

Interreg

ITALIA-SLOVENIJA



TRAIN



UNIONE EUROPEA
EVROPSKA UNIJA

Progetto standard co-finanziato dal Fondo europeo di sviluppo regionale
Standardni projekt sofinancira Evropski sklad za regionalni razvoj

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Virtual Biopsy

Vincent Torre - SISSA

Humanitas Milan (Miran Skrap)

SISSA (Laio, Torre)

Univ Genova (Verri)

Glance Vision Technology Srl

DataMind Srl

BioValley Investments

TUMOR PATHOLOGY

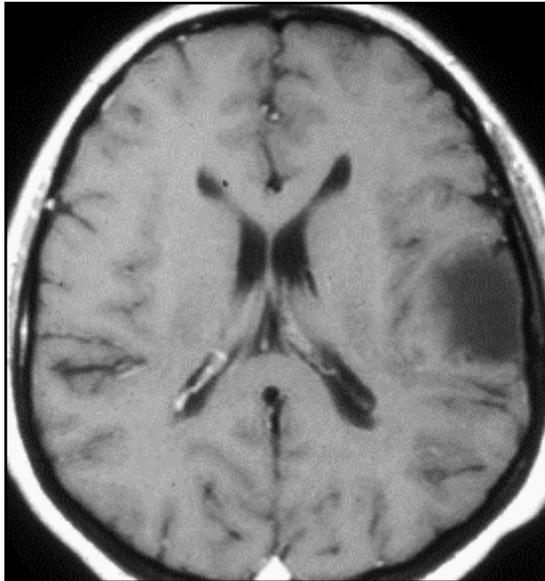
- **THE MOST IMPORTANT OPERATIVE PLATFORM IN NEUROSURGERY**
- it represent the 70 - 80 % of neurosurgical cases
- urgent or relatively urgent treatment
- the surgical experience still remain essential in spite of the many tools are available

BIG OPPORTUNITY

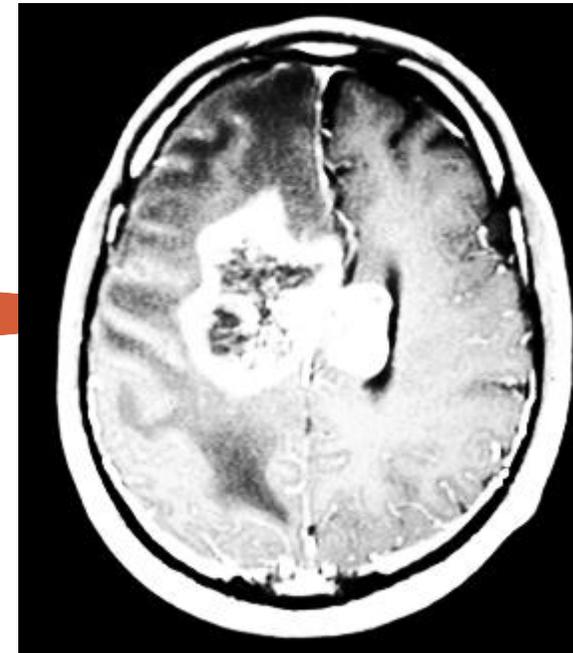
- for developing new technical devices
- for research and applications

GLIOMAS with low and high malignancy

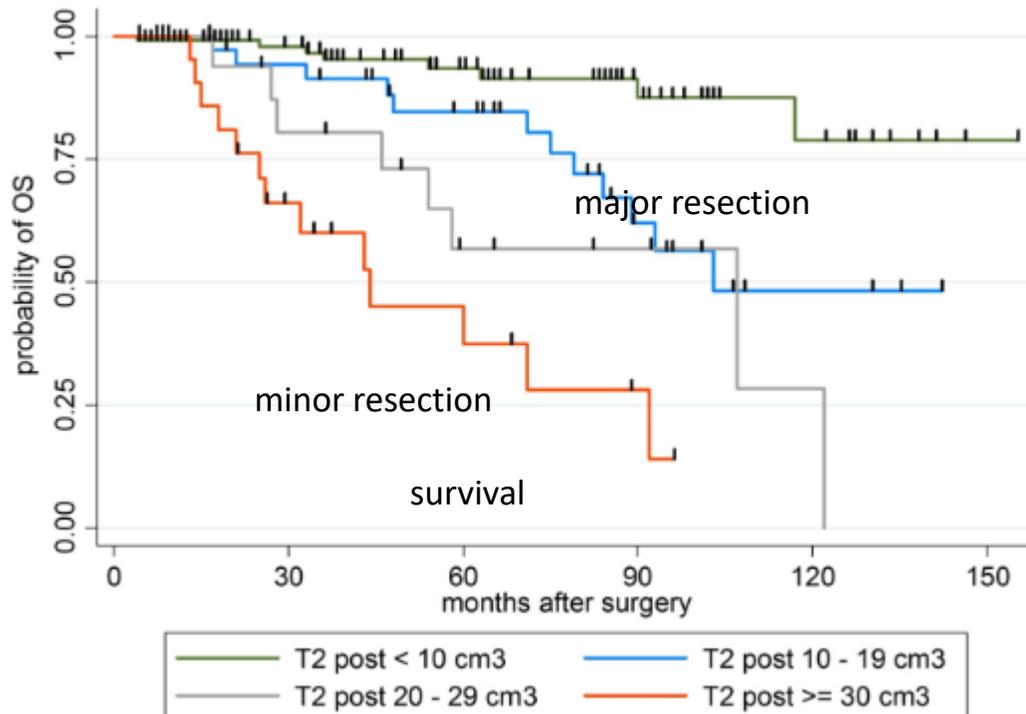
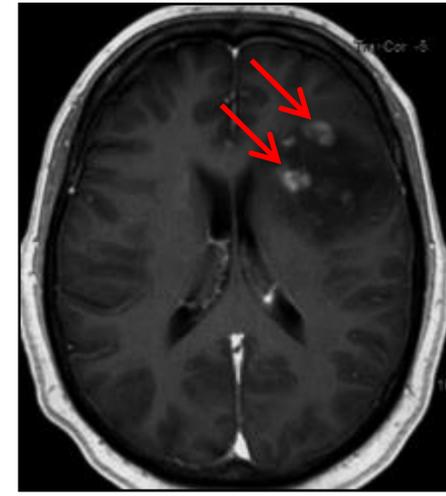
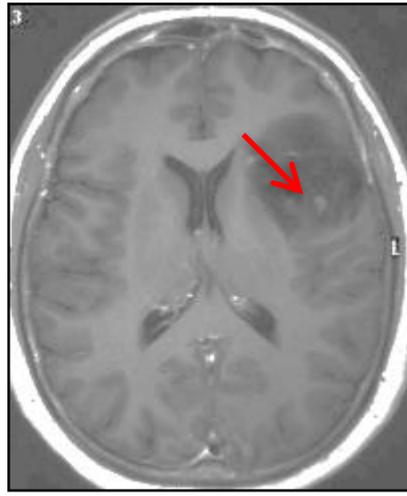
low grade



high grade



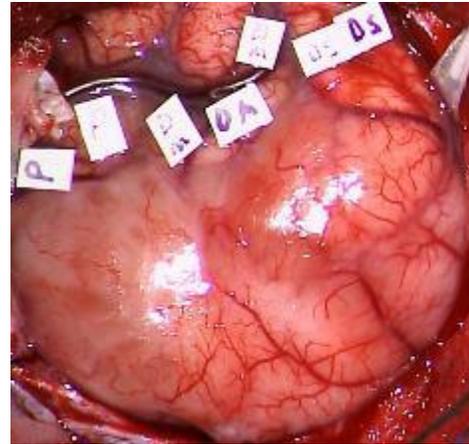
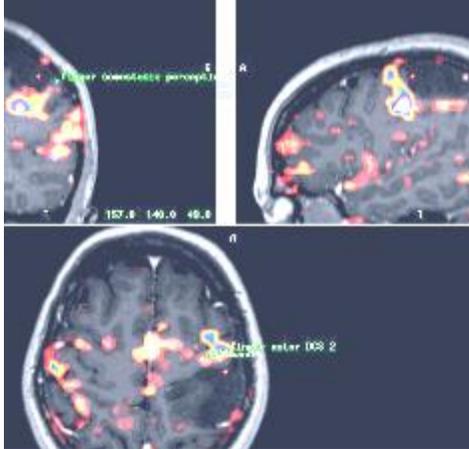
**the high grade are the most frequent tumors .The low grade is more rarely detected.
In few years also the low grade glioma will become highly malignant.**



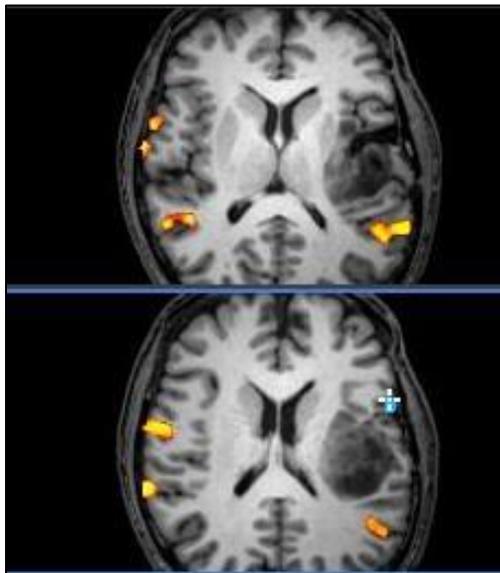
**TODAY THE BEST TREATMENT IS THE SURGICAL MAJOR POSSIBLE RESECTION .
THE LIMIT FOR A RADICAL RESECTION IS THE VICINITY OF AN IMPORTANT FUNCTIONAL AREA WHICH IS INFILTRATED BY TUMORAL CELLS. (language, movement ...)**

BIG EFFORT TO IDENTIFY THE FUNCTIONS IN THE BRAIN BEFORE AND DURING SURGERY

FUNCTIONAL MRI BEFORE SURGERY INTRAOPERATIVELY TO CONFIRM THE FUNCTIONAL LOCATION



quite simple for the movement



more complex for language and more cognitive functions.
We do an awake craniotomy to have the collaboration of the patient

Novel Biomarker (*gene analysis*)

Different prognosis is correlated with differences in transcriptome

RNA deep sequencing analysis



82 genes



Proteins involved in other solid cancer with Positive prognostic value

LGG BAD
79/82
up-regulated

LGG GOOD
3/82
up-regulated

ICAM1, IL1A, IL6, CXCL2, CXCL3, CCL20, PTGDS...

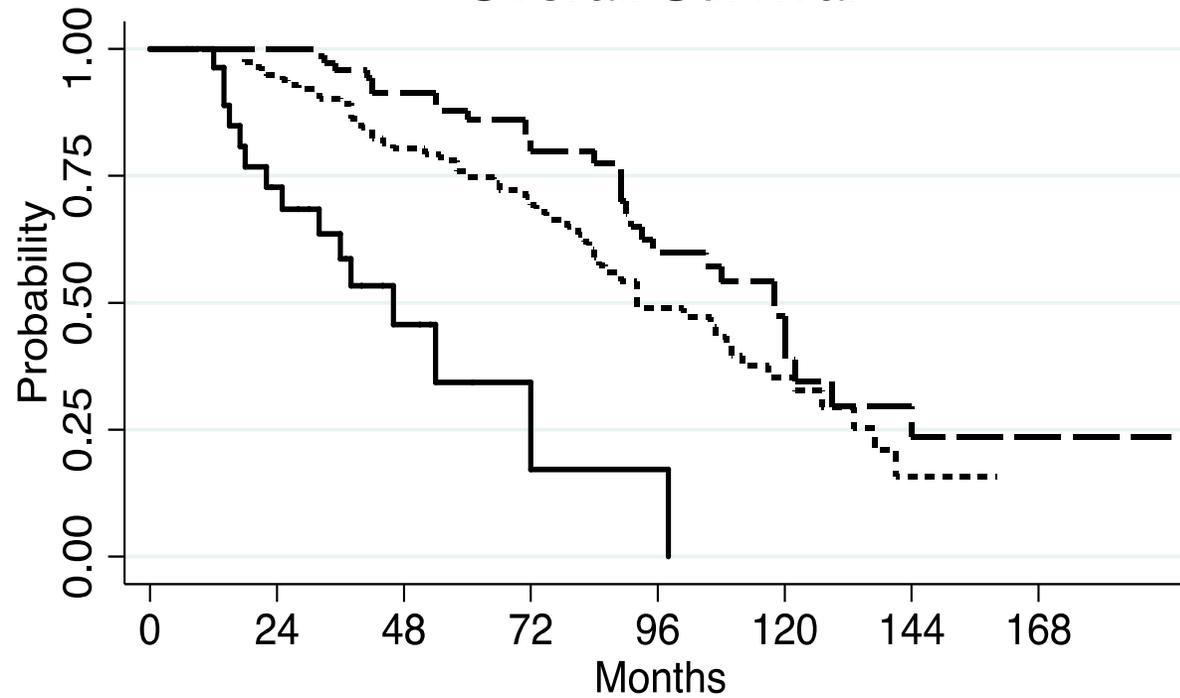
Functional analysis:
genes involved in the **inflammatory response**, in the **communication between innate and adaptive immune cells** and a **deregulation of pathways involved in metabolism**

NPTX1, ITGA8, TMEM119

The hallmarks of cancer comprise six biological capabilities acquired during the multistep development of human tumors.

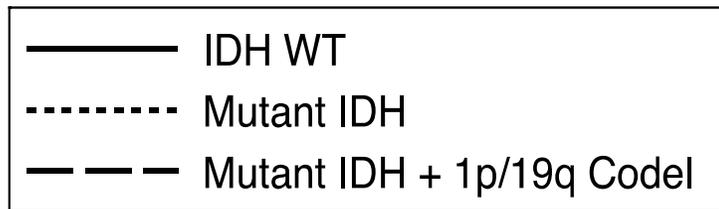


Overall Survival



Number at risk

	0	24	48	72	96	120	144	168
IDH WT	31	17	6	2	1	0	0	0
Mutant IDH	129	105	77	50	28	15	3	0
Mutant IDH + 1p/19q Codel	79	76	55	40	23	11	5	2



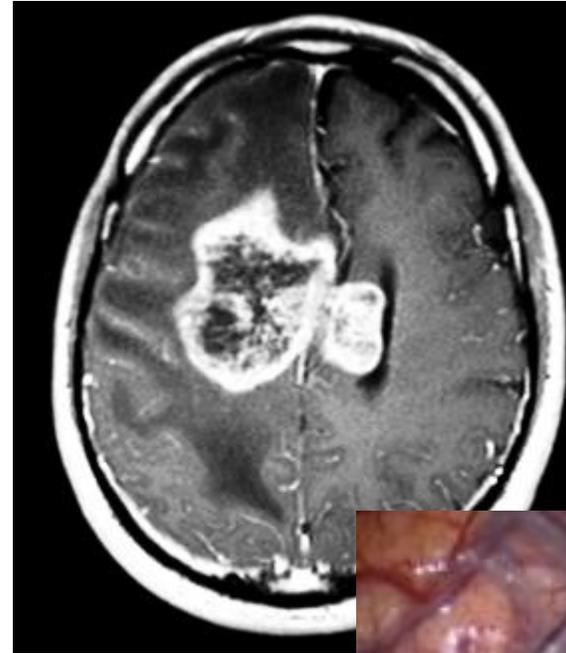
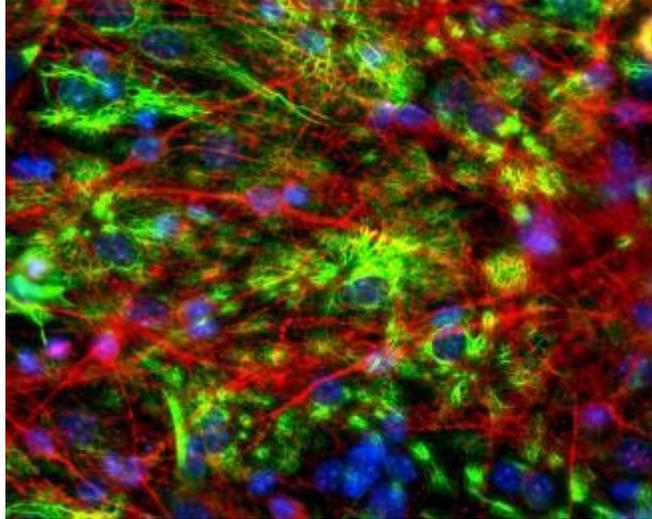
The key questions in Neurosurgery:

The patient has to be operated?

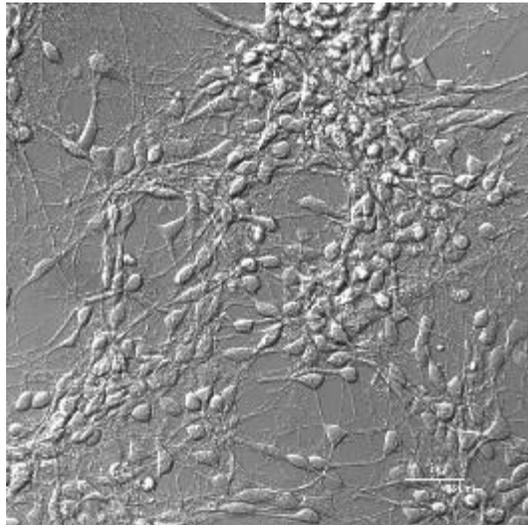
If so how much brain has to be removed?

Can we avoid a real biopsy and use Artificial Intelligence?

Artificial Intelligence for Biomedical Images



To understand almost automatically this kind of biomedical images



Clinical predictions from the data

LEARNING

Features



Ground
Truth

Extract features containing sufficient
information for reproducing the ground
truth observation

Clinical predictions from the data

LEARNING

Features



Ground
Truth

Extract features containing sufficient information for reproducing the ground truth observation

PREDICTING

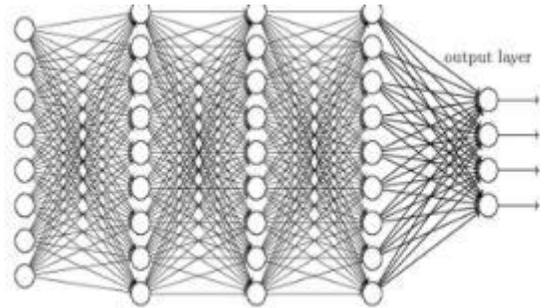
Features



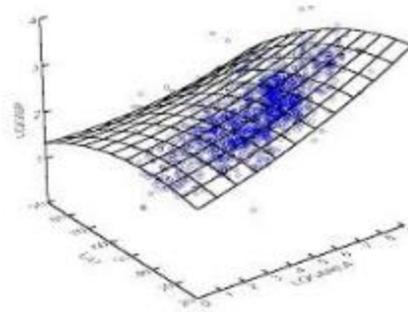
Prediction

Which tool should we use?

Neural networks. Deep learning.



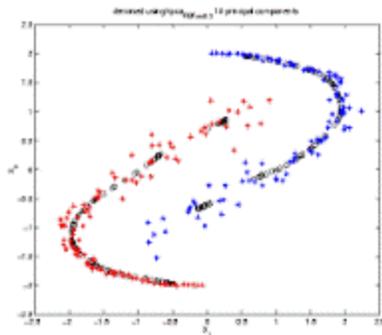
Multivariate regression.



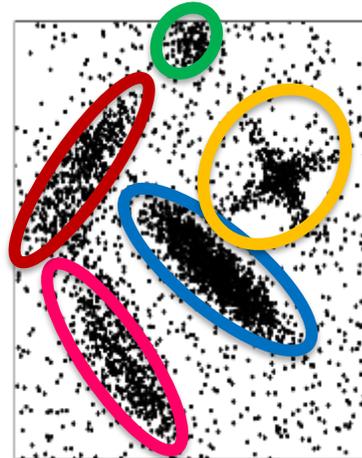
Bayesian inference

$$P(q|Y) = P(Y|q) P(q) / P(Y)$$

Kernel PCA

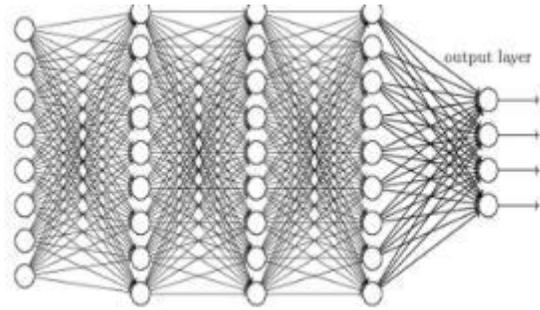


Clustering

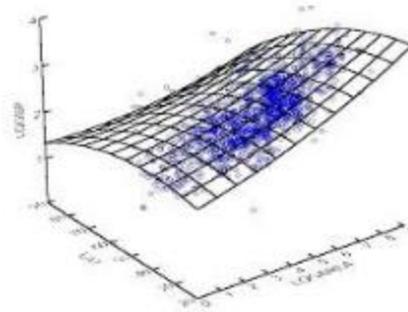


Which tool should we use?

Neural networks. Deep learning.



Multivariate regression.



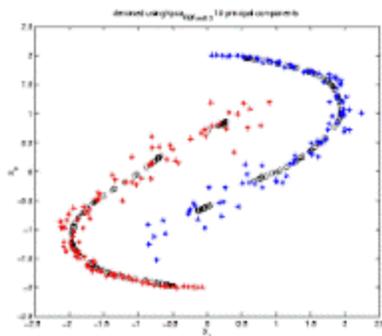
Threats:

- Irrelevant features (many)
- Inaccurate ground truth
- Censoring
- A relevant features is missing
- Too few patients
-

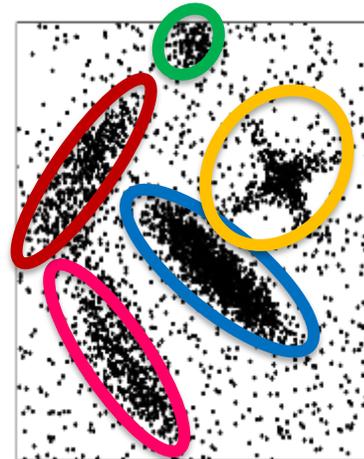
Bayesian inference

$$P(q|Y) = P(Y|q) P(q) / P(Y)$$

Kernel PCA

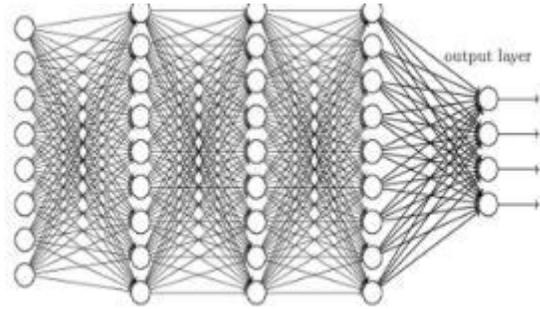


Clustering

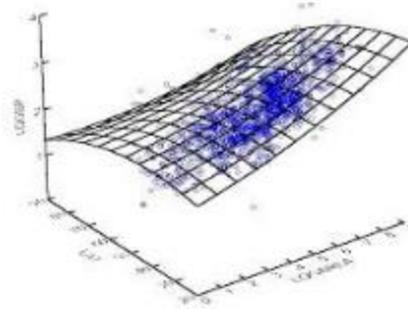


Which tool should we use?

Neural networks. Deep learning.



Multivariate regression.



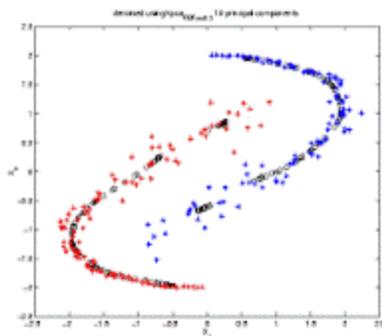
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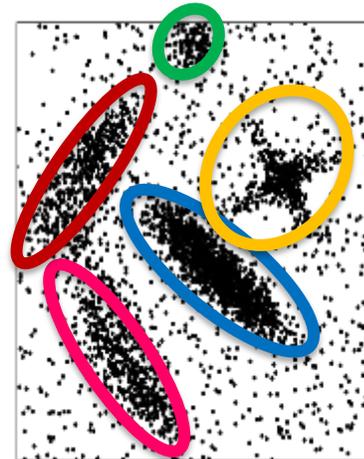
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Clustering

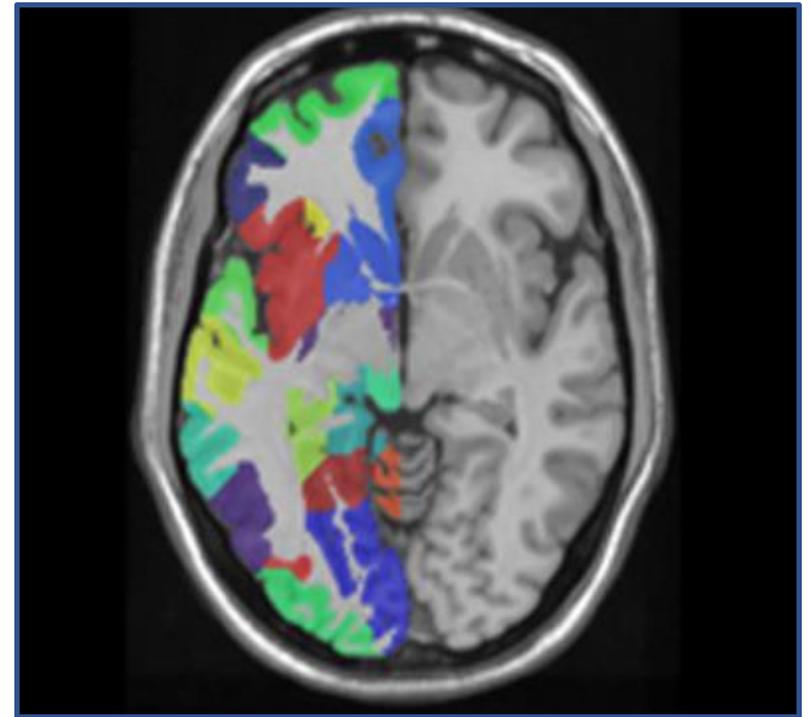
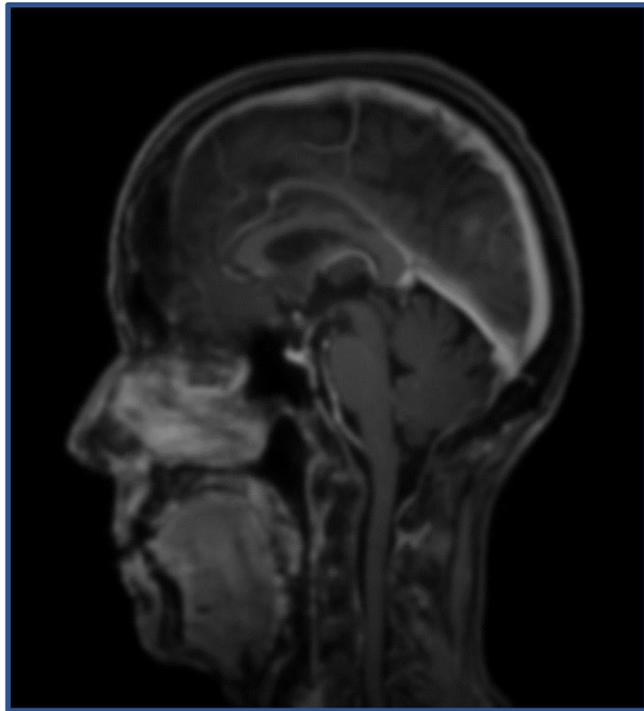


Our goal:

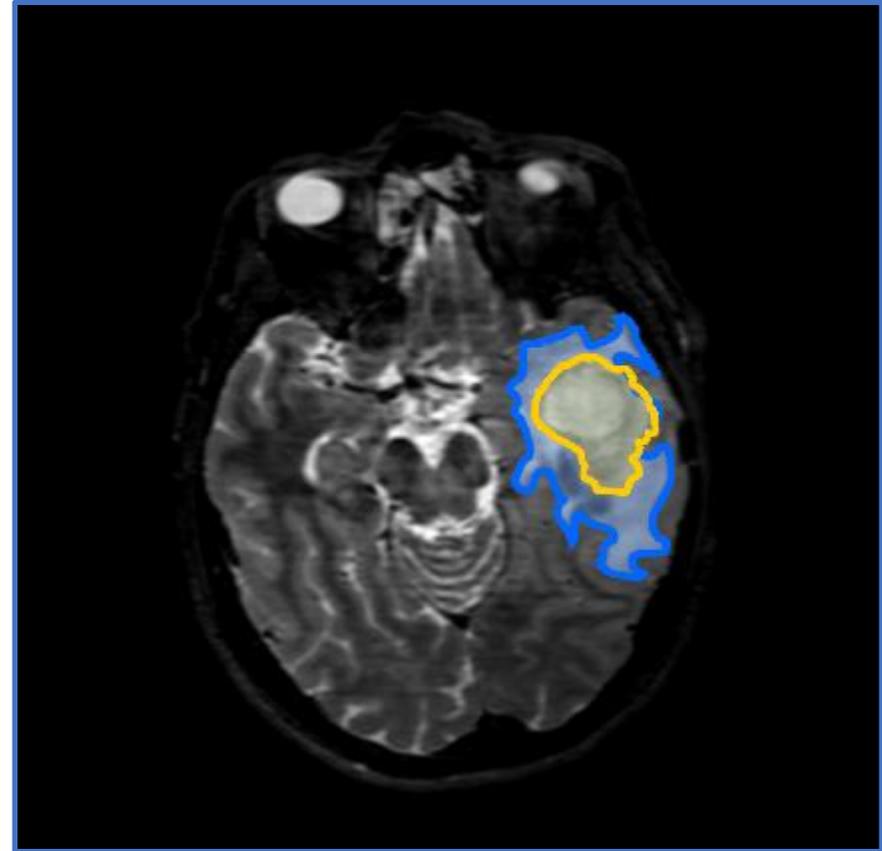
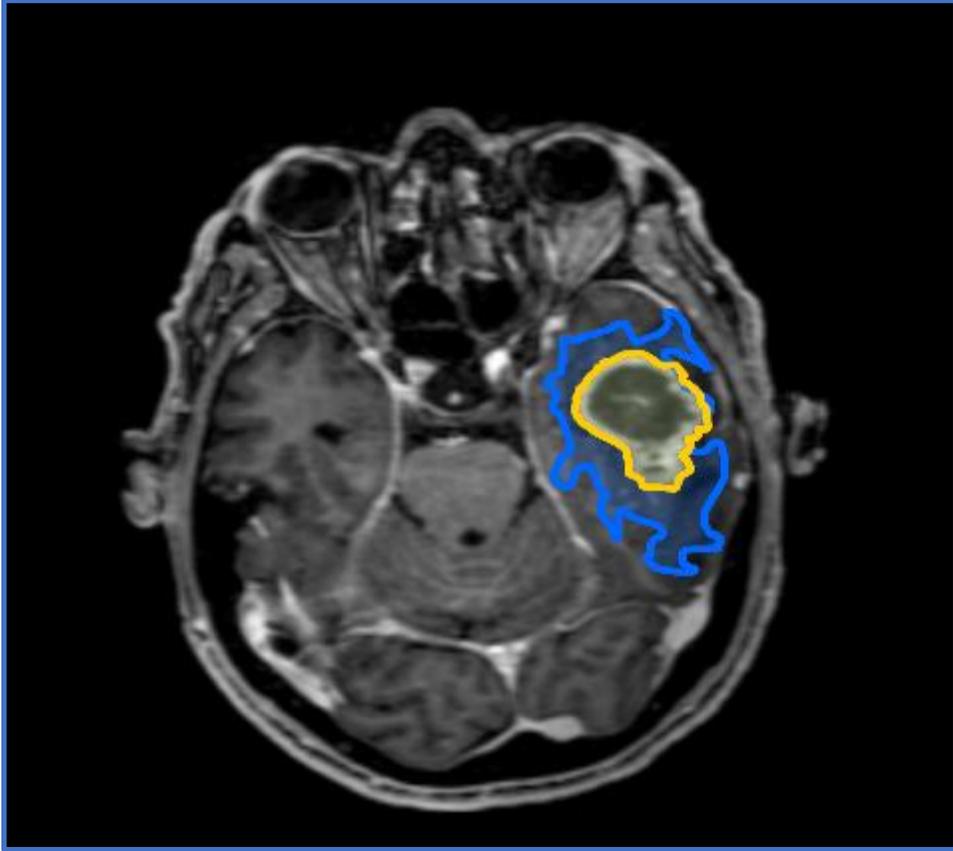
Finding the most threat-resistant prediction tool for the specific task of the project (virtual biopsy of gliomas)

What we have done so far

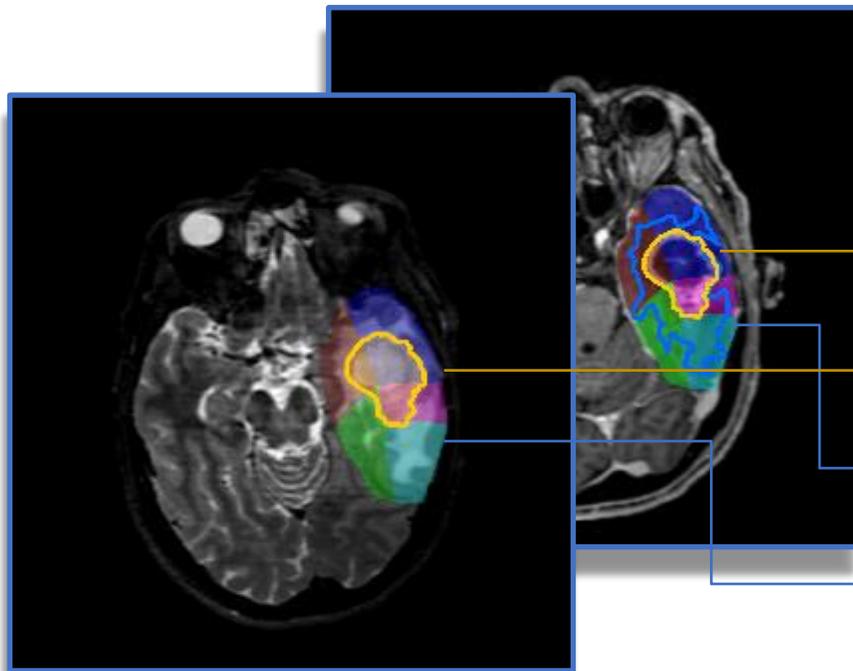
Brain Regions Map



Automatic Segmentation of Lesion and Edema



Multimodal Feature Extraction for Virtual Biopsy



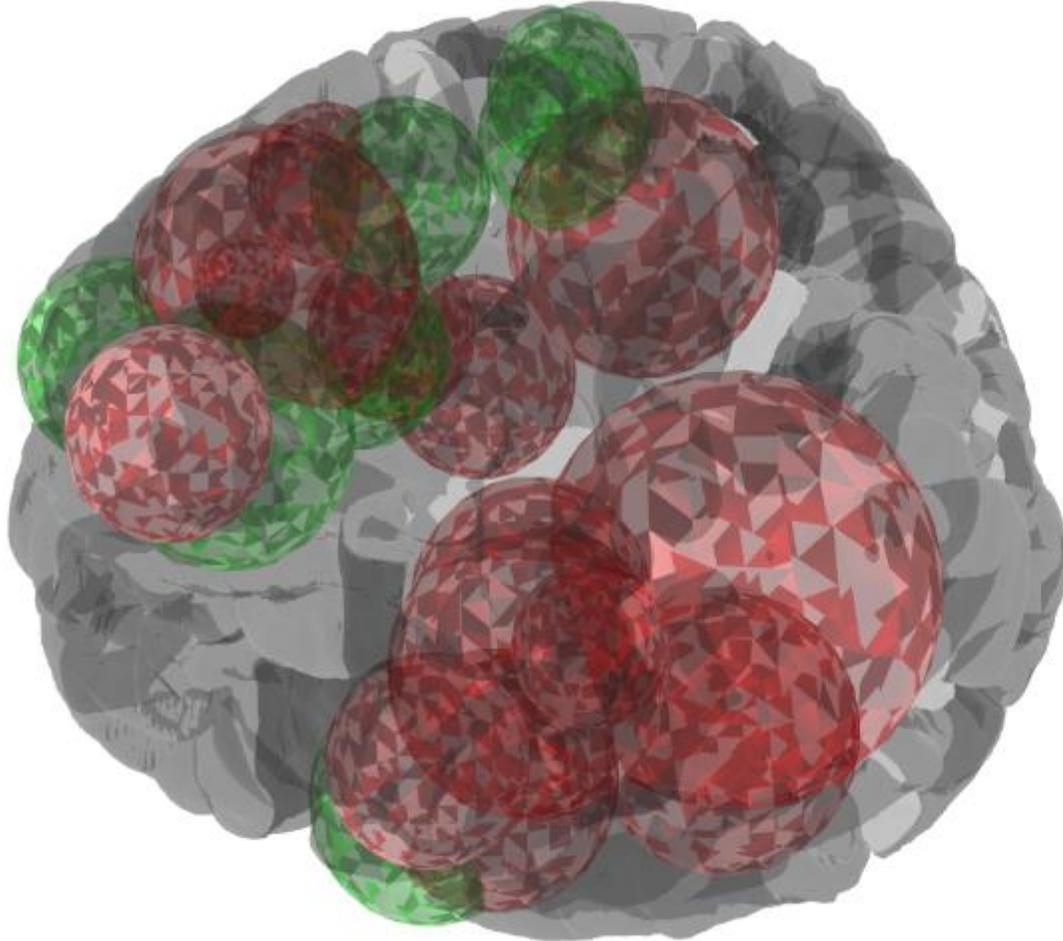
TEXTURAL FEATURES \cap R3	
TEXTURAL FEATURES \cap R2	
TEXTURAL FEATURES \cap R1	
TEXTURAL FEATURES	
GLCM_ANG2MOM_T1	0.082497
GLCM_ANG2MOM_T2	0.081803
GLCM_JOINT_AVG_T1	8.6954
GLCM_JOINT_AVG_T2	10.3851
GLCM_ROW_VAR_T1	578.4014
GLCM_ROW_VAR_T2	621.5863

TEXTURAL FEATURES	
GLCM_ANG2MOM_T1	0.09877
GLCM_ANG2MOM_T2	0.03852
GLCM_JOINT_AVG_T1	6.5424
GLCM_JOINT_AVG_T2	9.241
GLCM_ROW_VAR_T1	645.44
GLCM_ROW_VAR_T2	741.002

SHAPE FEATURES \cap R3	
SHAPE FEATURES \cap R2	
SHAPE FEATURES \cap R1	
SHAPE FEATURES	
SHIFT_CENTER_OF_MASS	0.8121
SPHERICAL_DISPROPORTION	0.212
MAXIMUM_DIAMETER_2D	8.775
COMPACTNESS	0.1967
ELONGATION	0.53
PERIMETER2SURFACE_RATIO	0.234

SHAPE FEATURES	
SHIFT_CENTER_OF_MASS	1.661
SPHERICAL_DISPROPORTION	0.1008
MAXIMUM_DIAMETER_2D	20.123
COMPACTNESS	0.004713
ELONGATION	0.88
PERIMETER2SURFACE_RATIO	0.0987

Mapping of glioma from patients on a reference brain



We can easily select:

- **Survival time**
- **Various genomic clinical data**
- **Location of glioma**

What we plan to achieve: best suggestions

- **For extent of removal (EOR)**
- **Combination of radiotherapy and chemotherapy**
- **Rehabilitation therapy**