# A Brain Metastasis Study with Machine Learning

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## The team

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## What is brain metastasis?

It happens when cancer cells travel from other parts of the body and form tumors in the brain. It is currently one of the most complicated forms of cancer to treat. But there is hope, early detection and effective treatment go a long way to have better odds.

# Our goals

We sought to resolve one of the most important questions patients have: "How much time do I have left to enjoy life?". Other goals such as helping doctors predict when a person is likely to relapse, and effective treatment methods were also important.

## What's our dataset like?

We worked on the MOLAB Brain Metastasis Dataset, a structured and anonymized dataset covering segmented Magnetic Resonance Imaging (MRI) scans, clinical data and morphological measurements of 75 patients.

There are 3 groups of files with structured and unstructured data.

- Clinical data: an excel spreadsheet with patient data and treatment history.
- Morphological measures: an excel file with tumor dimensions and MRI info.
- The MRI scans are in formats such as nifti and DICOM.

# Clinical data

| Variable                                | What it really means                                  |  |  |
|---|---|--|--|
| Patient Data                            | Section includes data such as age at 1st scan and sex |  |  |
| Lesion                                  | Tumors numbered in the order they were discovered     |  |  |
| Primary Tumor                           | Numbered 1 - 12 with subtype for breast & lung cancer |  |  |
| Whole Brain Radiation<br>Therapy (WBRT) | Includes dosage and period administered               |  |  |
| Stereotactic<br>Radiosurgery (SRS)      | A non-surgical radiation therapy.                     |  |  |
| Radiation Necrosis                      | Tissue breakdown due to radiation                     |  |  |
| Surgery                                 | Describes type (full, partial, unknown) and time      |  |  |
| Systemic Treatment                      | Drugs given and the time period                       |  |  |
| Death                                   | Measured in days. Cause is also given.                |  |  |
| MRI Follow up dates                     | Minimum 4 appointments, Maximum 19                    |  |  |

# Morphological measures

| Variable  | What it really means  |  |  |
|---|---|--|--|
| General data  | Patient ID number, info about image and equipment used  |  |  |
| Other measurement data  (Don't worry too much about this unless you're an MRI expert) | <ul> <li>SBS (Space between Slices) in millimeters</li> <li>SCS (Slice Thickness) in millimeters</li> <li>REPTIME (Repetition Time) in milliseconds</li> <li>CEVOLUME (Contrast-Enhancing Volume) VCE</li> <li>NECVOLUME (Necrotic (Non-Enhancing) Volume) Vn</li> <li>TOTALVOLUME V=VCE+VN</li> <li>CERIMWIDTH (Contrast-Enhancing (CE) Spherical Rim Width): based on CE areas' average width.</li> </ul> |  |  |
|   | <ul> <li>SURFACEREGULARITY: 0 to 1 for roundness.</li> <li>MAXDIAMETER3D: tumor's max. diameter.</li> </ul>   |  |  |

#### **MRI** scans

The dataset came with images that had already been processed (Figure 1). One of the benefits of working with this dataset were the clearly annotated images with dimensions.

PATIENT N10020 FEMALE AGE 44 TIME OF DEATH 1625 DAYS

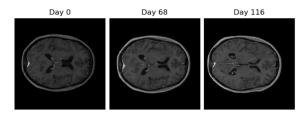


Figure 1: Sample MRI scan over time period

# Our strategy

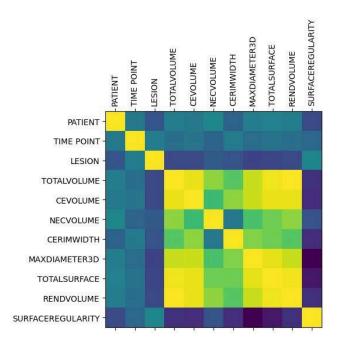
We'll run you through how we explored our data, decided on a Machine Learning (ML) approach and our results.

# Data preparation (pre-processing & cleaning)

Clinical data and morphological measures were structured differently in separate files. Organizing the data in one dataset made it easier for our models to understand. Also there were empty cells and data format issues to resolve.

## Data analysis

A whole lot of plots, graphs and code were needed to understand the relationship between our variables and know what we could predict with the most certainty. While working our data, we were made aware of factors that could affect the accuracy of our model, such as size, class imbalance and outliers (Figure 2 & 3).



**Figure 2**: Correlation matrix for Morphological Measures. High correlation between variables derived from each other. Aided selection of most pertinent variables for model training.

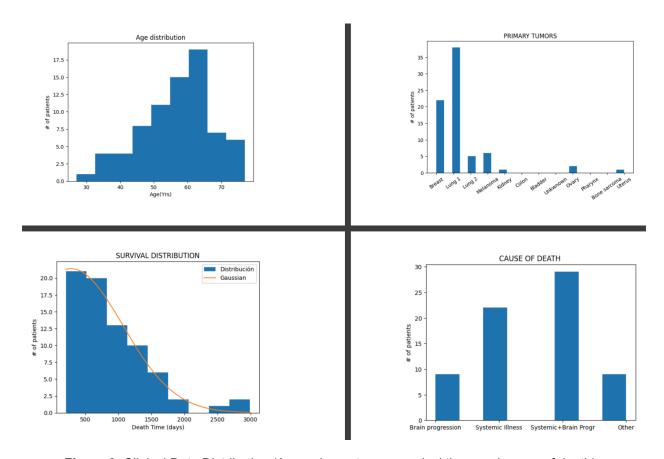


Figure 3: Clinical Data Distribution (Age, primary tumor, survival time, and cause of death).

## Prediction approach

It was challenging selecting which level to apply our model (patient, tumor, evolution over time or a combination). Figure 4 is an example for lesion volume. We saw it would be difficult to do a time series prediction as tumor evolution varied widely.

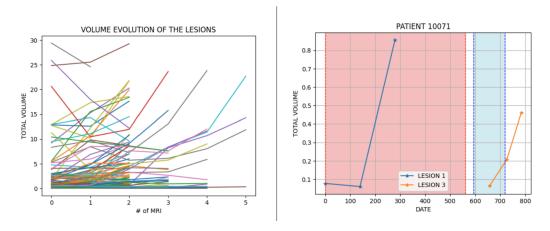
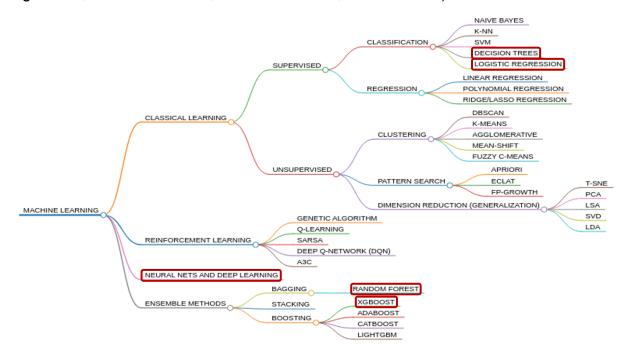


Figure 4: Temporal evolution of tumor total volume viewed by tumor and by patient

## **Model Selection**

Our small dataset size limited model selection. Figure 5 shows the main ML method groups with the ones we explored highlighted in red (Decision trees, Logistic Regression, Neural Networks, Random Forests, and XGBoost).



<u>Figure 5</u>: Machine learning methods concept map showing selected models from the main ML method groups (Classical, Reinforcement, Neural Networks/Deep Learning & Ensemble methods)

# Model training

Our main objectives were translated into variables for our models to predict.

- Objective 1: Predict <u>survival time</u> in days
- **Objective 2a**: Predict <u>lesion relapse</u> (for all patients)
- **Objective 2b**: Predict <u>lesion relapse</u> (only patients who had radiosurgery)

We chose a binary and multiclass approach to compare model performance. Various model parameters were used to arrive at optimal results.

## **Binary Classes**

#### Objective 1: Survival time

- Survival <500 days</li>
- 500 days or more

Objective 2a & 2b: Relapse (all patients & patients with radiosurgery)

Relapse: tumor growth > 30%No relapse: tumor growth < 30%</li>

#### Multiclasses

#### Objective 1: Survival time

- Survival <500 days</li>
- >= 500 or <1500 days
- >= 1500 days

Objective 2a & 2b: Relapse (all patients & patients with radiosurgery)

- Relapse: tumor growth > 30%
- No relapse: tumor growth 0 30%
- Improvement/tumor shrinkage: tumor growth < 0%

# Input data summary

| Objective | Size   | Input  | Predicted variable                       |
|-----------|--|--|--|
| 1         | 75 rows<br>5 columns                               | sex (categorical) age (numerical discrete) gpa (numerical discrete) nlesions (categorical ordinal) type (categorical ordinal)  | survival days<br>(numerical<br>discrete) |
| 2a & 2b   | 345 rows<br>(2a)<br>105 rows<br>(2b)<br>13 columns | sex (categorical) age (numerical discrete) gpa (numerical discrete) cermwidth (numerical continuous) surfaceregularity (numerical continuous) totalvolume (numerical continuous) srs (numerical continuous) days_since_srs (numerical discrete) wbrt (numerical continuous) days_since_wbrt (numerical discrete) | relapse<br>(categorical<br>boolean)      |

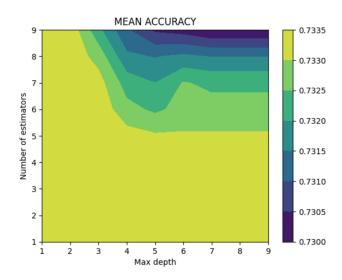
# Results

We summarized results of different trials. More information is available on GitHub.

# Objective 1 (Predict Survival Time) - Model Training Results (Binary)

| Model               | Accuracy | AUC* | Comments   |
|---------------------|----------|------|--|
| Logistic regression | 71       | ı    | Seeds: 10000   |
| Decision Tree       | 72       | 67   | Tree depth of 4 performed best                                   |
| Random Forest       | 73       | -    | Estimators: 15, Iterations: 5000                                 |
| XGBoost             | 73       | 75   | Estimators: 4, depth: 4, iterations: 10000                       |
| Neural networks     | 75       | -    | Epochs: 5, Seeds: 1000 (higher uncertainty than previous trials) |

<sup>\*</sup>AUC (Area Under ROC Curve)



**Figure 6**: Selection of parameters for best performing model (XGBoost)

# Objective 1 (Predict Survival Time) - Model Training Results (Multiclass)

| Objective         | Class      | Results  |
|-------------------|------------|--|
| 1 (survival time) | Multiclass | Model accuracy varied between 35 - 46%.  XGBoost showed the best performance |
|                   |            | XGBoost showed the best performance  |

# Objective 2a Summary Predict lesion relapse (all patients)

| Objective                  | Class      | Results   |
|----------------------------|------------|---|
| 2a (relapse, all patients) | Binary     | Model accuracy varied between 47 - 58%.  Decision trees showed the best performance |
| 2a (relapse, all patients) | Multiclass | Model accuracy varied between 43 - 50%.  Best performance with XGBoost.             |

## Objective 2b Summary Predict lesion relapse (patients with radiosurgery)

| Objective                       | Class      | Results   |
|---------------------------------|------------|---|
| 2b (relapse, patients with srs) | Binary     | Model accuracy varied between 52 - 59%.  Best performance with Logistic Regression. |
| 2b (relapse, patients with srs) | Multiclass | Model accuracy varied between 33 - 41%.  XGBoost showed the best performance        |

## Conclusion

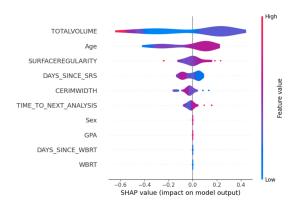
Our model performed best for predicting survival days, we expect results can be improved with more data. Predicting relapse gave poorer results given higher variance. Also there was generally poorer model performance on multiclass compared to binary classifications. Model performance depended on the task, emphasizing the importance of experimentation with several models to compare results.

We recognize that there are factors that impact both outcomes that are not captured in our dataset. Still it serves as a good starting point for similar studies on diseases with relatively small populations.

We must add that these are promising results. With only 75 patients we have been able to predict with an accuracy of 75% their survival time. In the case of predicting relapses, it is obvious that we are just beginning and accuracy can be improved with additional data and more details. We also expect advanced approaches for model adjustment to yield more favorable outcomes.

## Explainable ML

Our model is designed to make predictions that are critical to people's lives and their decisions for the future. So we made sure it would be transparent both to us and patients. To that end, we've added the SHAP (SHapely Additive exPlanations) values, links to the data and our <u>code</u>. Why? Because we know it's harder to trust Al when it's shrouded in mystery.

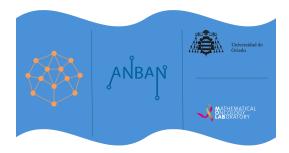


**Figure 7**: SHAP value (impact on model output)

**<u>Disclaimer</u>**: models are fallible and should NEVER be used without professional advice.

## How we did it

With teamwork and a lot of help from our <u>coordinator</u>, instructors, mentors, the <u>organizers</u> of <u>SaturdaysAl</u> Asturias, our <u>hosts</u>, and the wonderful people at <u>MOLAB</u>.



Some of us knew little about Python and in just 12 weeks together, we trained ML models. Hopefully, our story helps you on your journey to making lives better with artificial intelligence. We look forward to your feedback and comments on our ML project.



We acknowledge ideation and visualization support from Generative AI - ChatGPT, Bing Copilot, and DALL-E.

# Next steps

For anyone looking to join our fight against brain metastases, here are some avenues we would have liked to explore.

- We discovered the cause of death was a variable that could be predicted during our data exploration. However, we were not able to advance this option due to time constraints.
- Varying the threshold for percentage tumor growth to define as a relapse. We used 30% growth as our criteria.
- Augment the dataset size with Generative Adversarial Networks.
- We did not achieve better results by separating patients that had surgery from the rest. Notwithstanding, it is worth exploring whether splitting the dataset by other criteria will yield better results.

## Resources

- MOLAB
- MOLAB brain metastasis dataset
- Brainlab.org
- Brain metastases: A documentary