Politecnico di Torino

UCLouvain
École polytechnique de Louvain

# Assessing microstructural brain differences in epileptic patients with vagus nerve stimulation via diffusion MRI, tractography and machine learning

Supervisor:
Santa DI CATALDO
Francesco PONZIO
Benoît MACQ
Alexandre BERGER
Nicolas DELINTE

Author:
Michele CERRA

# Outline

- Introduction
  - Objectives
  - Epilepsy and Vagus Nerve Stimulation
  - Diffusion Magnetic Resonance Imaging
- Methods
  - Dataset
  - Radiomics analysis
    - Regions' extraction
    - Radiomics feature selection
    - Selection of interpretable features
  - Deep Learning analysis
- Conclusions

# Objectives

1. Classifying non-responder patients to VNS.
2. Understanding which brain regions are involved in the action of VNS.
3. Understanding which microstructural brain characteristics are involved in the action of VNS.

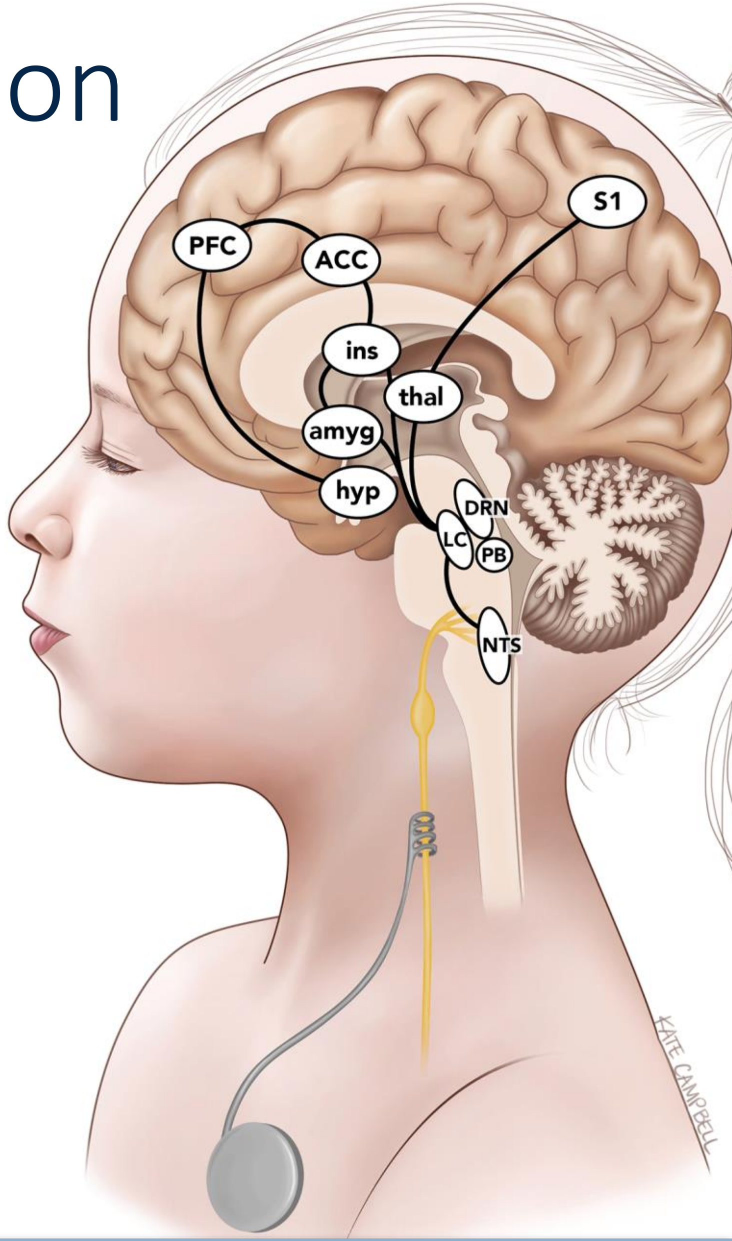
# Epilepsy and Vagus Nerve Stimulation

Treatments for epilepsy typically involves medications, but in cases of drug-resistant patients, other treatments such as neurostimulation therapies can be considered.

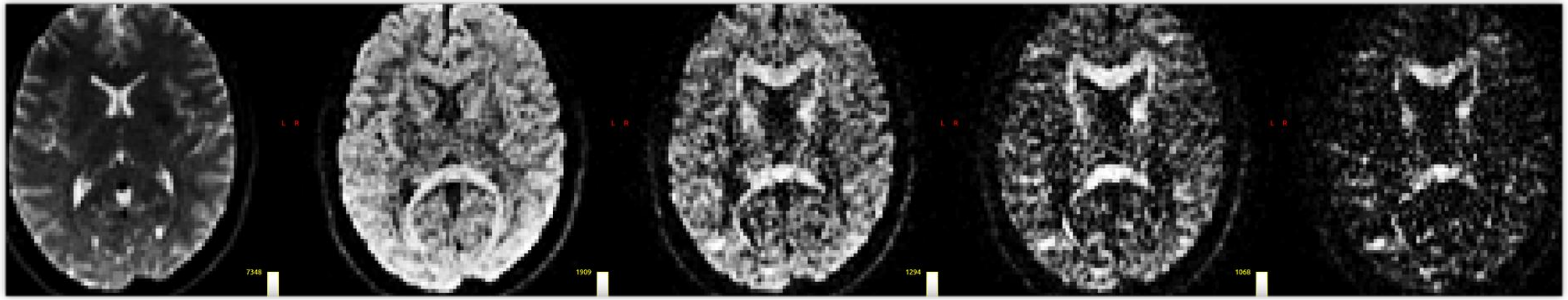
Vagus Nerve Stimulation (VNS) is one of the many neurostimulation therapies.

Patients to VNS can be divided by the reduction of seizure frequency ($\mathrm{rsf}$):

- Responder patients (R): $\mathrm{rsf} > 50\%$
- Partial Responder patients (PR): $30\% \leq \mathrm{rsf} \leq 50\%$
- Non-Responder patients (NR): $\mathrm{rsf} < 30\%$

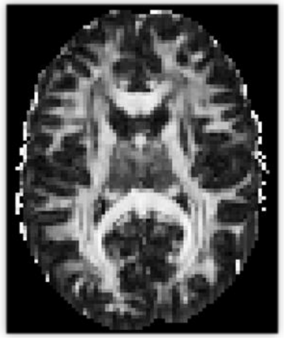


# Diffusion Magnetic Resonance Imaging

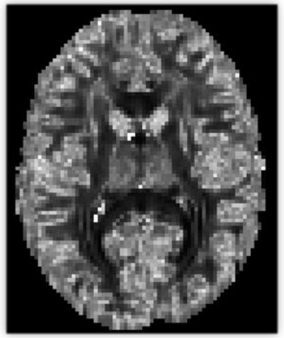


# Microstructural Metric Models

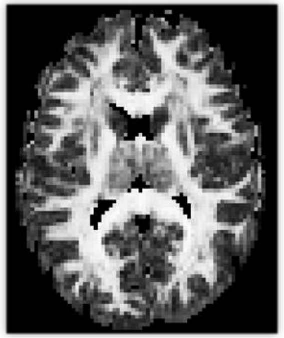
Diffusion Tensor  Imaging (FA)



NODDI (ODI)



DIAMOND (wFA)



Microstructure Fingerprinting (fvf)

# Outline

- Introduction
  - Objectives
  - Epilepsy and Vagus Nerve Stimulation
  - Diffusion Magnetic Resonance Imaging
- Methods
  - Dataset
  - Radiomics analysis
    - Regions' extraction
    - Radiomics feature selection
    - Selection of interpretable features
  - Deep Learning analysis
- Conclusions

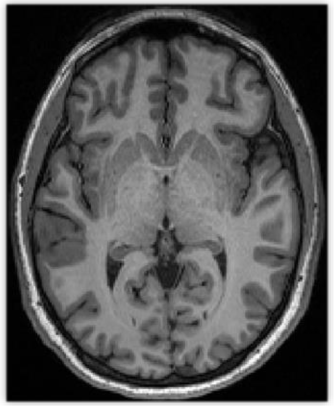
# Dataset

## Subjects

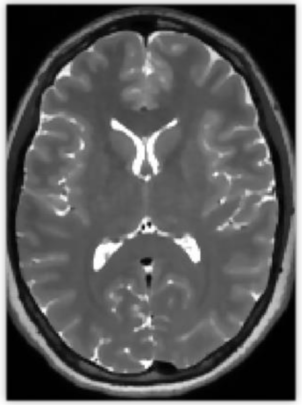
The study was composed of 19 subjects with drug-resistant epilepsy.

- 8 Responders (R)
- 4 Partial responders (PR) (considered as Responders)
- 7 Non-responders (NR)

T1 slice



T2 slice



## Data acquisition

For each subjects were acquired:

- T1-anatomical volume
- T2-weighted volume
- Diffusion weighted MRI volumes

dMRI slice

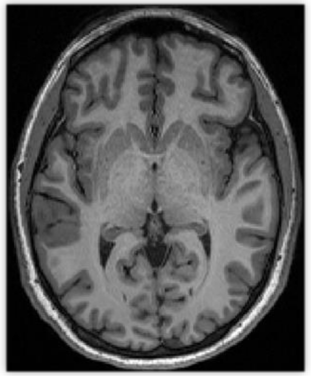
# Outline

- Introduction
  - Objectives
  - Epilepsy and Vagus Nerve Stimulation
  - Diffusion Magnetic Resonance Imaging
- Methods
  - Dataset
  - Radiomics analysis
    - Regions' extraction
    - Radiomics feature selection
    - Selection of interpretable features
  - Deep Learning analysis
- Conclusions

# Regions' extraction

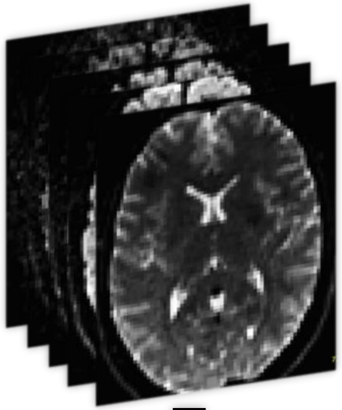
Different 3D brain regions have been segmented for radiomics feature extraction.

T1 volume

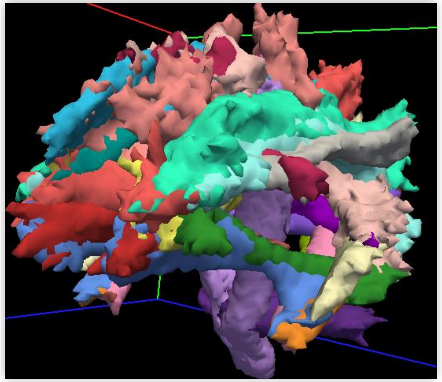


FreeSurfer:
Cortical parcellation
Subcortical segmentation

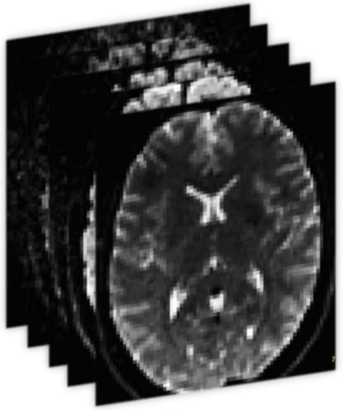
dMRI volumes



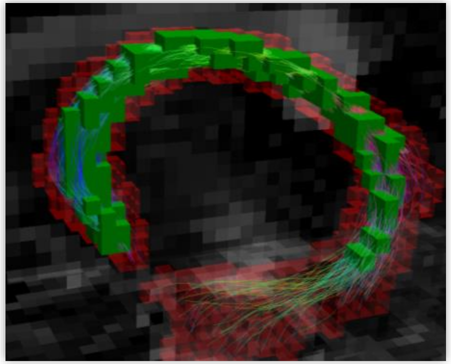
TRACULA:
White Matter segmentation



dMRI volumes



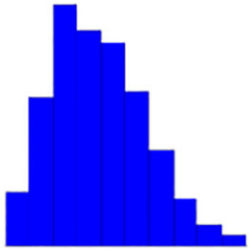
MRtrix3:
Specific regions



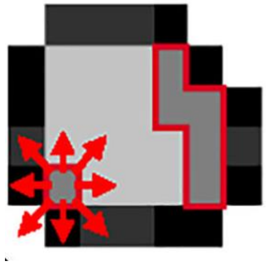
# Radiomics feature selection

Radiomics technique can extract from a single region statistical, textural, shape and wavelet features that can reach the hundreds.

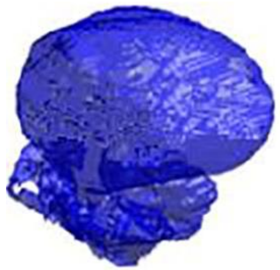
Statistical features



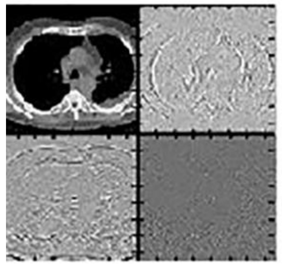
Textural features



Shape features



Wavelet features



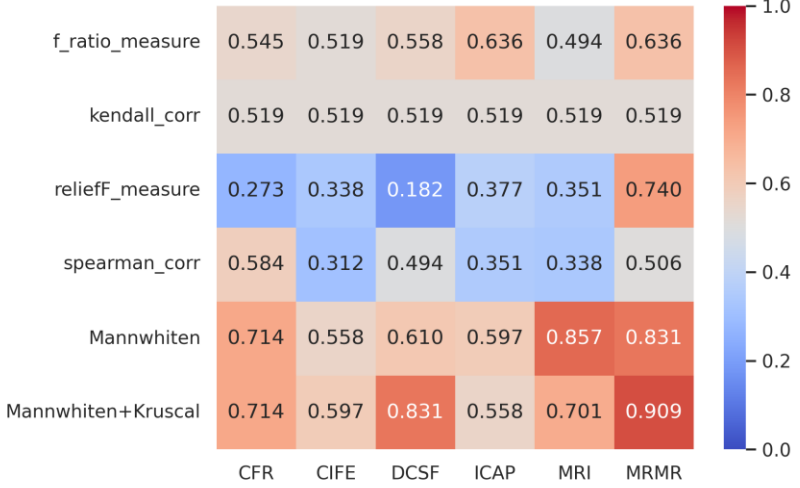
Considering all the possible regions and microstructural maps, dimensionality reduction is necessary to extract representative and informative features.

Different combinations of univariate and multivariate filters are used to select the features.

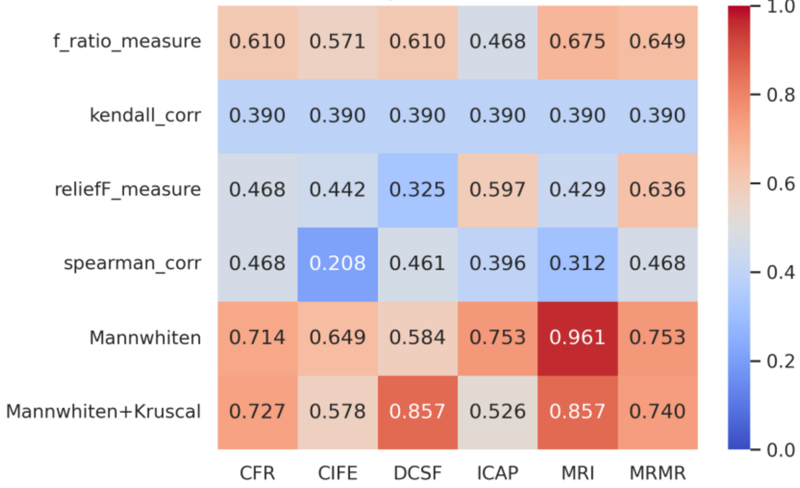
Model selection was done by a Leave One Out Cross Validation.

# Results – Radiomics

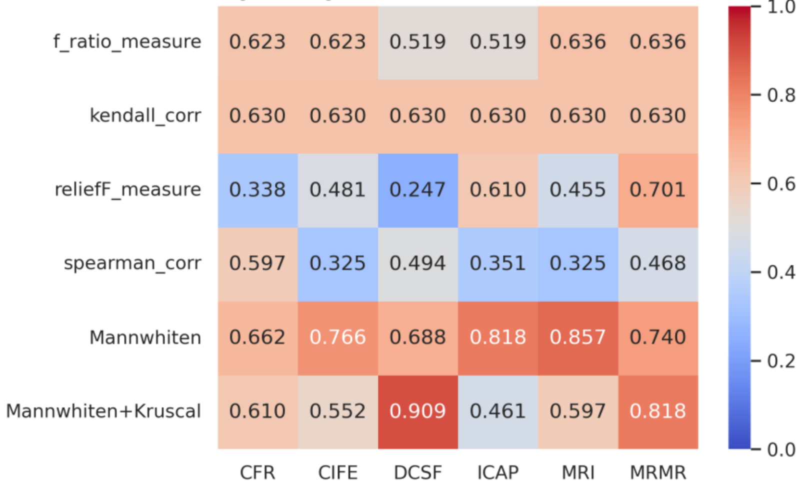
Neural Network AUC-ROC score + SFS(1, 15)



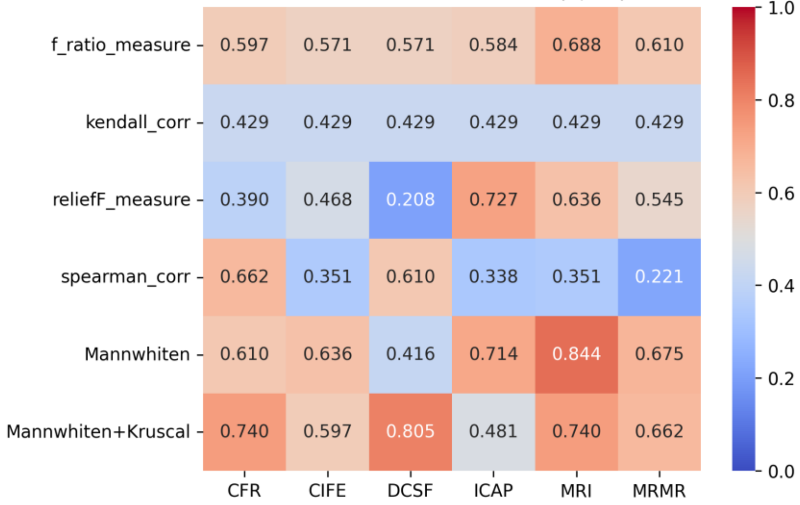

Gaussian Naive Bayes AUC-ROC score + SFS(1, 15)



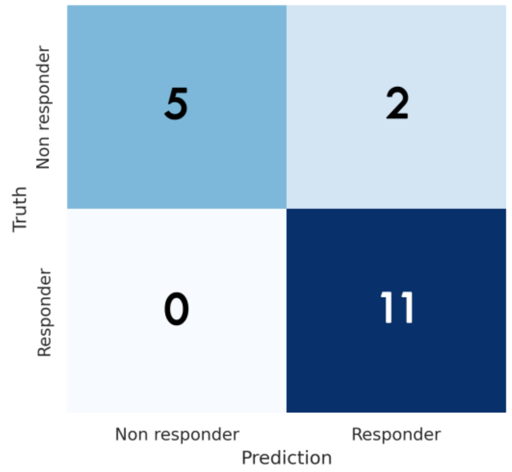

Logistic Regression AUC-ROC score + SFS(1, 15)




SVM AUC-ROC score + SFS(1, 15)

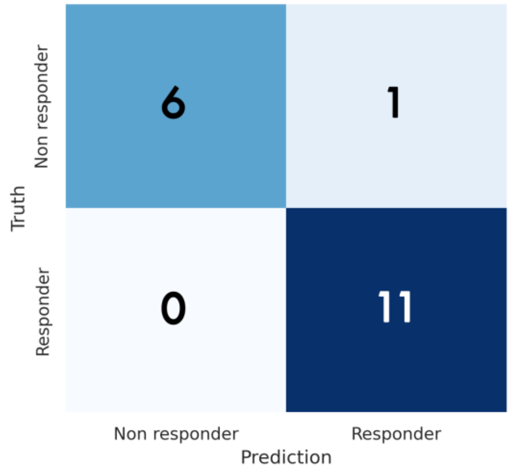


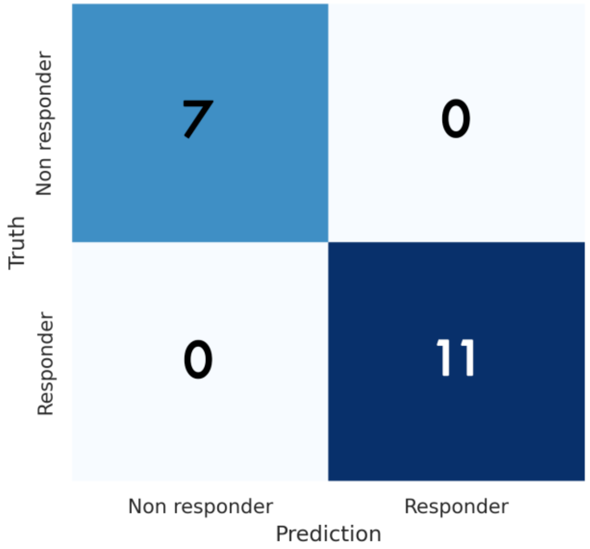
# Results – Radiomics




Gaussian NB
Mannwhiten + Kruskal + DCSG + SFS
Val AUC = 0.961
Val Acc = 0.857

Gaussian NB
Mannwhiten + MRI+ SFS
Val AUC = 0.857
Val Acc = 0.929

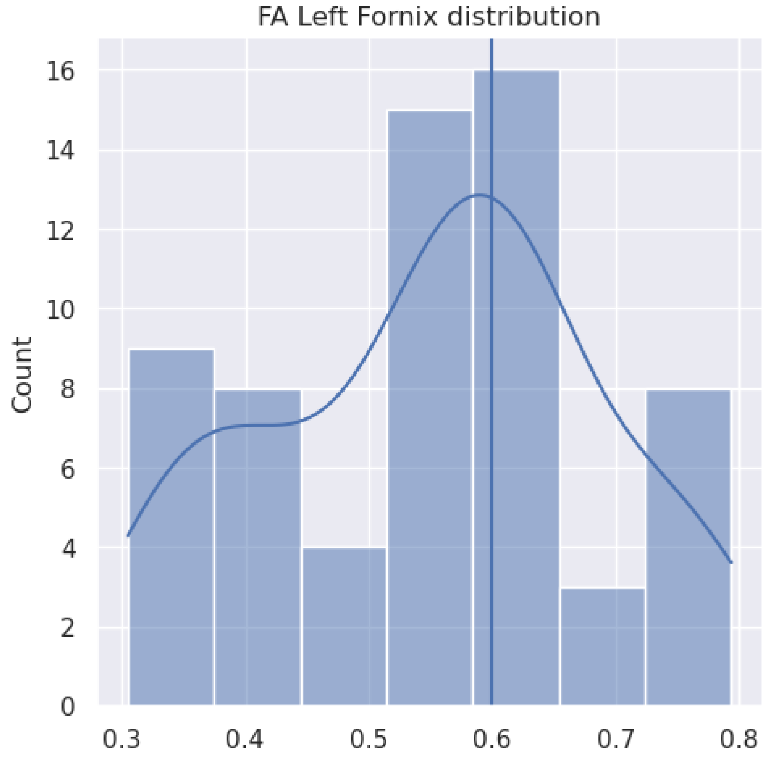


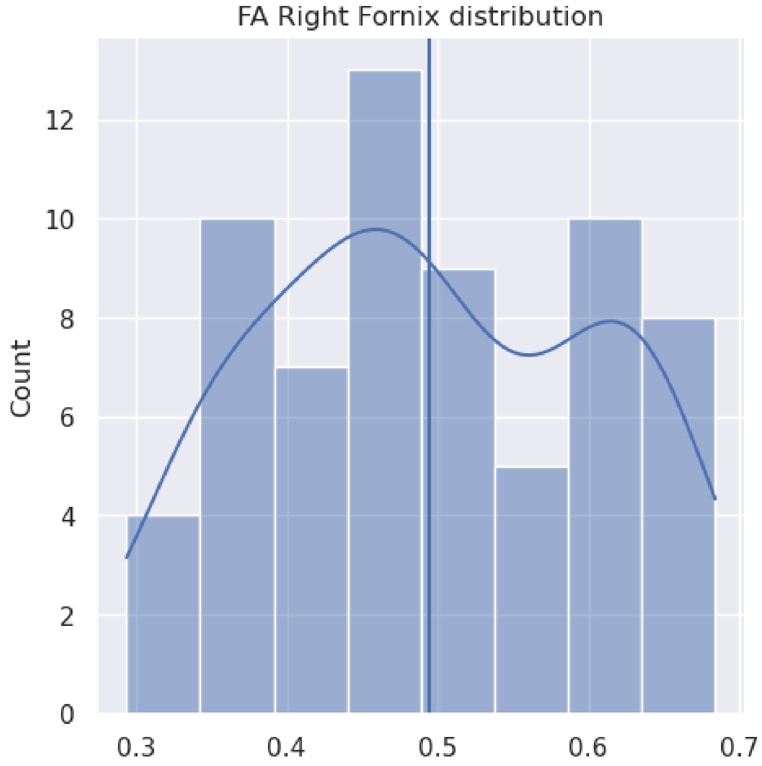




Gaussian NB
Ensemble
Val AUC = 1
Val Acc = 1

# Selection of interpretable features

Selecting only the first four moments of metric distribution in the region allows for the biological interpretation of the results.



# Statistical and multivariate analyses

Statistical tests are used to assess differences in interpretable microstructural features between R and NR to VNS:

- Mann-Whitney U rank test
- Kruskal-Wallis test
- Barnard’s exact test

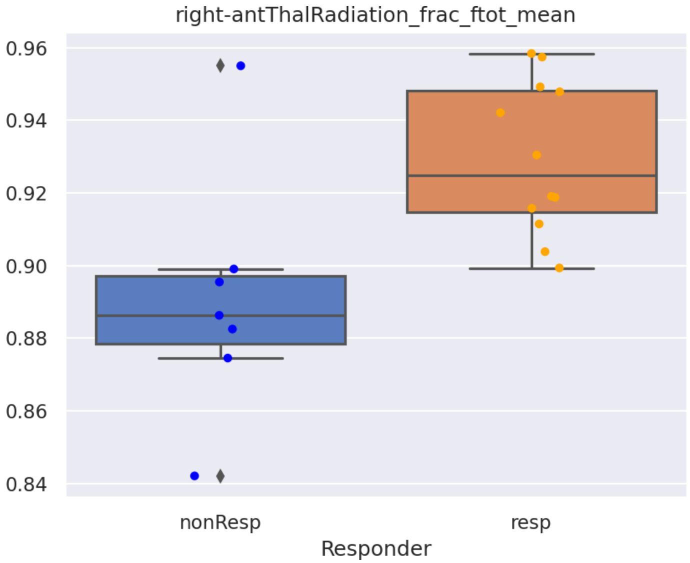
These tests are the corresponding non-parametric tests of t-test, ANOVA and Chi2.

A multivariate analysis was performed to obtain interacting features for classifying NR to VNS by extracting the most important features using Sequential Feature Selection.

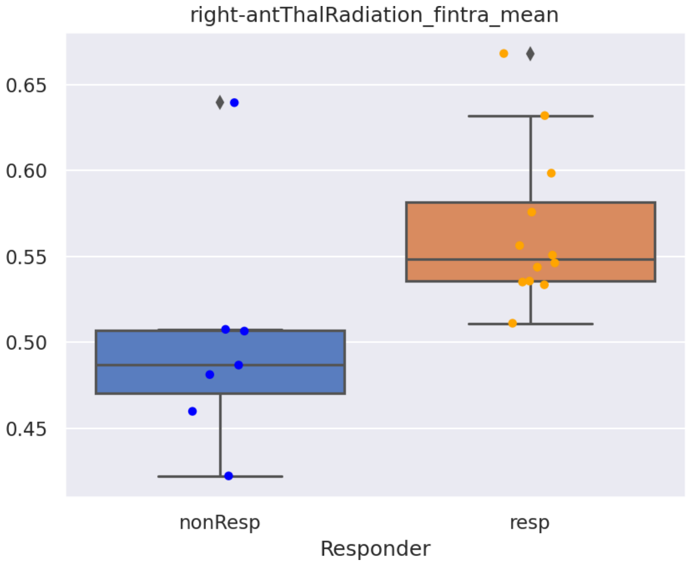
Model selection was done by a Leave One Out Cross Validation.

# Results – Statistical Analysis

The fraction of fascicles of fibres in the right anterior thalamocortical radiation were found lower in NR subjects respect to R.




p-value = 0.00262



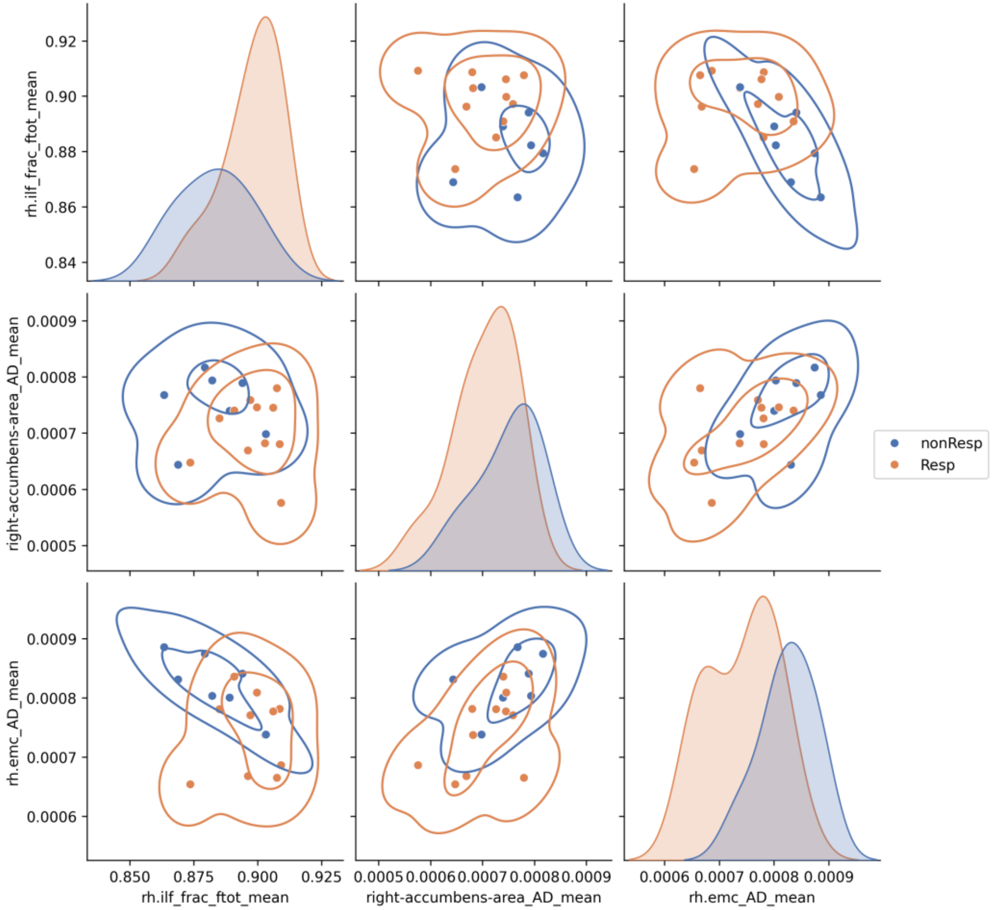

p-value = 0.00359

Damaged fibre fascicles were found in the posterior thalamocortical radiation and fornix.

# Results – Multivariate Analysis

Most frequently selected features by SVM with polynomial kernel:

1. Fiber fraction of right inferior longitudinal fascicle
2. AD mean of right accumbens area
3. AD mean of right extreme capsule




Val accuracy = 1; Val AUC = 1

# Outline

- Introduction
  - Objectives
  - Epilepsy and Vagus Nerve Stimulation
  - Diffusion Magnetic Resonance Imaging
- Methods
  - Dataset
  - Radiomics analysis
    - Regions' extraction
    - Radiomics feature selection
    - Selection of interpretable features
  - Deep Learning analysis
- Conclusions

# Pretrained model

We use a 3D deep learning model to classify NR and R directly from a selected microstructural map, without defining any regions.

A pretrained UNesT model for T1 image segmentation was selected for this study.

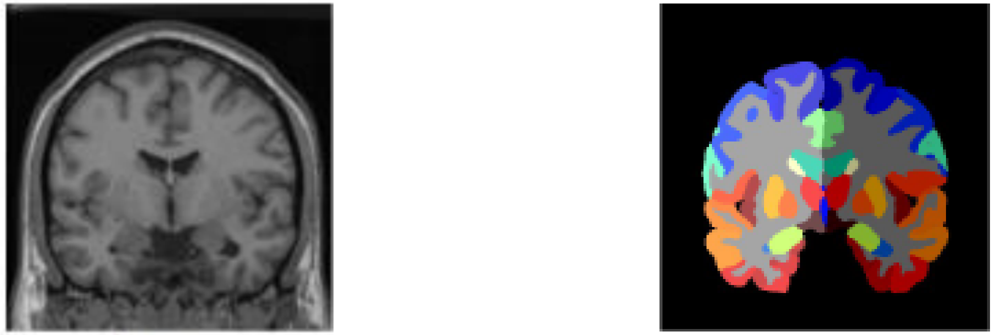
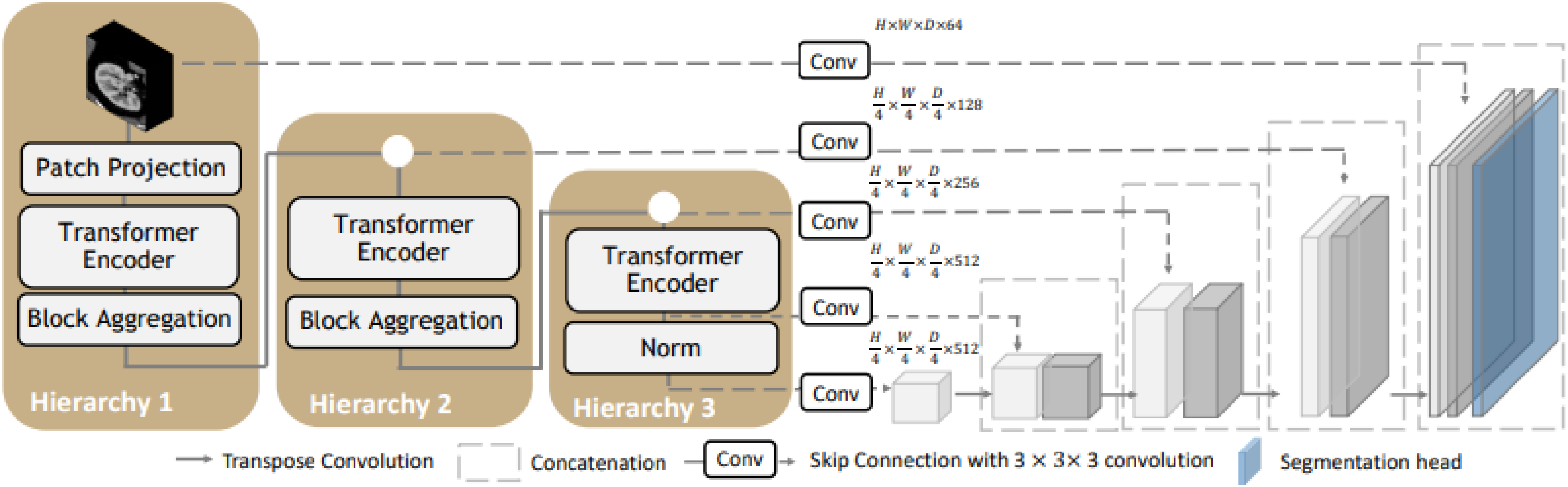


Image UNesT-L

The pretrained model is finetuned to adapt it to microstructural maps instead of anatomical maps.

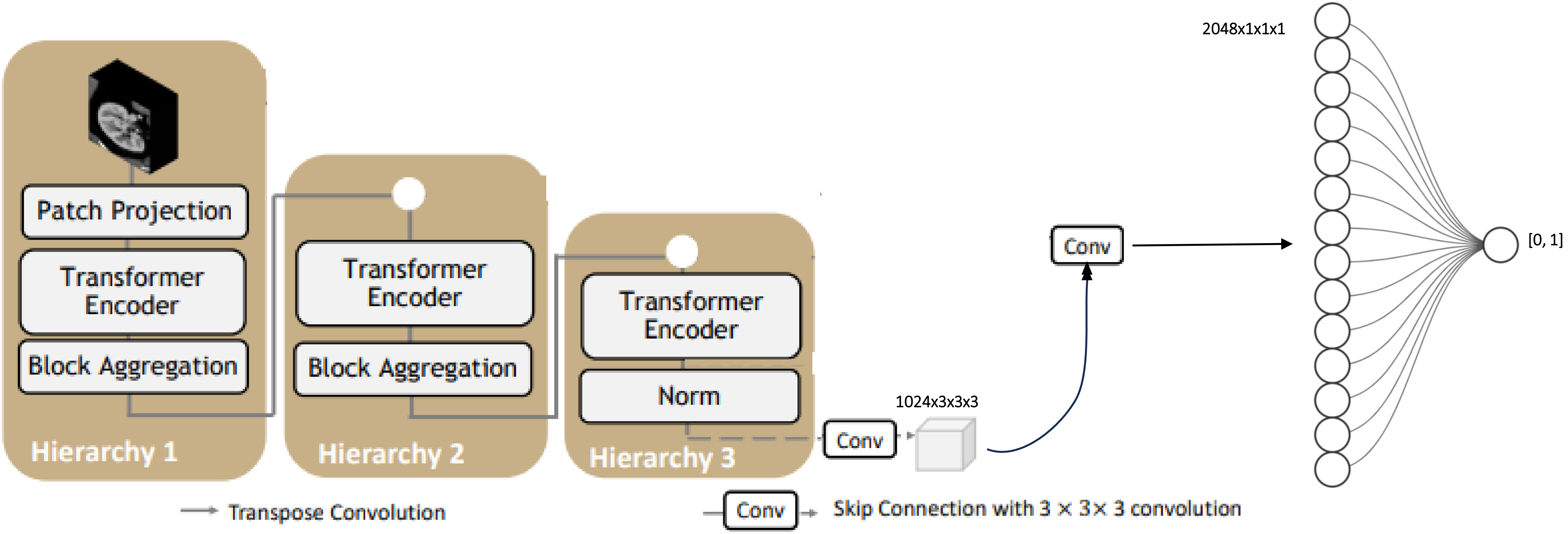
# UNesT for classification task

The model task is transformed from segmentation to classification.



# UNesT for classification task

The model task is transformed from segmentation to classification.

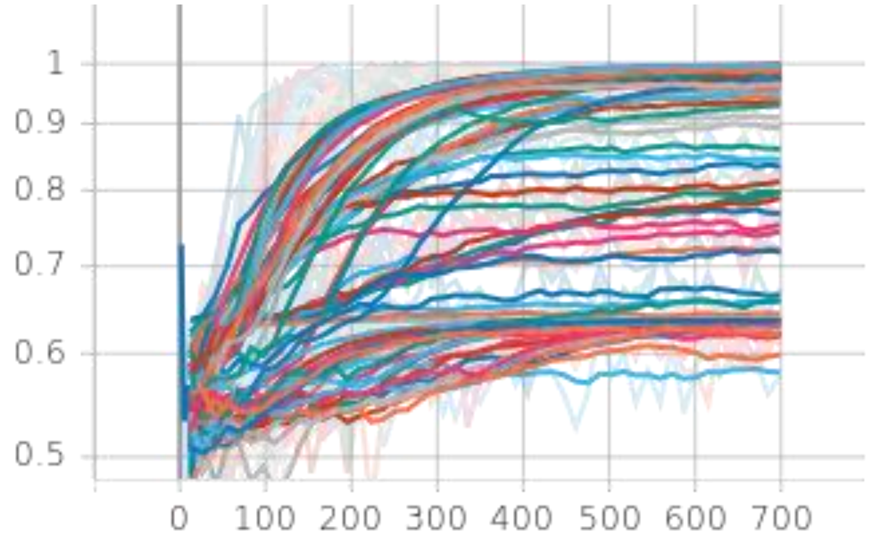


# Results – 3D Deep Learning Classification

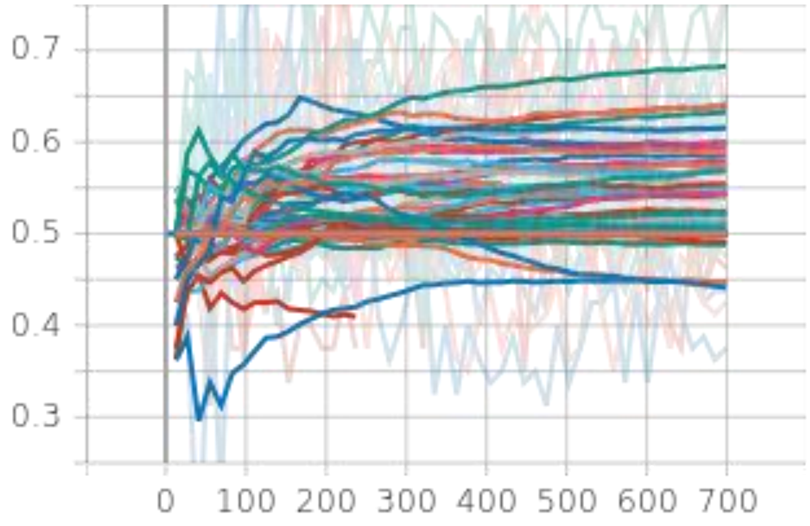
Different scheduler learning rates, step sizes, gamma factors were tried.

The size of the training and validation sets have been augmented by 20 times.

The training set reached an accuracy of 1 and the validation set had an accuracy of 0.7.




Training set accuracy scores




Validation set accuracy scores

# Outline

- Introduction
  - Objectives
  - Epilepsy and Vagus Nerve Stimulation
  - Diffusion Magnetic Resonance Imaging
- Methods
  - Dataset
  - Radiomics analysis
    - Regions' extraction
    - Radiomics feature selection
    - Selection of interpretable features
  - Deep Learning analysis
- Conclusions

# Conclusions

1. Classifying non-responder patients to VNS.

✓ Great potential of radiomics features.
✗ Lack of generalization in 3D deep learning model (small dataset).
✗ Impossibility to predict non-responders before implantation (non-longitudinal acquisitions).

2. Understanding which brain regions are involved in the action of VNS.

✓ Fornix and anterior thalamocortical radiation have presented patterns to discriminate non-responders.
It is possible to interpret the decision-making of CNN through the class activation map.

3. Understanding which microstructural brain characteristics are involved in the action of VNS.

✓ DTI and NODDI metrics had lower p-values in univariate analysis, while no changes in proportion were recorded in multivariate feature selection.
✗ Impossibility to input more than one metric map at a time in the 3D deep learning model.