AI3011 | Spring 2025

MULTI-VIEW LEARNING FOR PARTIAL DATA MODALITIES IN GLIOBLASTOMA SURVIVAL PREDICTION

Group 41

PROBLEM STATEMENT

GLIOBLASTOMA

The most aggressive kind of 'Glioma', a type of primary brain tumour

SURVIVAL PREDICTION

IS IMPORTANT

Approximately ***250,000*** *new cases worldwide each year* [1]

But Median Survival is about ***12 - 15*** *months* [1]

Heterogeneity of the disease makes prognosis difficult

- ✓ **Allows Physicians to make** ***personalized treatment plans***
- ✓ **Allow patients to make** ***informed*** ***informed*** **about their quality of life**
- ✓ ***Avoid ineffective treatments*** **and cope with possible outcomes.**

[1] *Papacocea SI, Vrinceanu D, Dumitru M, Manole F, Serboiu C, Papacocea MT. Molecular Profile as an Outcome Predictor in Glioblastoma along with MRI Features and Surgical Resection: A Scoping Review. Int J Mol Sci. 2024 Sep 8;25(17):9714.*

.........BUT THIS DOESNT ALWAYS WORK!

Studies show that Survival predictions by Physicians tend to be *TOO OPTIMISTIC* [2]

Survival Prediction is rather subjective !!

Varies with Physician Experience

2 Islam M, Wijethilake N, Ren H. Glioblastoma multiforme prognosis: MRI missing modality generation, segmentation and radiogenomic survival prediction. Comput Med Imaging Graph. 2021b;91:101906.

.........BUT THIS DOESNT ALWAYS WORK!

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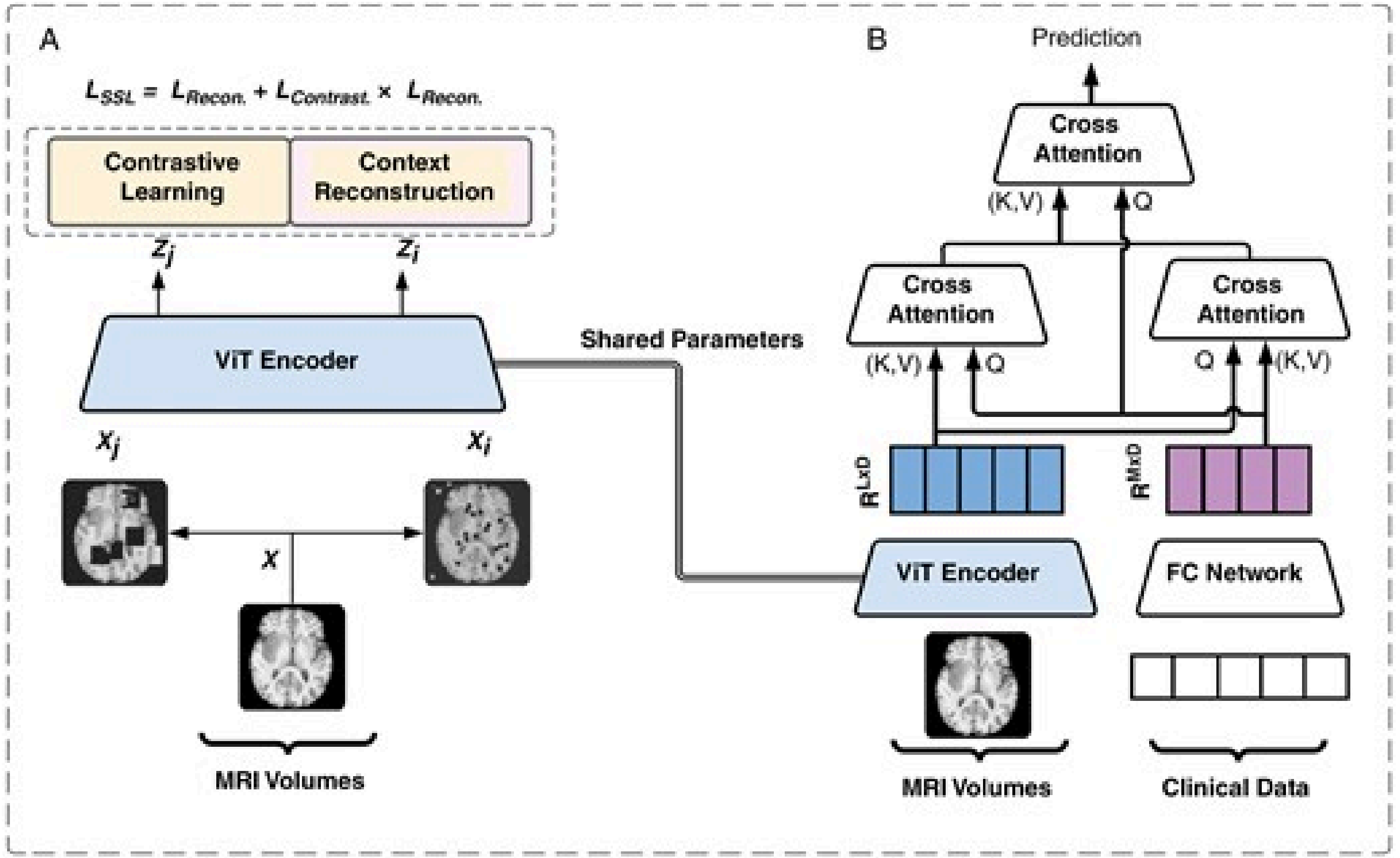
Varies with Physician Experience

ARTIFICIAL INTELLIGENCE & MACHINE LEARNING

EUROPEAN ASSOCIATION OF NEURO-ONCOLOGY

Comprehensive multimodal deep learning survival prediction enabled by a transformer architecture:
A multicenter study in glioblastoma



Ahmed Gomaa, Yixing Huang, Amr Hagag, Charlotte Schmitter, Daniel Höfler, Thomas Weissmann, Katharina Breininger, Manuel Schmidt, Jenny Stritzelberger, Daniel Delev, Roland Coras, Arnd Dörfler, Oliver Schnell, Benjamin Frey, Udo S Gaipl, Sabine Semrau, Christoph Bert, Peter Hau, Rainer Fietkau, Florian Putz, Comprehensive multimodal deep learning survival prediction enabled by a transformer architecture: A multicenter study in glioblastoma, Neuro-Oncology Advances, Volume 6, Issue 1, January-December 2024, vdae122, https://doi.org/10.1093/noajnl/vdae122

PAPER 1

METHODOLOGY

Model employs self-supervised learning techniques to effectively encode the high-dimensional MRI input for integration with nonimaging data using cross-attention

OBSERVATIONS

The transformer model outperformed 3D-CNN-based models, improving survival prediction accuracy and distinguishing between favorable and unfavorable outcomes.

PERFORMANCE METRICS

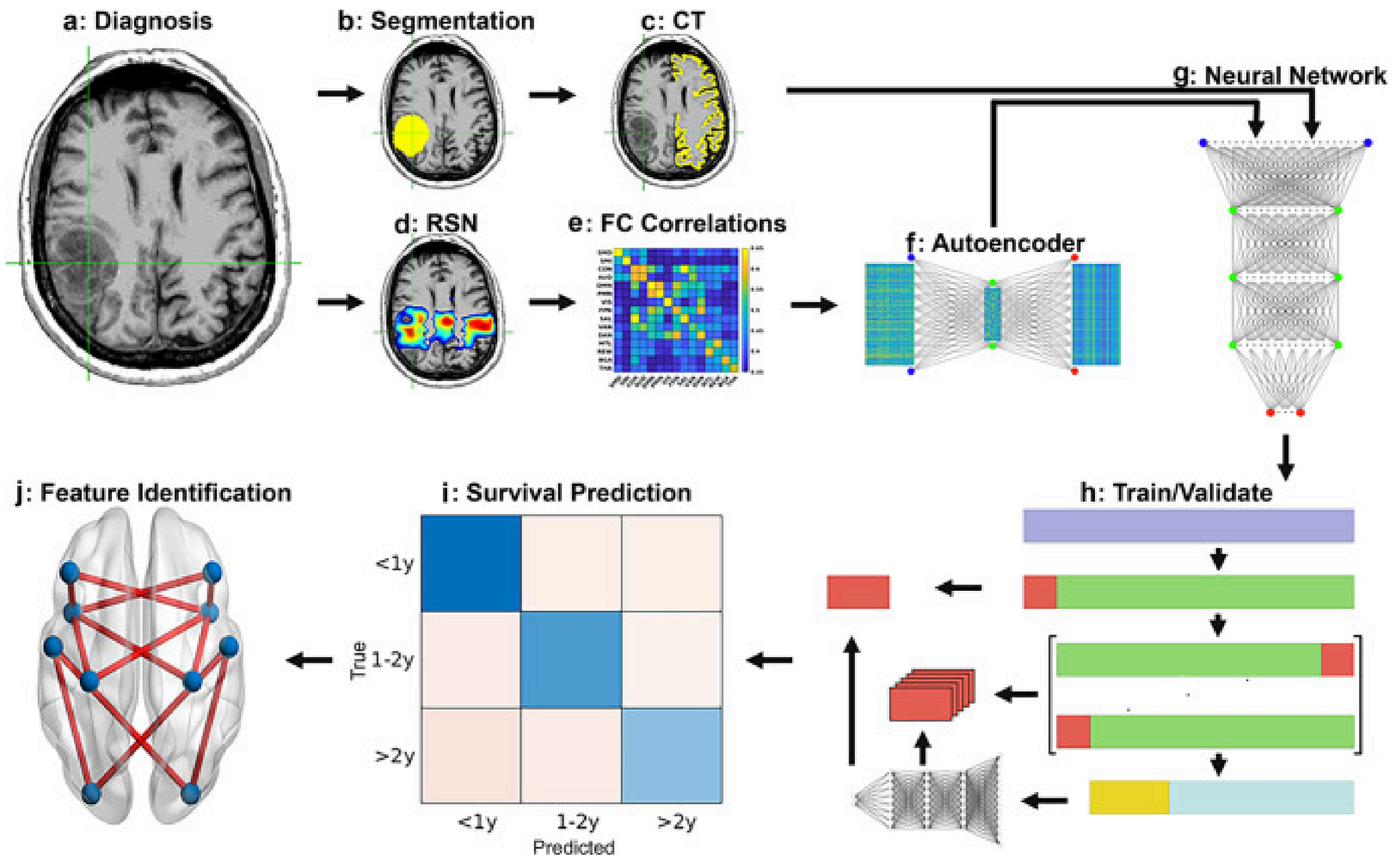
- *UPenn-GBM: Cdt = 0.707*
- *UCSF-PDGM (Imaging-only): Cdt = 0.578, (Multimodal): Cdt = 0.672*
- *RHUH-GBM: Cdt = 0.618*

ANALYSIS

The model demonstrated superior performance in integrating multimodal data, showing better generalizability and potential clinical value for glioblastoma survival prediction. Yet it lacked interpretability.

Springer

Predicting survival in glioblastoma with multimodal neuroimaging and machine learning



Luckett PH, Olufawo M, Lamichhane B, Park KY, Dierker D, Verastegui GT, Yang P, Kim AH, Chheda MG, Snyder AZ, Shimony JS, Leuthardt EC. Predicting survival in glioblastoma with multimodal neuroimaging and machine learning. J Neurooncol. 2023 Sep;164(2):309-320. doi: 10.1007/s11060-023-04439-8. Epub 2023 Sep 5. PMID: 37668941; PMCID: PMC10522528.

PAPER 2

METHODOLOGY

A deep neural network was trained to classify GBM patient survival using demographics, cortical thickness (CT), and resting-state fMRI data from 133 patients. Permutation feature importance identified key survival predictors.

OBSERVATIONS

Strong demographic predictors included age and sex, while key CT predictors were the superior temporal sulcus and parahippocampal gyrus. Key FC predictors involved somatomotor, visual, and cingulo-opercular networks.

PERFORMANCE METRICS

- *Accuracy: 90.6%*
- *Key CT predictors: Superior temporal sulcus, parahippocampal gyrus, pericalcarine, pars triangularis, middle temporal regions*
- *Key FC predictors: Somatomotor, visual, cingulo-opercular networks*

ANALYSIS

Machine learning effectively predicts GBM survival using neuroimaging data alone, revealing structural and functional brain changes linked to patient outcomes.


THERE IS STILL A GAP!!!

Current Models are Promising
BUT LIMITED BY

POOR GENERALIZABILITY

Dependence on Complete Multi-modal data [3]

LACK INTERPRETABILITY

Black Box Problem [3]

Our Goal is to tackle:

Patients with Partial Data Modalities are not able to utilise such models and the lack of interpretability of these models makes the adoption for those who do, difficult.

Allows Survival Predictions even in the absence of complete data

Allows Better Clinical adoption due to explainibility

Helps Identify Relevant Biomarkers and Patterns for Medical Research

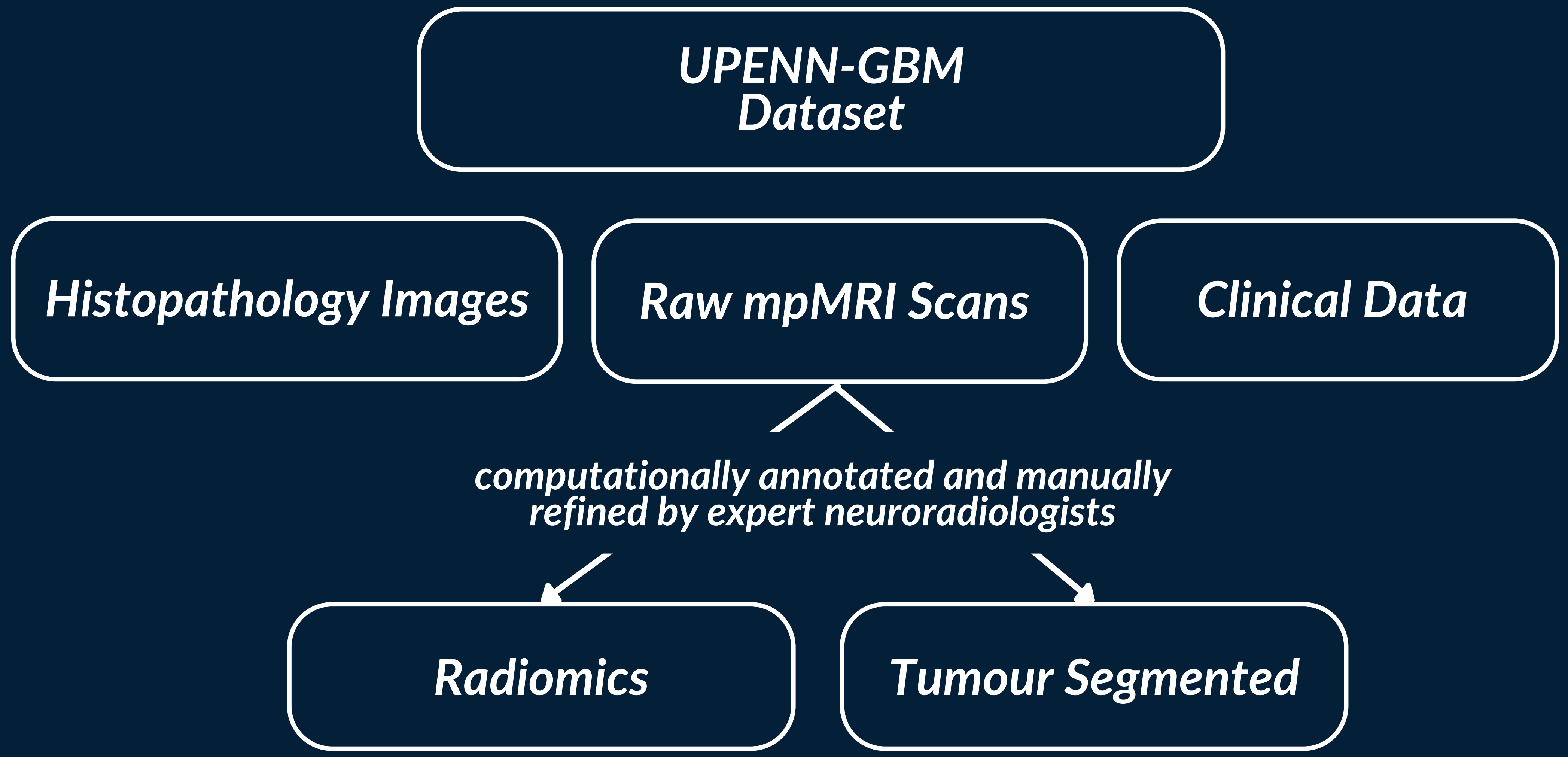
3 Poursaeed, R., Mohammadzadeh, M. & Safaei, A.A. Survival prediction of glioblastoma patients using machine learning and deep learning: a systematic review. BMC Cancer 24, 1581 (2024). https://doi.org/10.1186/s12885-024-13320-4

DESCRIPTION OF THE DATASET

University of Pennsylvania Health System

630 Patients of *de novo* Glioblastoma

2006 - 2018



Credit to Authors :

Bakas, S., Sako, C., Akbari, H., Bilello, M., Sotiras, A., Shukla, G., Rudie, J. D., Santamaría, N. F., Kazerooni, A. F., Pati, S., Rathore, S., Mamourian, E., Ha, S. M., Parker, W., Doshi, J., Baid, U., Bergman, M., Verma, R., Ha, S. M., & Davatzikos, C. (2022). The University of Pennsylvania glioblastoma (UPenn-GBM) cohort: Advanced MRI, clinical, genomics, & radiomics. Scientific Data, 9(1), 453. TCIA

WHY THIS DATASET ??

Largest, Most Comprehensive Publicly Available Dataset of GBM

Includes *diverse* multimodal data (imaging, tissue analysis, etc.)

Consistent acquisition protocols and well-recorded high-quality data

ETHICAL CONCERNS

Data was collected with appropriate ethical approvals

Informed Consent !

Personal Identification Data has been removed

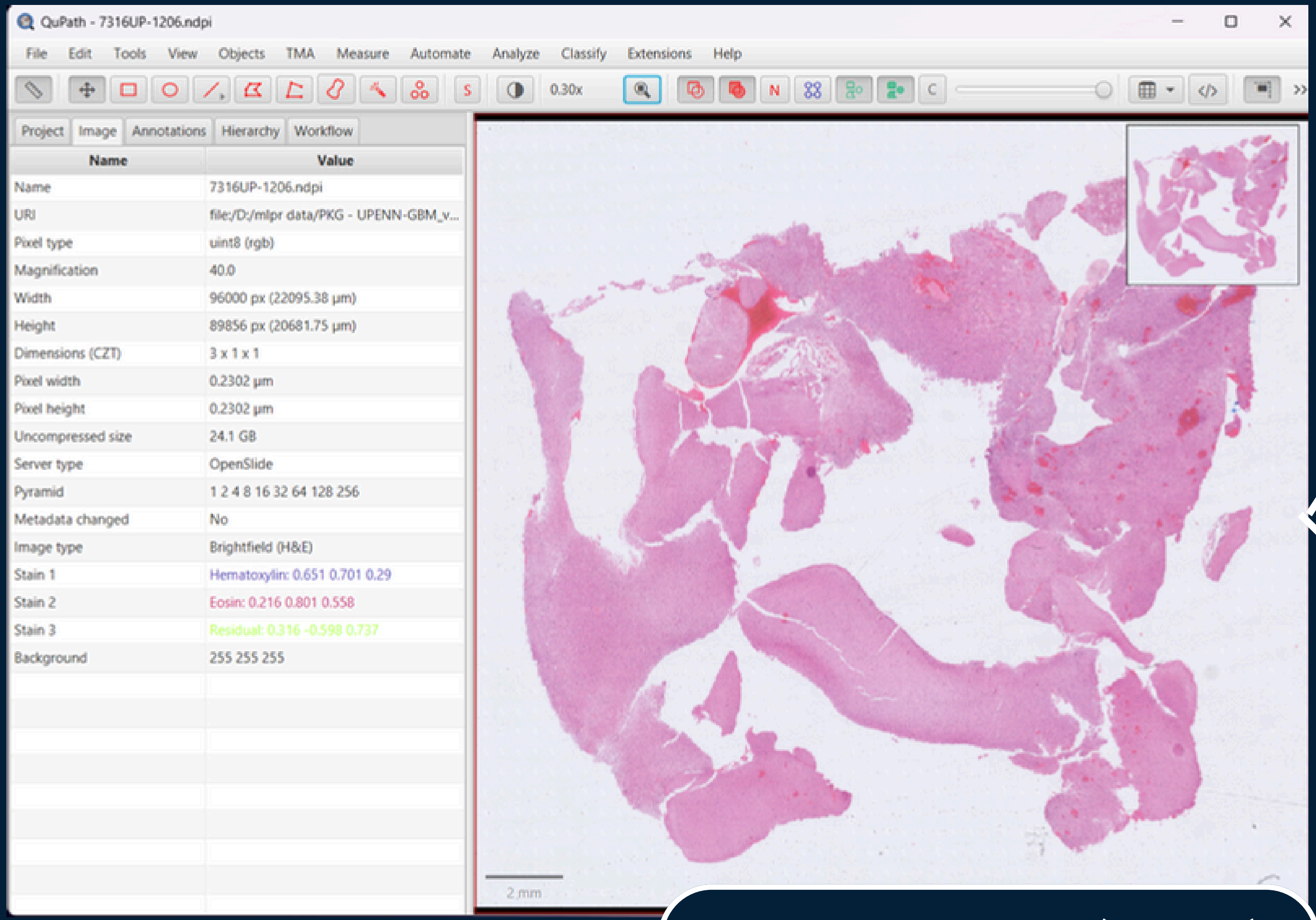
Follows *strict compliance* with data-sharing policies (HIPPA)

**Credit to Authors*

DATA PRE-PROCESSING

HISTOPATHOLOGY IMAGES ⊂ DATASET

Data Type : *Histopathology*
Format : *NDPI*
Size: *149 GB*
Subjects: *34 (71 total slides)*

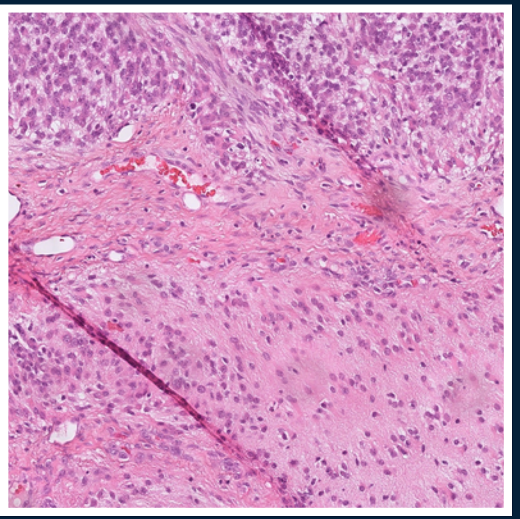


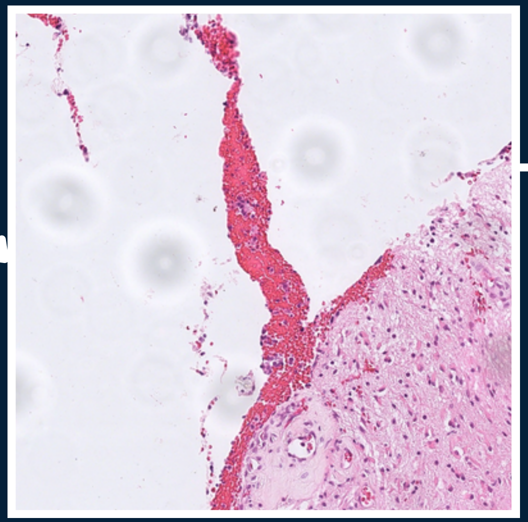
Some image is 3-3.5 GB!

Original Image (NDPI)

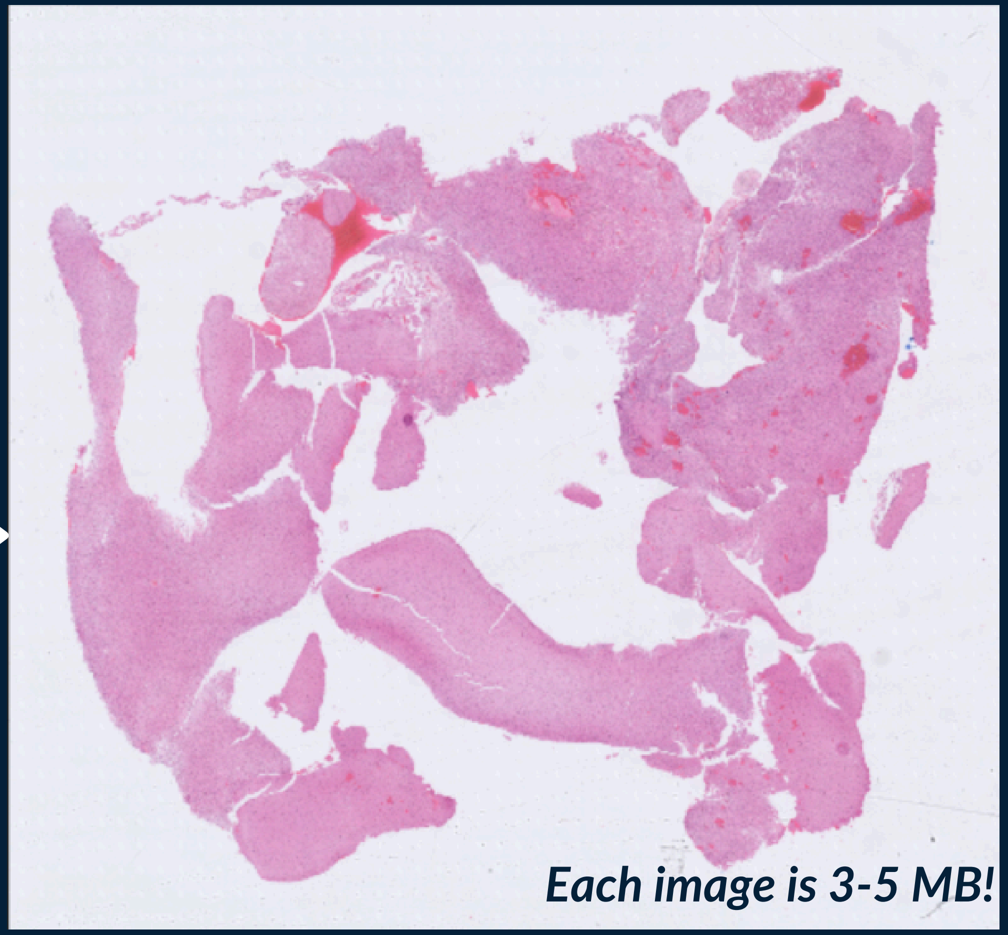
Pre-Processing : ***Tiling and Merging***

Split large images into smaller patches → *Recombined tiles* → *Compressed*





Preprocessed Image :



Each image is 3-5 MB!

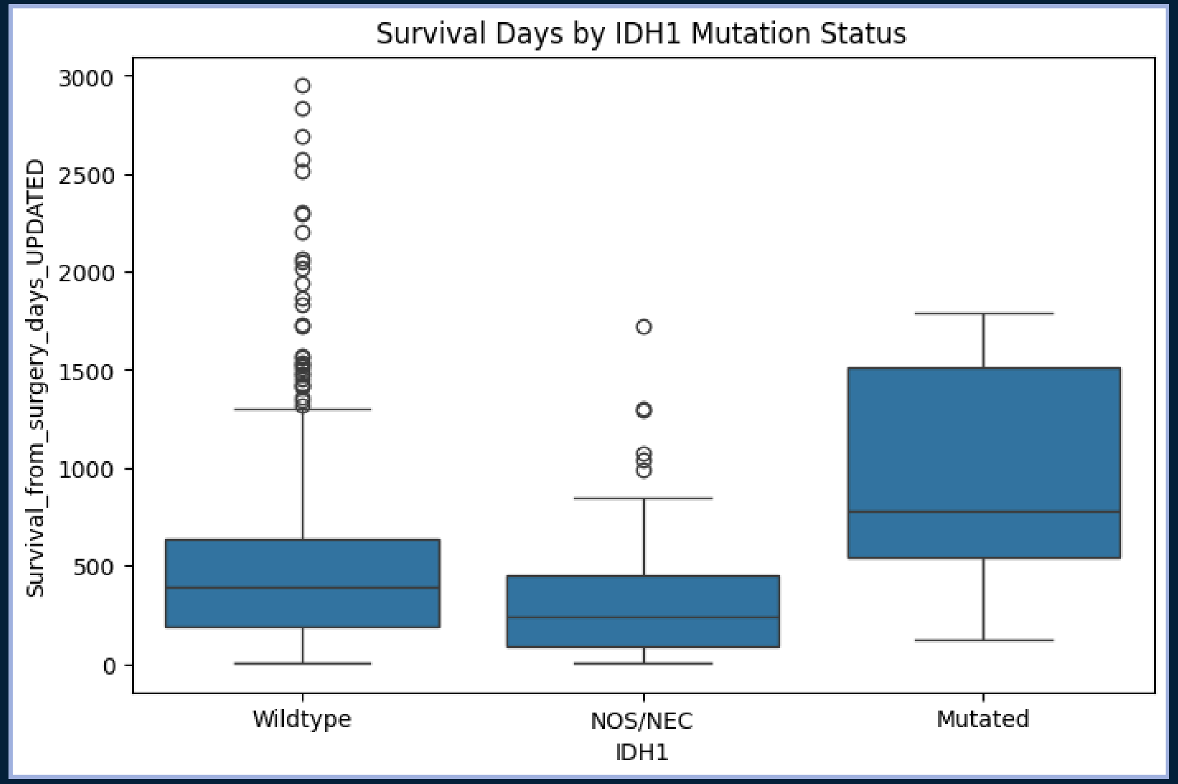
CLINICAL DATA ⊂ DATASET

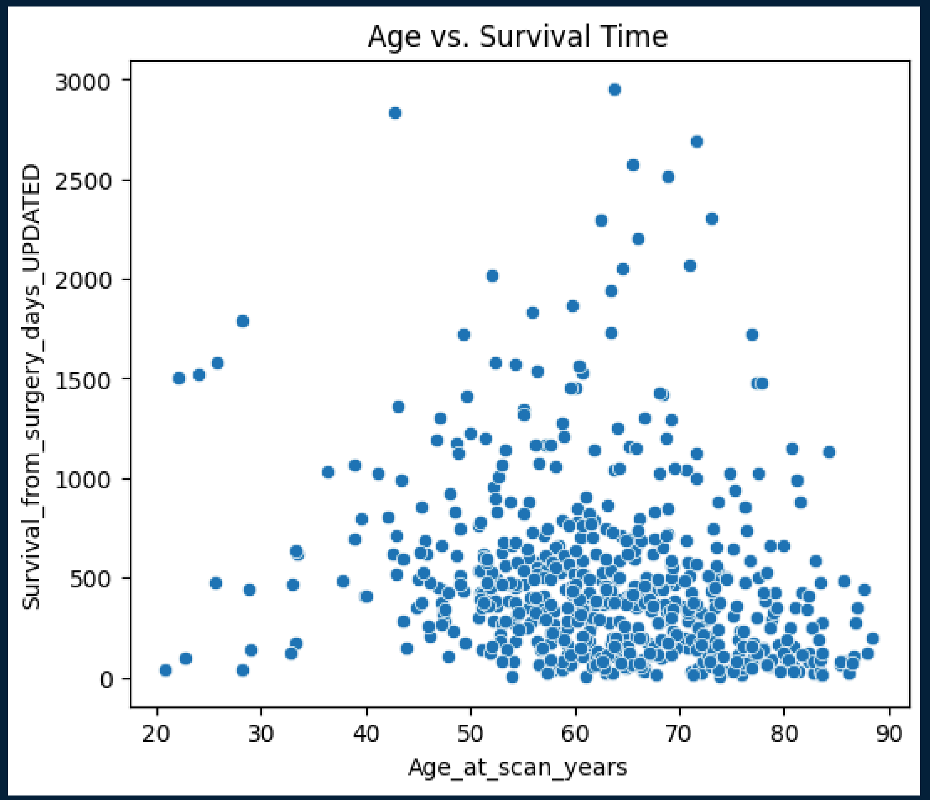
Data Type :
Format : *CSV*
Size: *35 KB*
Subjects: *671*

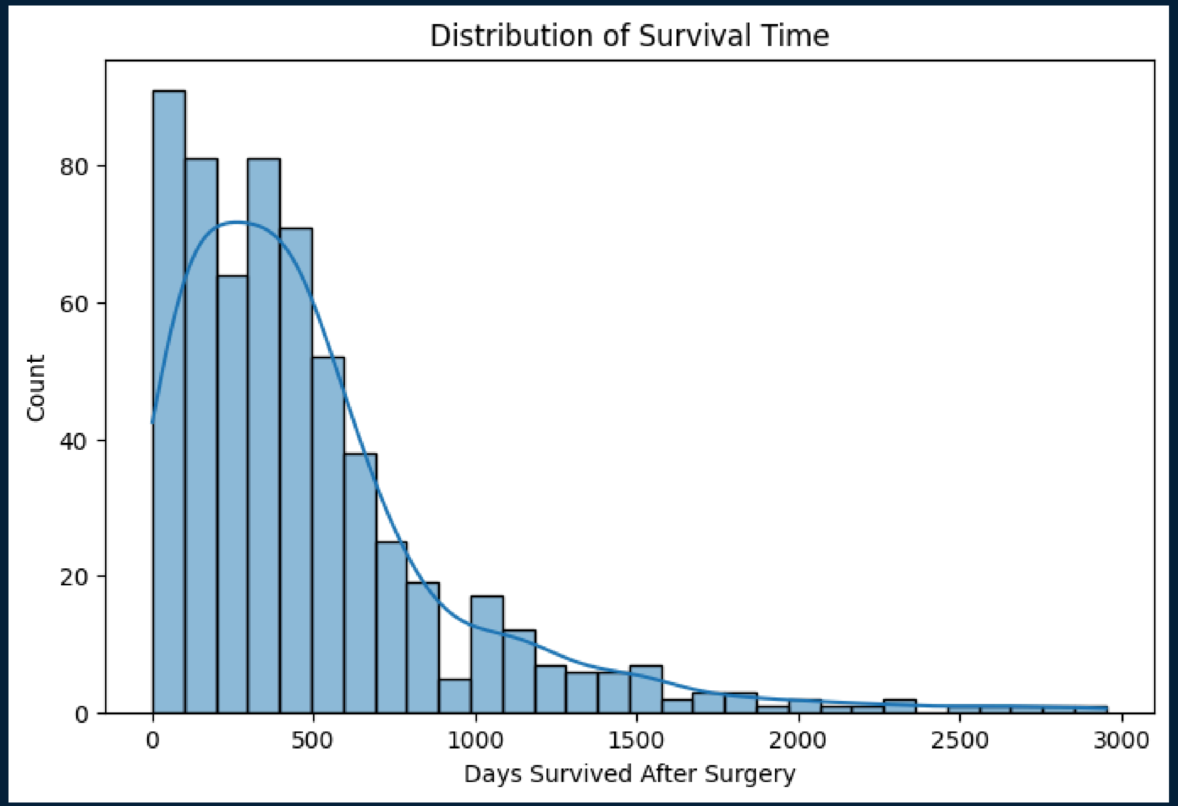
- *Demographics*
- *Survival Data*
- *Time points*
- *Clinical Factors*
- *Genetics and Biomarkers*

Pre-Processing :

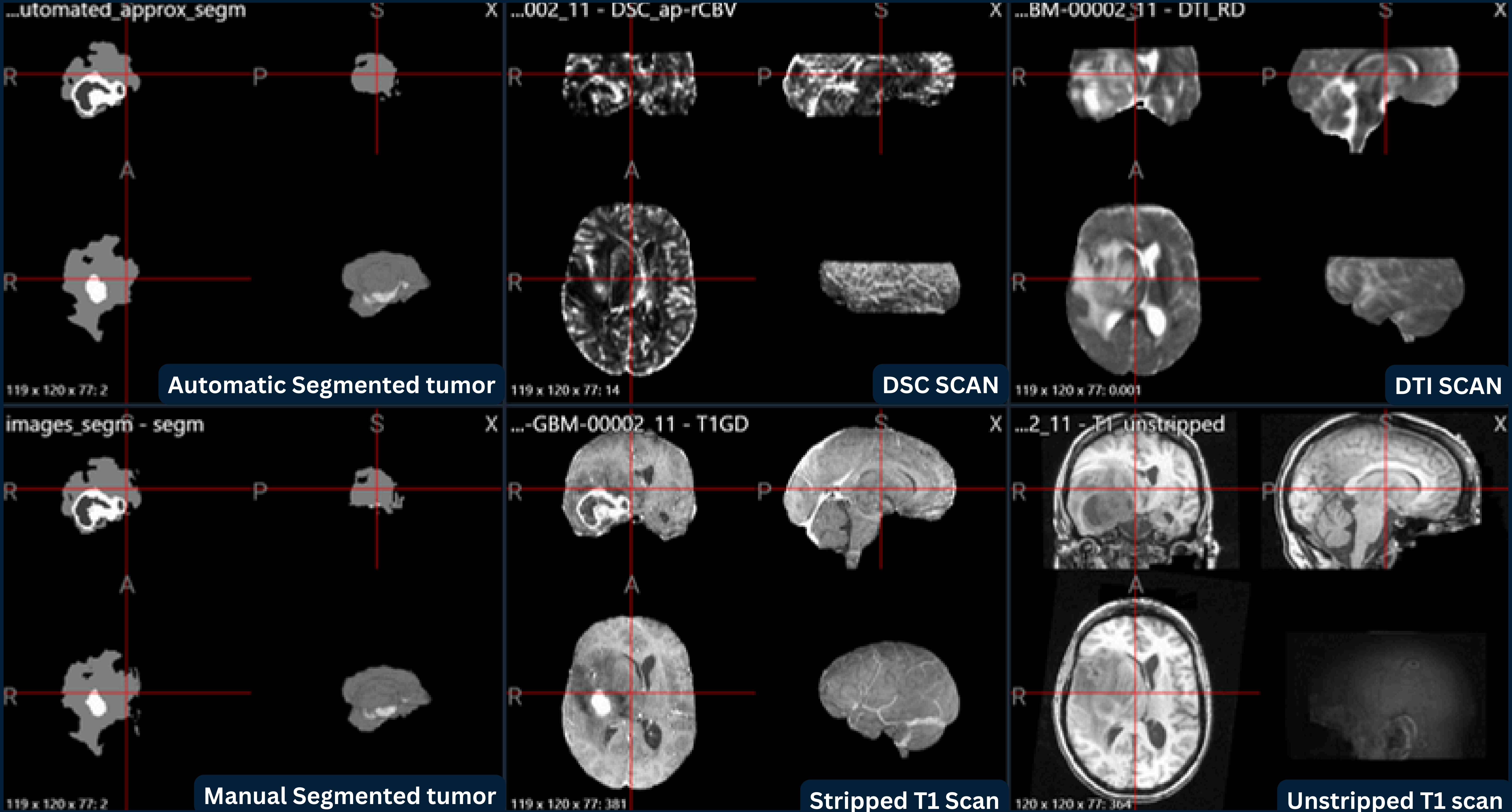
- *Removing null values*
- *Outlier detection*
- *Correlation analysis*
- *Derived Summary Statistics*







NIFTI IMAGES ⊂ DATASET



NIFTI IMAGES ⊂ DATASET

Data Type : *3D Brain Scans*
Format : *NIFTI*
Size: *69.6 GB*
Subjects: *671*

Pre-Processing :
Features we extracted using SK-Image on NIFTI files

non_automated.csv > data

```
File,Mean_Intensity,Std_Intensity,Min_Intensity,Max_Intensity,Voxel_Count,Volume_mm3,Bounding_Box,Surface_Area,Compactness,Contrast,Dissimilarity,Homogeneity,Energy,Correlation,ent
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```

Feature	Meaning	Use Case
Mean Intensity	Average brightness of tumor	Identifies tumor type
Std Intensity	Variation in intensity	Measures heterogeneity
Min/Max Intensity	Range of intensities	Detects necrotic cores
Voxel Count	Number of voxels in tumor	Measures tumor size
Volume (mm^3)	Tumor size in physical units	Tracks growth
Bounding Box	3D tumor dimensions	Assesses spread
Surface Area	Tumor surface size	Shape analysis
Compactness	Shape compactness	Classifies morphology
Contrast	Intensity variation	Detects heterogeneity
Dissimilarity	Local intensity difference	Differentiates solid vs soft tumors
Homogeneity	Uniformity of texture	Identifies structured tumors
Energy	Uniform intensity pattern	Measures structure
Correlation	Predictability of intensities	Detects organized structures
Entropy	Intensity randomness	Measures tumor complexity

Features Extracted and Their Relevance

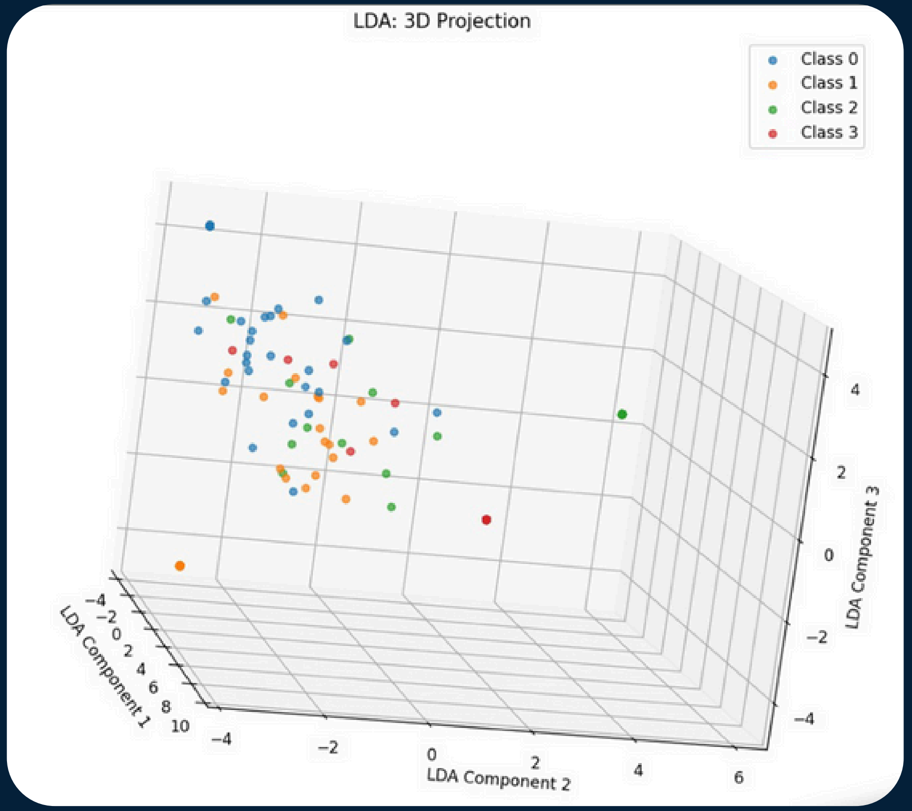
RADIOMICS ⊂ DATASET

Data Type : *Radiomics of the Tumour*

Format : *CSV*

Size: *34 MB*

Subjects: *671 (67 CSVs)*



Pre-Processing :

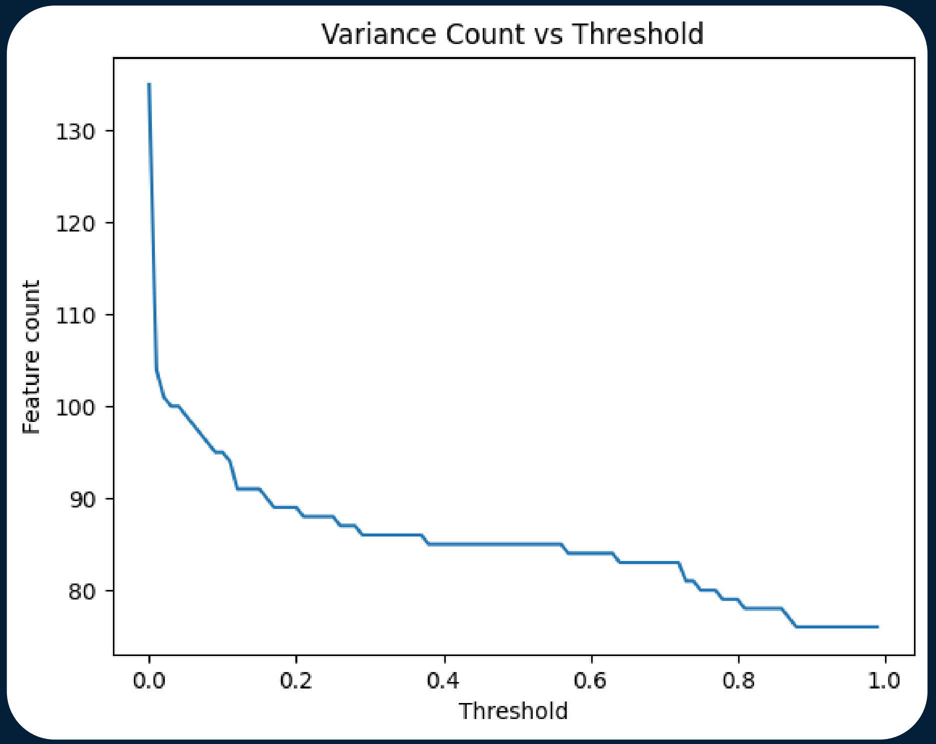
Removed duplicates and null values.

Imputed missing values using regression

Applied Z-score normalization.

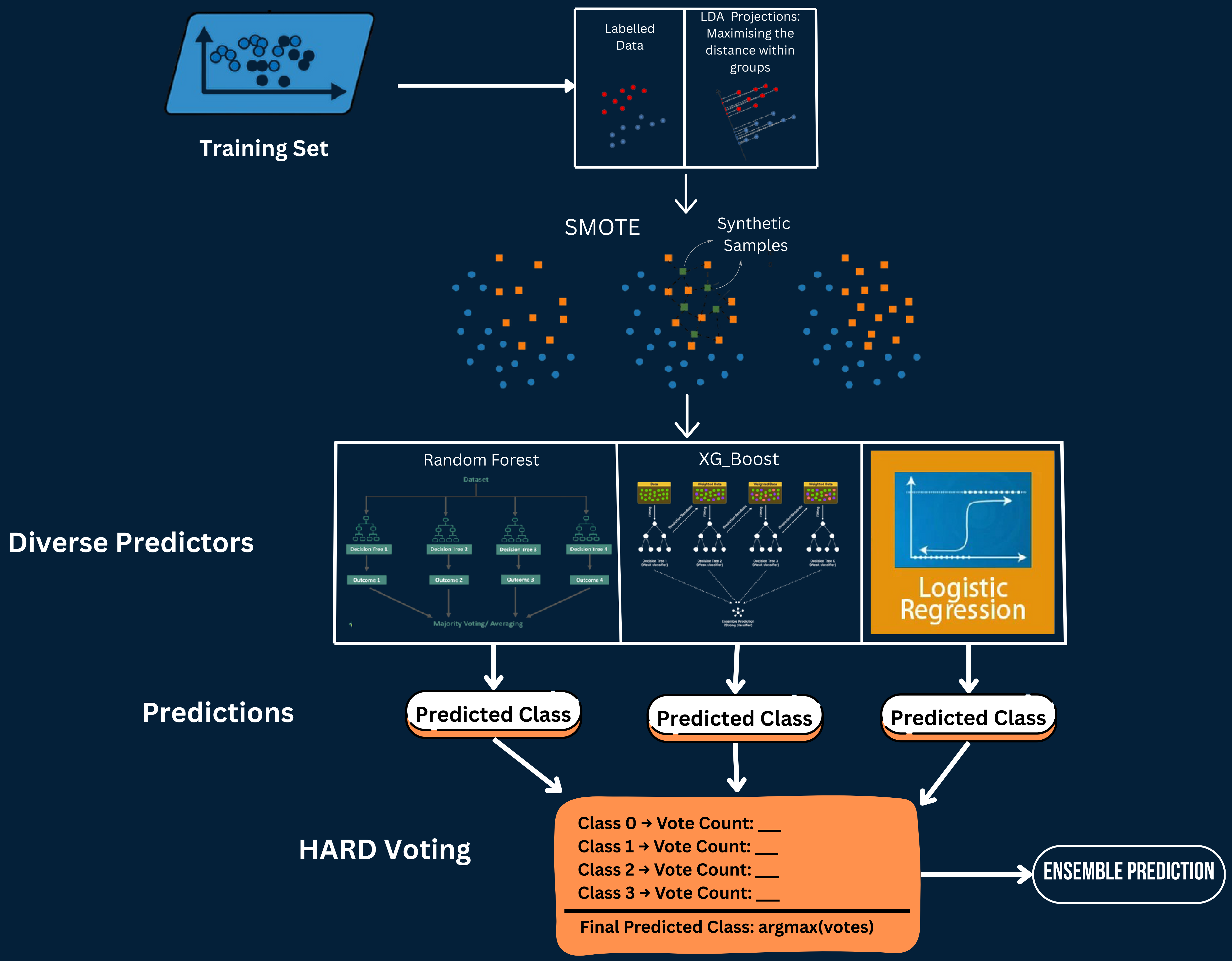
Performed Linear Discriminant Analysis with 3 components.

Allowed us to pick 300 modalities out of, 9400 and map them along 3 final features.



OUR MODEL !

VOTING CLASSIFIER MODEL ARCHITECTURE



WHY THIS?

SMOTE

It fixes the natural imbalances in medical datasets by oversampling the under-represented classes.

In effect, boosted our balanced accuracy by 12%.

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LDA

Proved ***best for feature extraction*** *compared to PCA, RF feature selection, and high-variance features.*

Increased accuracy by 30% *and c-index by 0.16 .*

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WHY THIS?

HARD VOTING

Robust method for multiple modalities where different models perform uniquely for specific modality patterns.

Enhanced accuracy by 6% and balanced accuracy by 8%

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*It **fixes the natural imbalances** in medical datasets by oversampling the under-represented classes.*

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***Robust method for multiple modalities** where different models perform uniquely for specific modality patterns.*

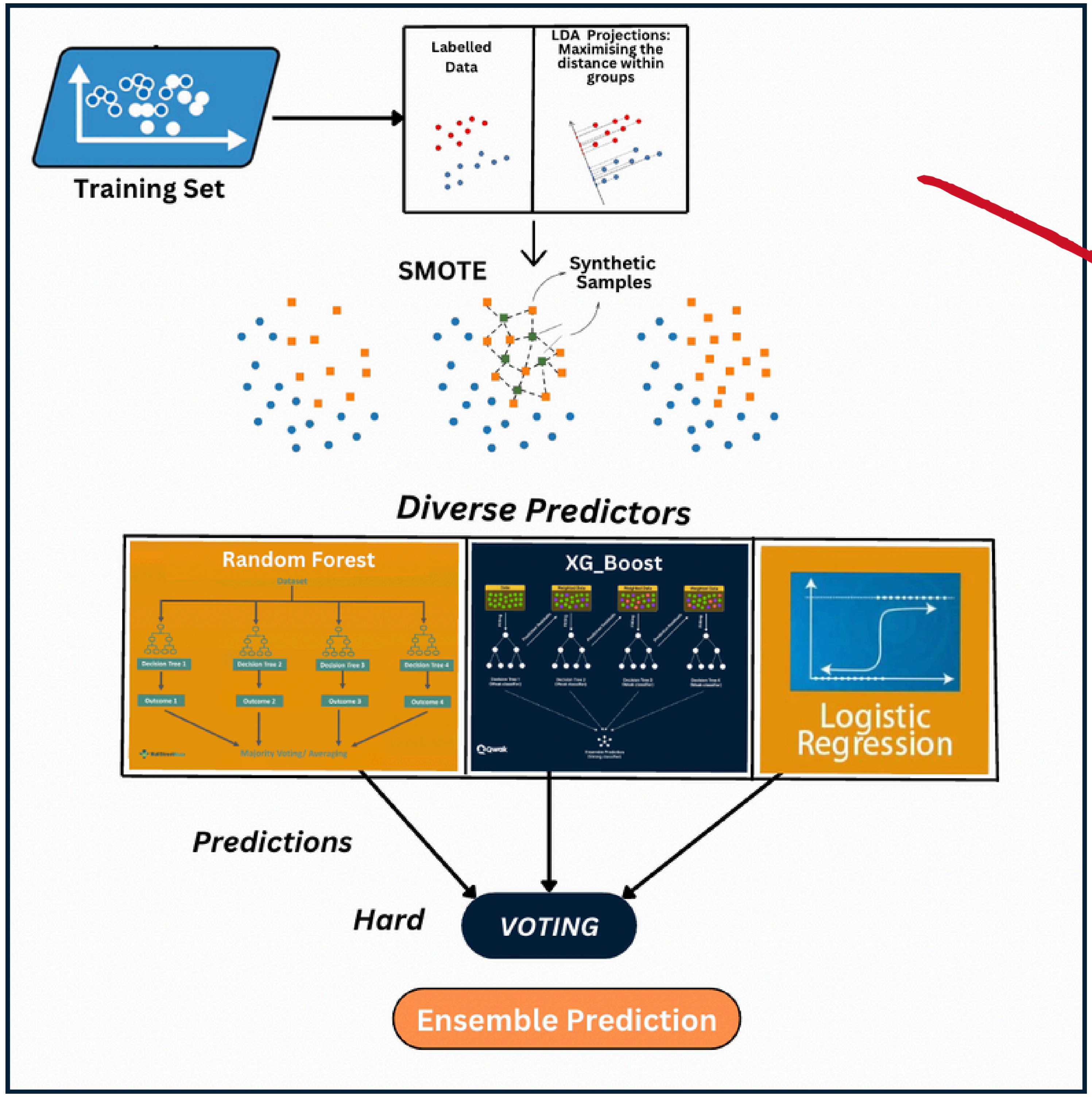
*Enhanced **accuracy by 6%** and **balanced accuracy by 8%***

EXTERNAL VALIDATION

*To check for high variance issues (**over-fitting**) and ensure **generalizability**.*

Proved robustness of the model to new and fewer modalities.

Enhanced interpretability and generalization to inconsistency in modalities for survival prediction of GBM patients.



OUR SOLUTION

METHODOLOGY

- *Train multiple Decision Trees on random subsets (Bootstrap Aggregation).*
- *Use majority voting (classification) or averaging (regression) for final prediction.*

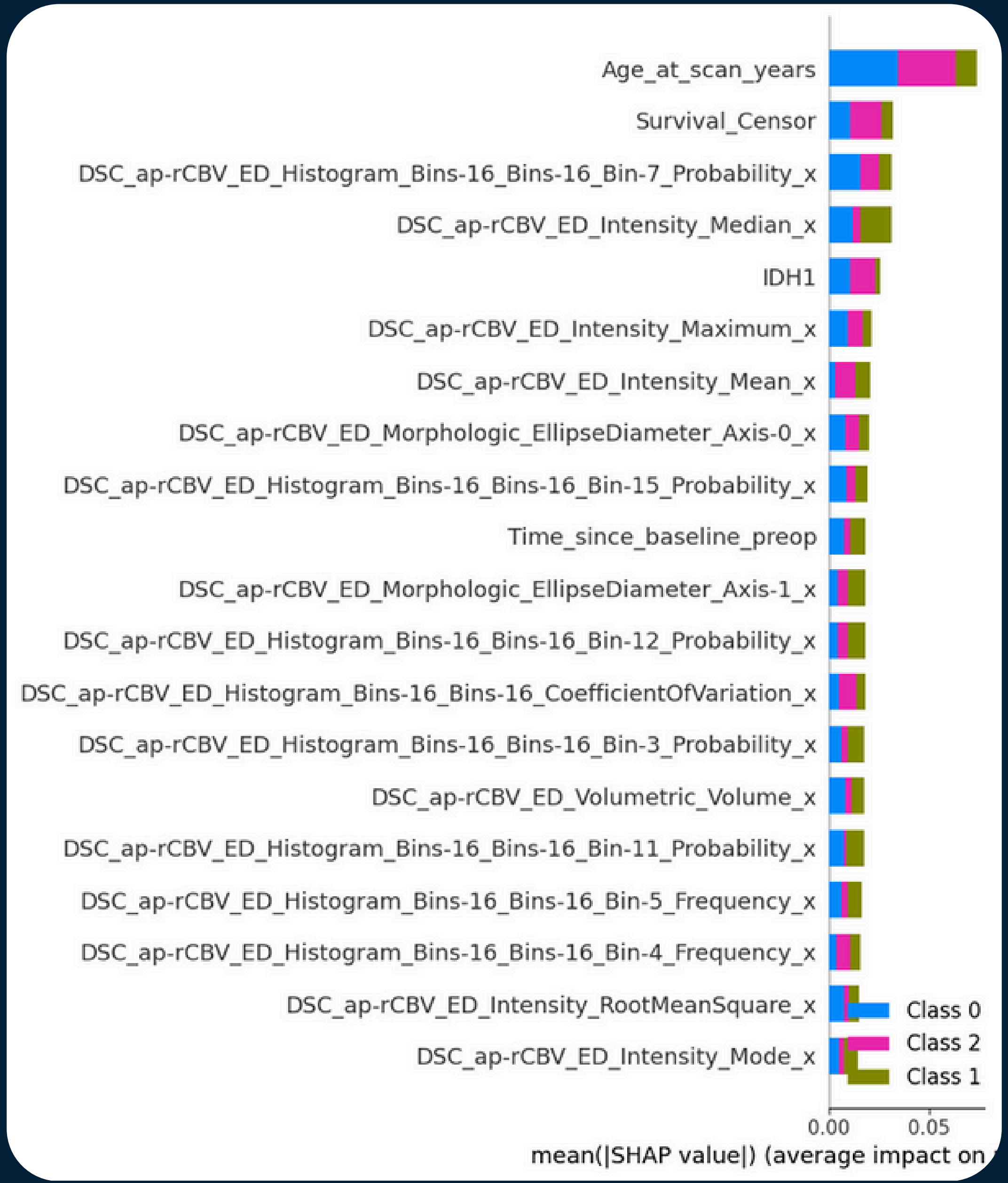
PERFORMANCE METRICS

- *Accuracy: 97%*
- *Balanced Accuracy: 94%*
- *Concordance Index: 0.88*
- *f1- score: 0.94-0.97*
- *ROC-AUC: 0.99*

EXPECTED OUTCOME

- ***Clinical Interpretability** and feature contribution (Using SHAP)*
- ***Accurate Prediction** with Varying Modalities*
- ***Generalizability** across varying datasets*
- ***Quantification** of Feature Importance (LDA Coefficients)*

INTERPRETABILITY ASPECTS



Using SHAP on RandomForest Classifier for ***Feature contribution mapping*** *for each class.*

	Feature	Importance
1	Age_at_scan_years	17.927916
4	IDH1	13.444819
5	MGMT	12.917231
0	Gender	8.627960
3815	T1GD_NC_Histogram_Bins-16_Bins-16_MeanAbsolute...	6.333860
4103	T1_ET_Histogram_Bins-16_Bins-16_MeanAbsoluteDe...	6.306016
8	Time_since_baseline_preop	6.056273
4453	T2_ED_GLSZM_Bins-16_Radius-1_GreyLevelVariance_x	5.768656
2896	DTI_TR_NC_Intensity_MeanAbsoluteDeviation_x	5.388300
1264	DSC_PSR_NC_GLCM_Bins-16_Radius-1_AutoCorrelati...	5.248733
3184	FLAIR_ET_Intensity_MeanAbsoluteDeviation_x	5.189719
3243	FLAIR_ET_Histogram_Bins-16_Bins-16_Mode_x	5.075271
7	GTR_over90percent	5.037397
3733	T1GD_ET_GLSZM_Bins-16_Radius-1_GreyLevelVarian...	4.96004[illegible]

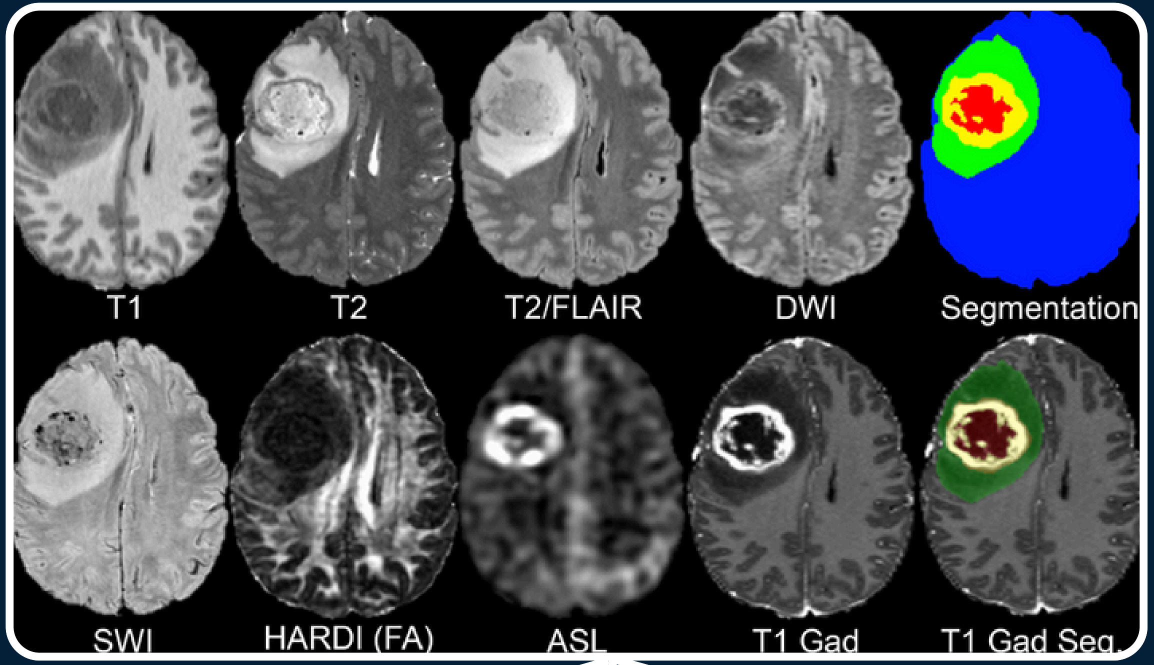
Cumulation of LDA Coefficient's magnitude to ***quantify importance*** *of each feature with respect to others in the modalities used for prediction.*

EXTERNAL VALIDATION DATASET

The University of California San Francisco

495 Patients of *de novo* Glioblastoma

2015-2021



23 MRI Scans per Patient

130 Radiomic + 16 Clinical features extracted

Segmented Tumor Masks

Credit to Authors :

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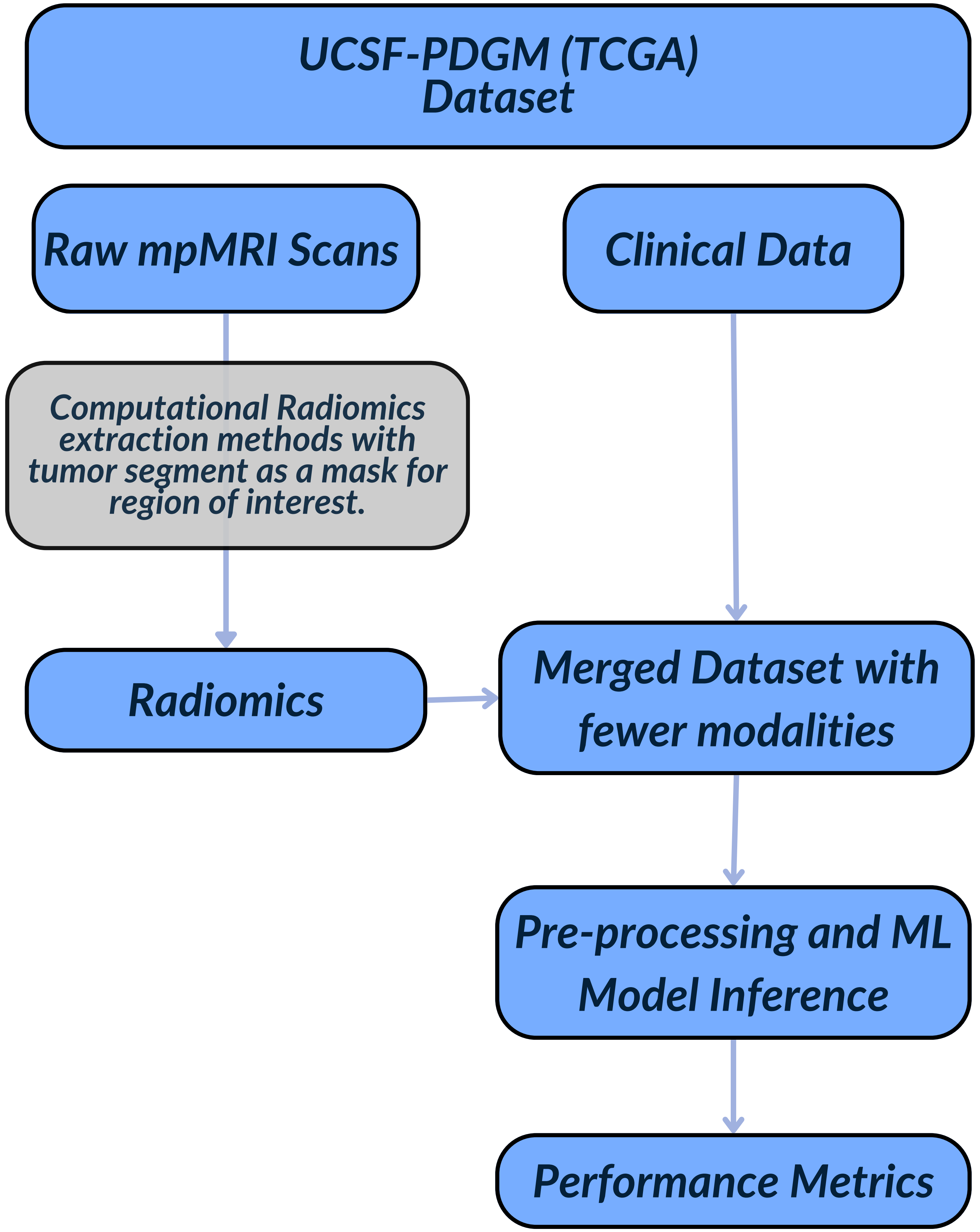

VALIDATION RESULTS

OBSERVATIONS

- *Extraction of radiomics from raw MRI scans is* ***computationally expensive.***
- *A* ***mask was needed*** *to limit the modalities to a specific region of interest.*
- *All papers with these datasets seems to have neglected the* ***curse of dimensionality***.
- ***LDA coefficient based importance*** *was used to extract 94 features from a pool of 1678 features after stacking all various scans.*

PERFORMANCE METRICS

- *Accuracy:* **92%**
- *Balanced Accuracy:* **91.6%**
- *Concordance Index:* **0.8658**
- *f1- score:* **0.91**
- *ROC-AUC:* **0.9710**

DEPLOYABILITY & FUTURE CHALLENGES

Technical

Designed for deployability, the model uses lightweight ML algorithms (RF, XGBoost) that are **fast to train and easy to export**

Interpretability is enhanced through LDA and SHAP, enabling clinicians to visualize and **understand key features.**

Standardized preprocessing pipelines ensure consistent performance across institutions.

Clinical

Good performance in accuracy and C-Index **supports clinical adoption.**

Demonstrates **strong generalizability** by performing well across diverse data types and modalities, even with **partial inputs**.

Challenge

Highly compute expensive feature extraction method **limits scalability**

CHALLENGES FACED

Too Many Features, Not Enough Data!

We had a lot of features but relatively few data points, which could lead to overfitting.

So, we reduced the number of features using LDA and selected only the most useful ones.

Traditional ML Trade-offs

Models like Random Forest and XGBoost are easier to understand, but they might miss complex patterns.

We accepted this trade-off to keep things interpretable and used SHAP to add deeper insights.

Clinical Deployment Barriers

Real-world adoption needs validation, updates, and clinician trust.

Addressed through explainability tools (SHAP), standardized pipelines, and modular design for easy updates.

THANK YOU!