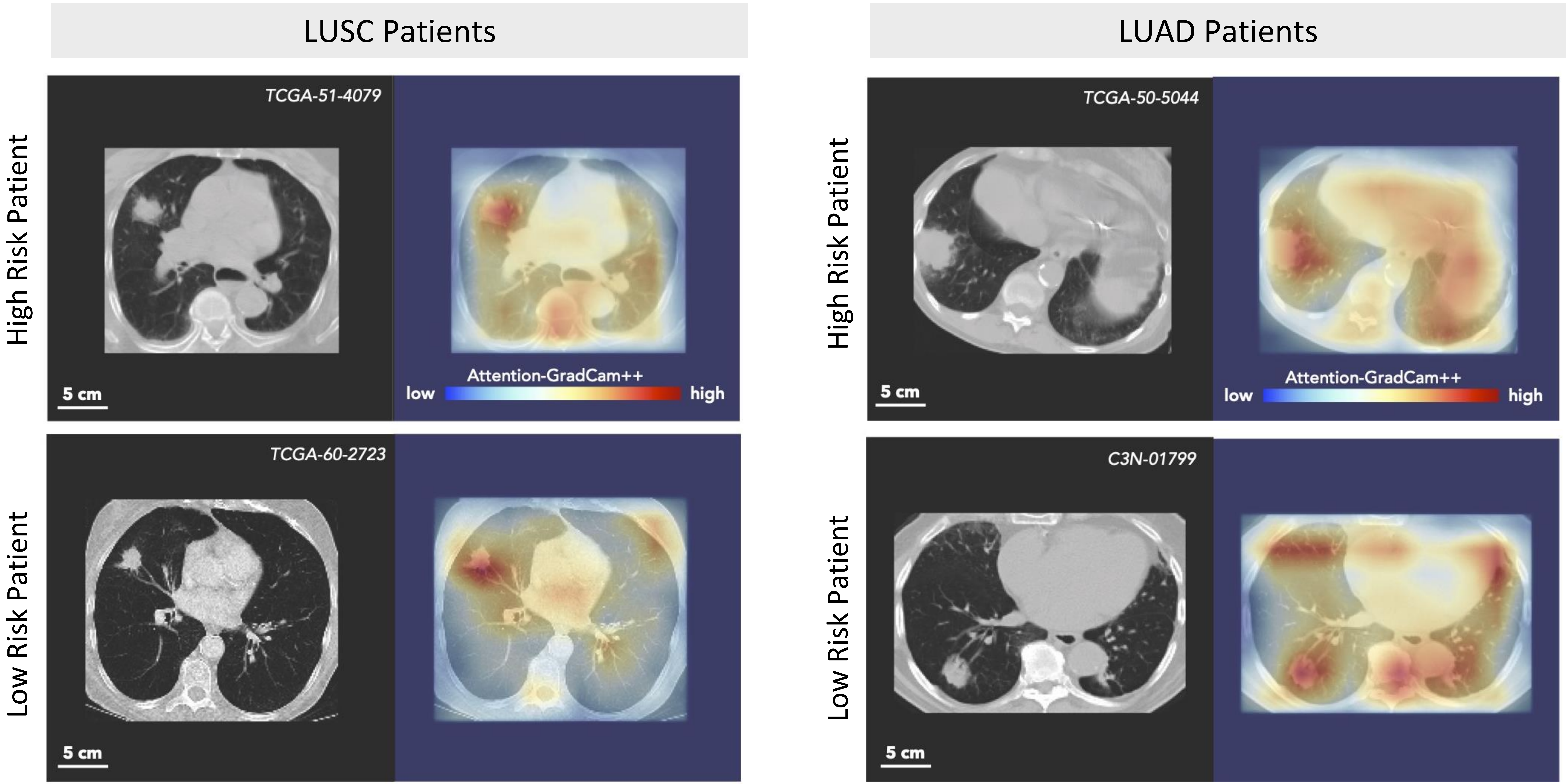
Lipkova et al., Cancer Cell, 2023

Interpretability Genomics



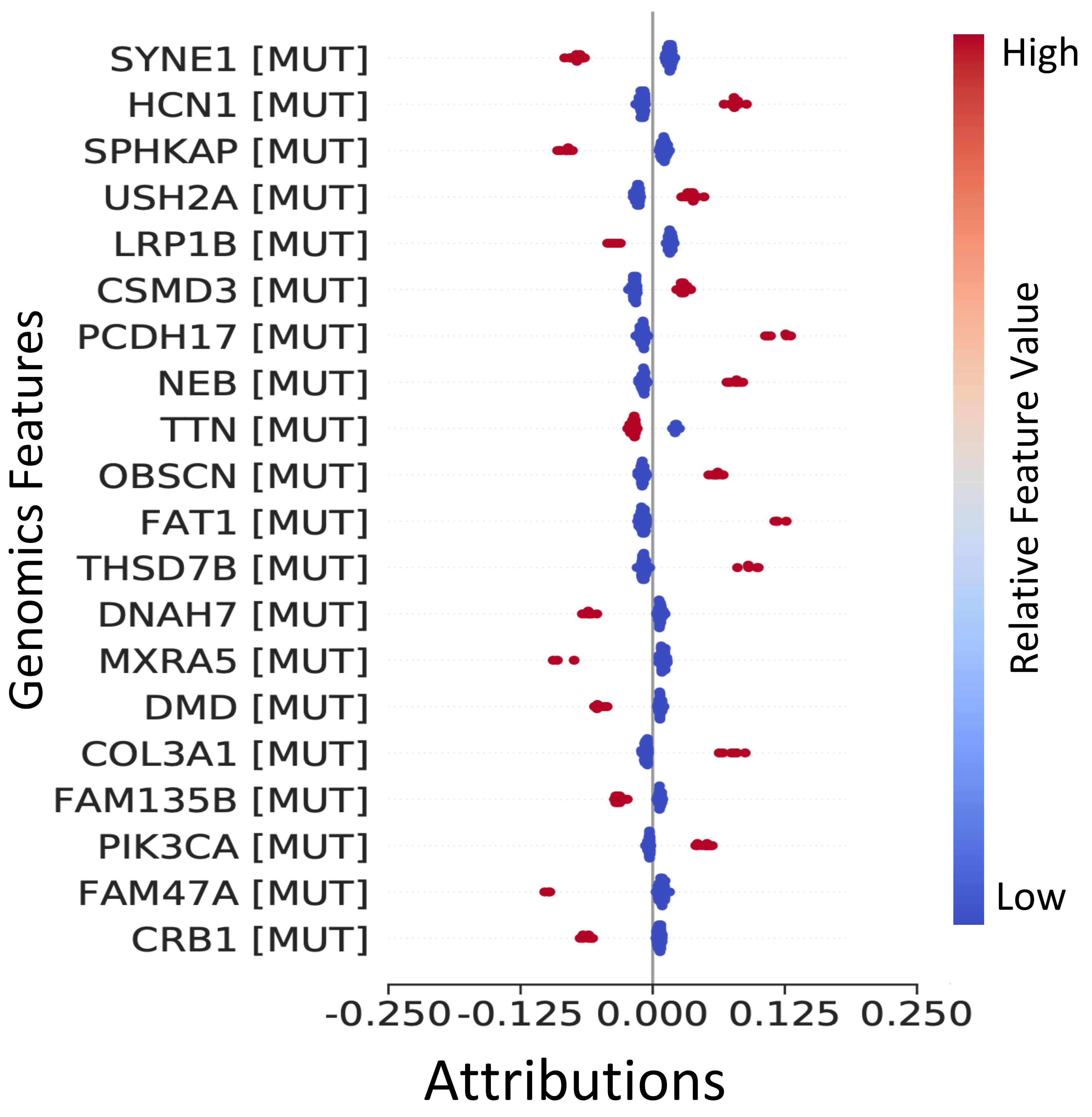
Interpretability Histology

Interpretability Radiology

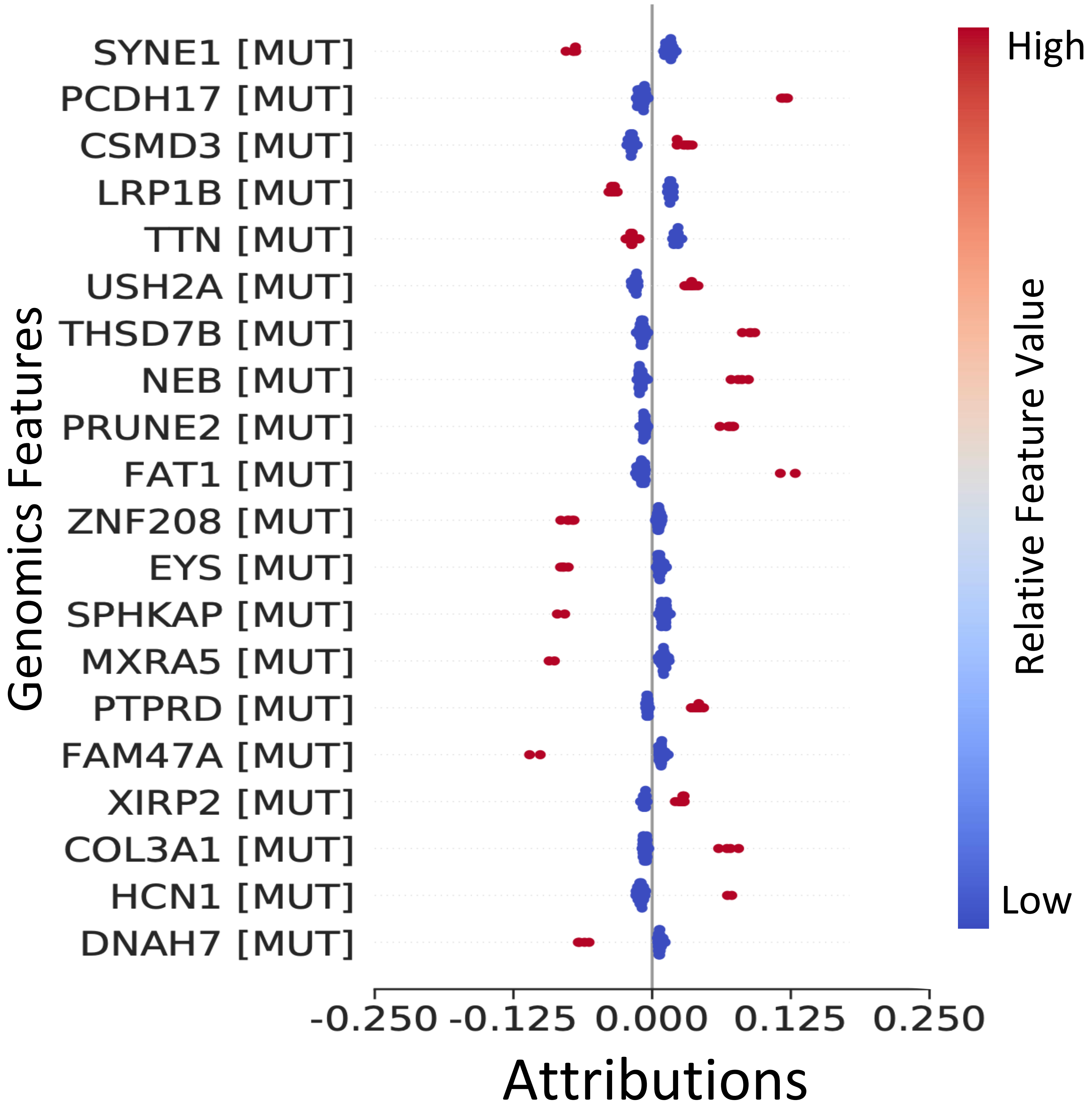


Interpretability Genomics

LUSC Global



LUAD Global



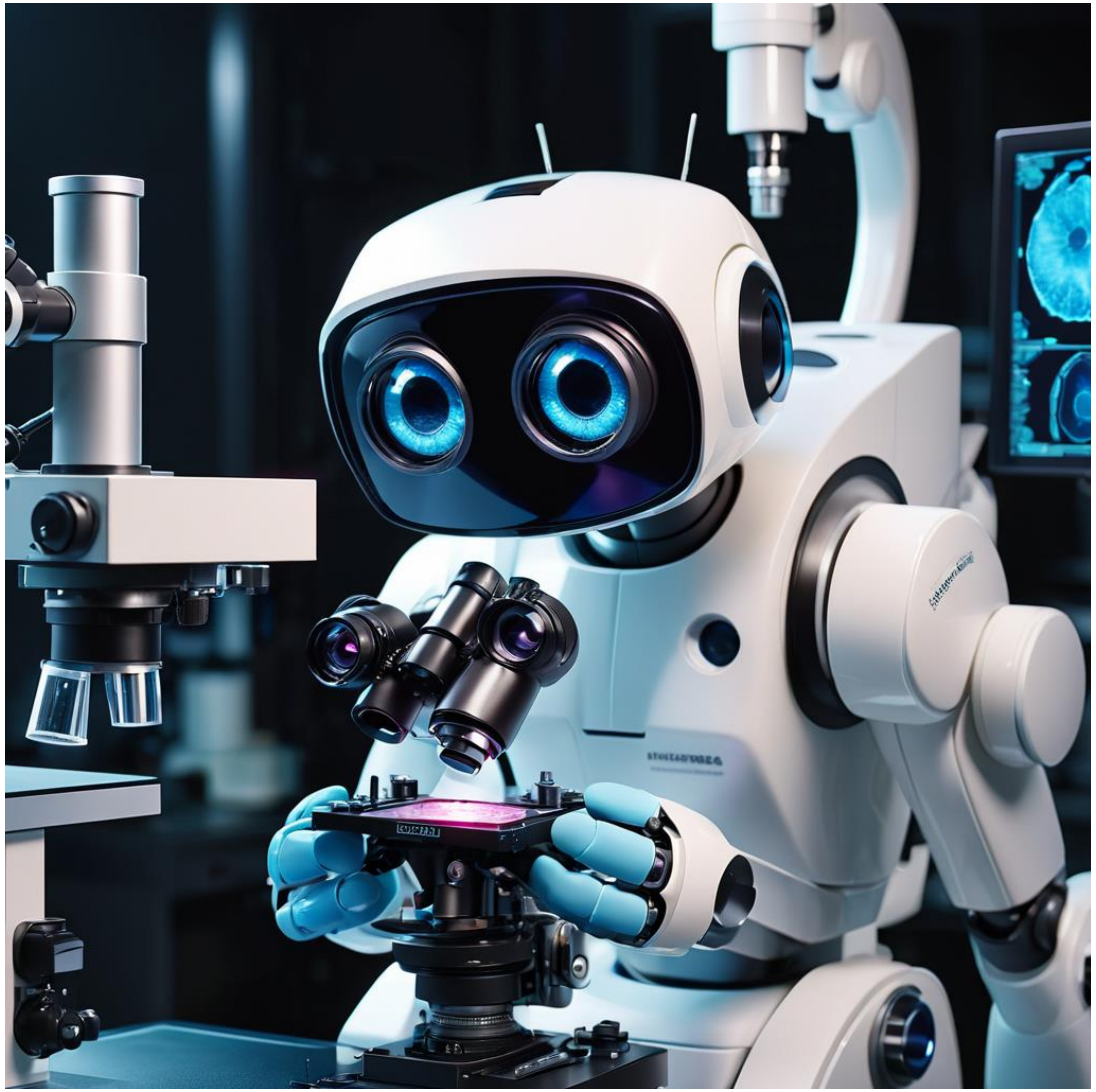
Conclusion

AI BASED MULTIMODAL FUSION

- Leverage **complementary** & **shared information** in data to provide **more accurate** and **robust predictions**
- **Interpretability**: features correlation with poor and favorable outcome
- **Independently identify prognostic factors**
- Suitable for **diverse disease model and data types**
- Open source framework

LIMITATIONS / FUTURE WORK

- Larger multimodal cohort:
  - more efficient multimodal fine-tuning
  - more advanced fusion methods
  - multimodal feature extraction
- Missing and incomplete data handling
- External validations for other cancer types



https://github.com/MultimodalFusion

Thank you

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