



Artificial Intelligence in Medicine

next steps towards the development of robust AI algorithms and validation on realistic use cases



Radiomic and DL in tcMRgFUS

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Trans-cranial Magnetic Resonance guided Focused Ultrasounds (tcMRgFUS)

- Use of ultrasounds suitably focused on the target
- Thermal Ablation of the target
- No surgery needed
- Guided by MRI



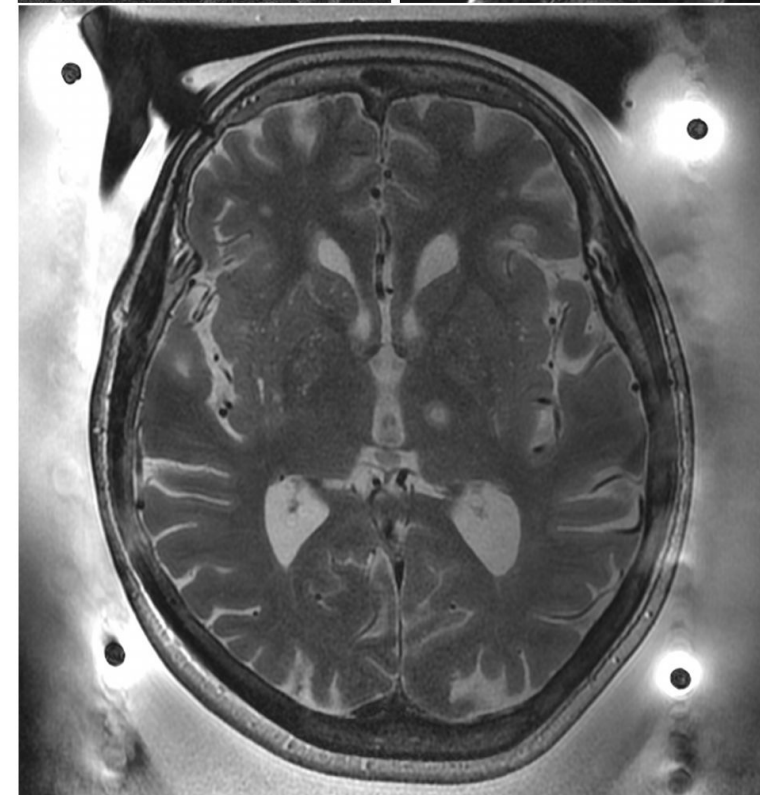
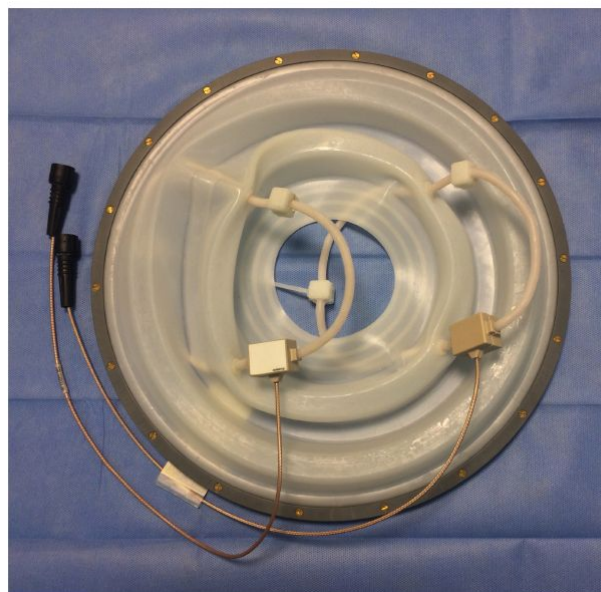
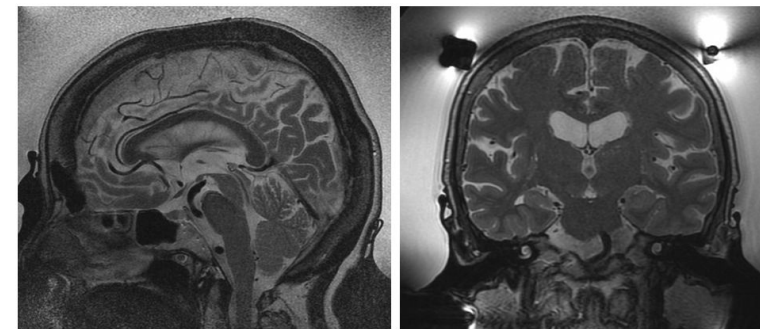
Courtesy of Insightec, Israel



Trans-cranial Magnetic Resonance guided Focused Ultrasounds (tcMRgFUS) at University Hospital Palermo

First Italian site for neurological surgery through tcMRgFUS

World First site for neurological surgery through tcMRgFUS at 1.5T





Trans-cranial Magnetic Resonance guided Focused Ultrasounds (tcMRgFUS)

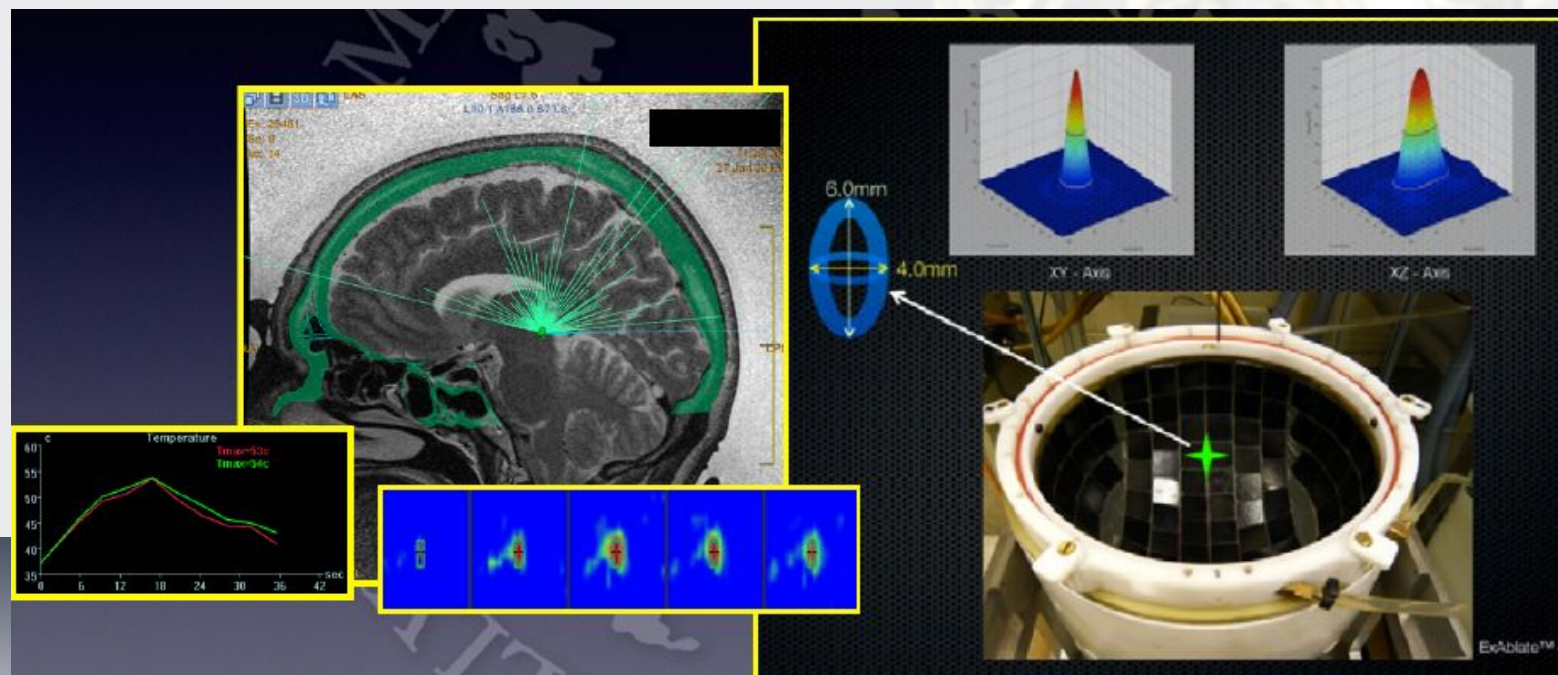
Focused Ultrasounds produced by an helmet with various transducers

It can induces neurostimulation or thermal ablation



Magnetic resonance imaging

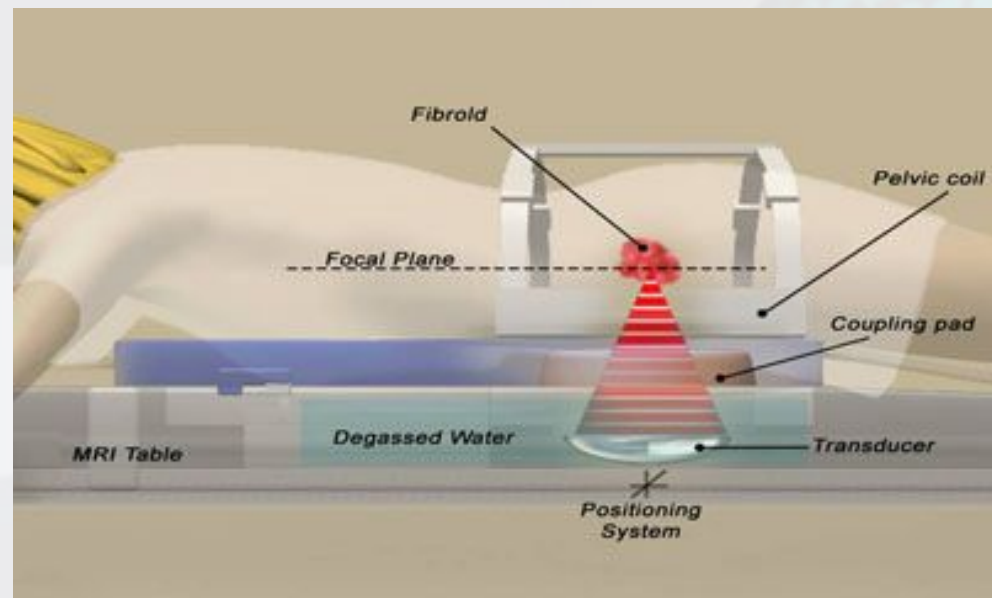
- **Multiplanar imaging for screening and follow-up**
- **Guide for FUS**
- **Thermometry**





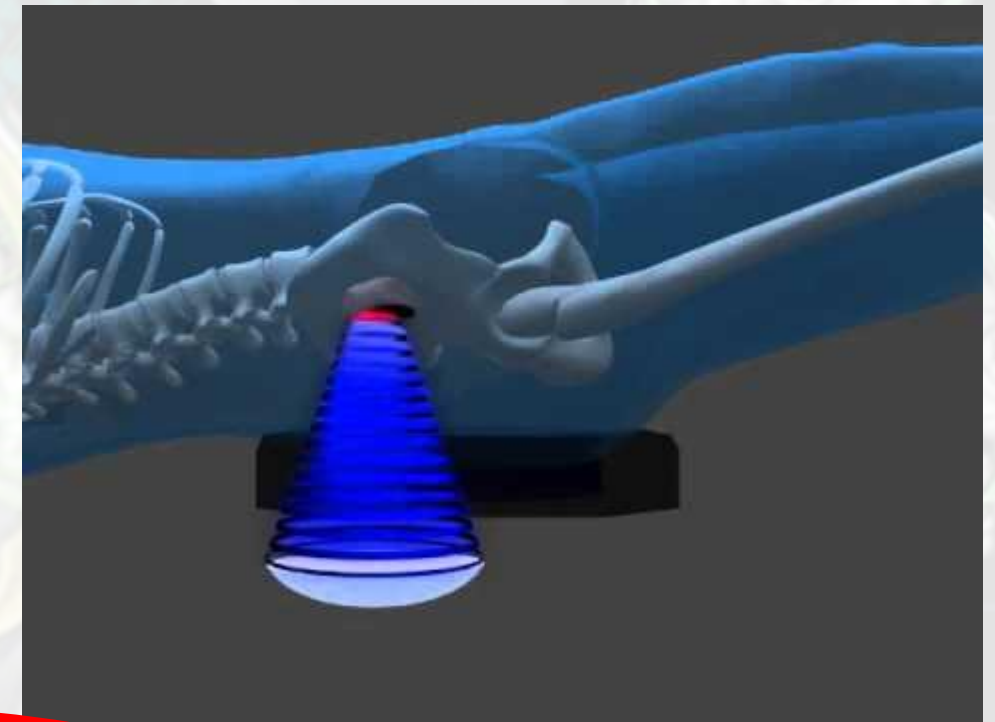
Some FDA approved treatments

Uterine fibroids



<https://veintreatment.weillcornell.org/uterine-fibroids/treatment/magnetic-resonance-guided-focused-ultrasound>

Bone metastasis



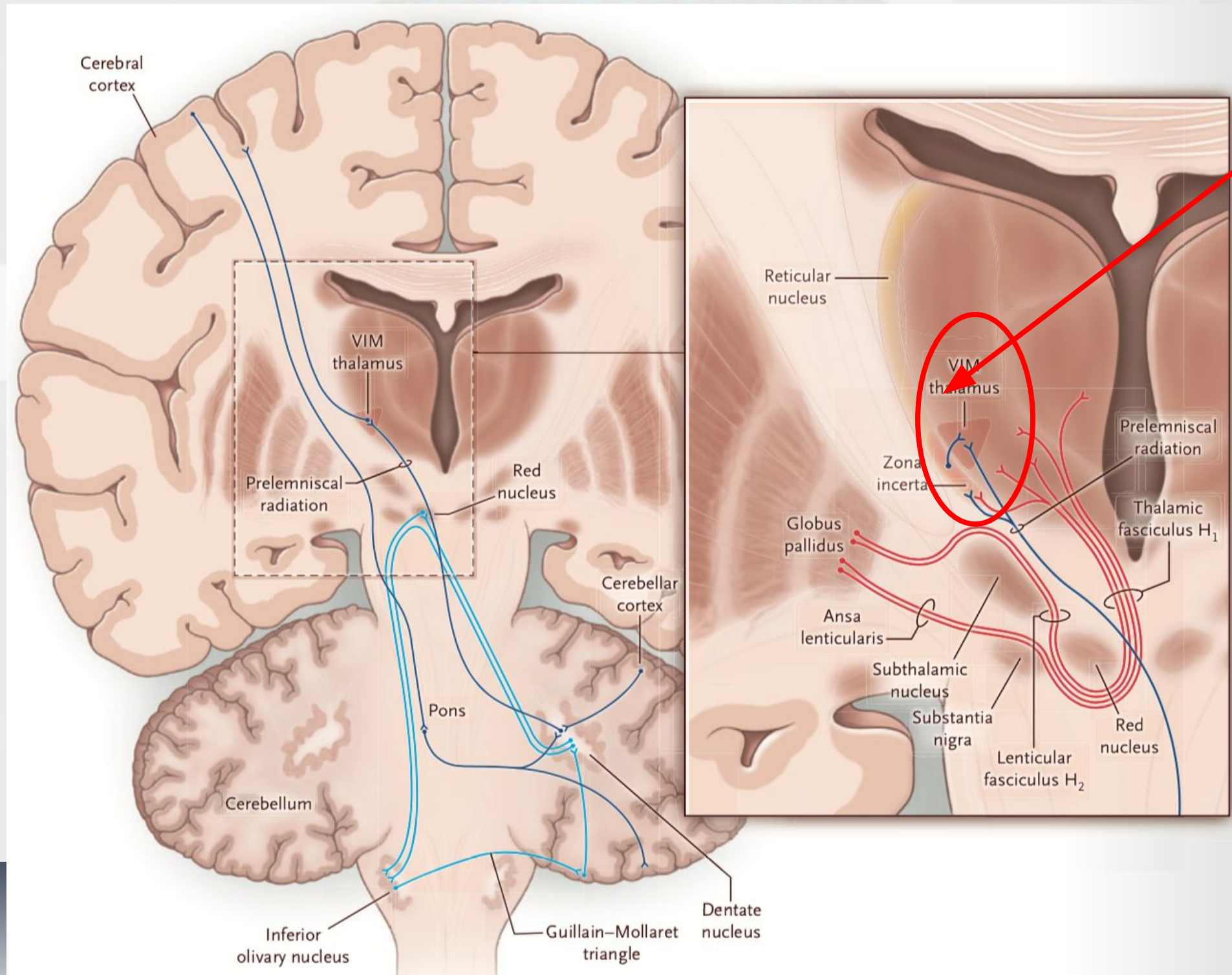
www.fusfoundation.org

Essential tremor





Cerebellar-thalamo-cortical tract



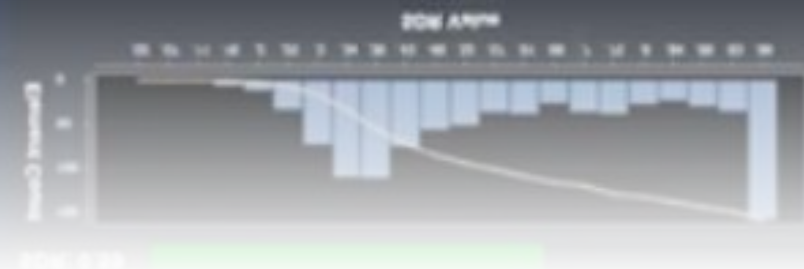
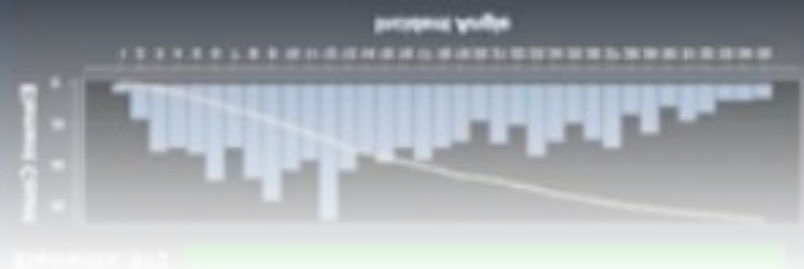
**Ventral
InterMediate
(VIM)
nucleus:**

**target to be
ablated!**



Target of this work

THE AIM OF THIS WORK IS THE PRELIMINARY RESULTS OF APPLICATION OF RADIOMICS APPROACH TO MR IMAGES OF PATIENTS WITH ESSENTIAL TREMOR IN ORDER TO FIND CORRELATIONS WITH CLINICAL DATA

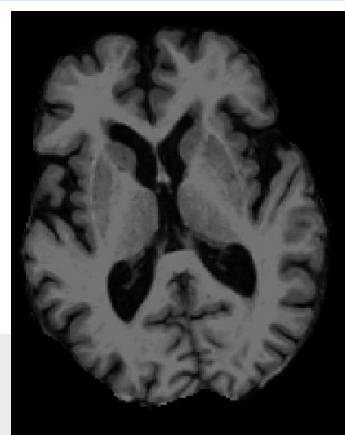




Flow chart of analysis

Radiomics + Machine Learning

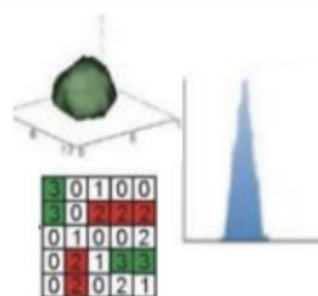
Imaging



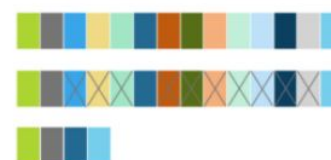
Segmentation



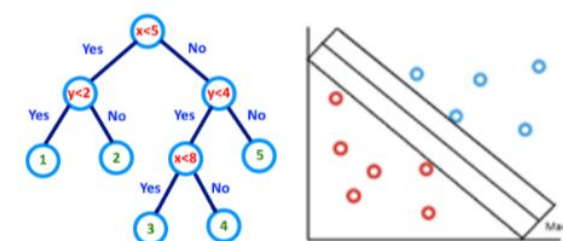
Feature extraction



Feature selection



ML algorithms





Materials and methods

Data from 40 patients affected by essential tremor

| | Average (SD) | Median | Range |
|-----------------------|-------------------------------------|--------|---------|
| Age | 67 (10) y | 69 y | 44-84 y |
| Gender | 32 Males 8 Females | | |
| Disease duration | 28 (17) | 24 y | 4-68 y |
| Tremor prevalent side | 21 right 8 left 11 both sides | | |



MRI data available

T1-weighted imaging



T1 BRAVO Sequence
 $1 \times 1 \times 1 \text{ m}^3$

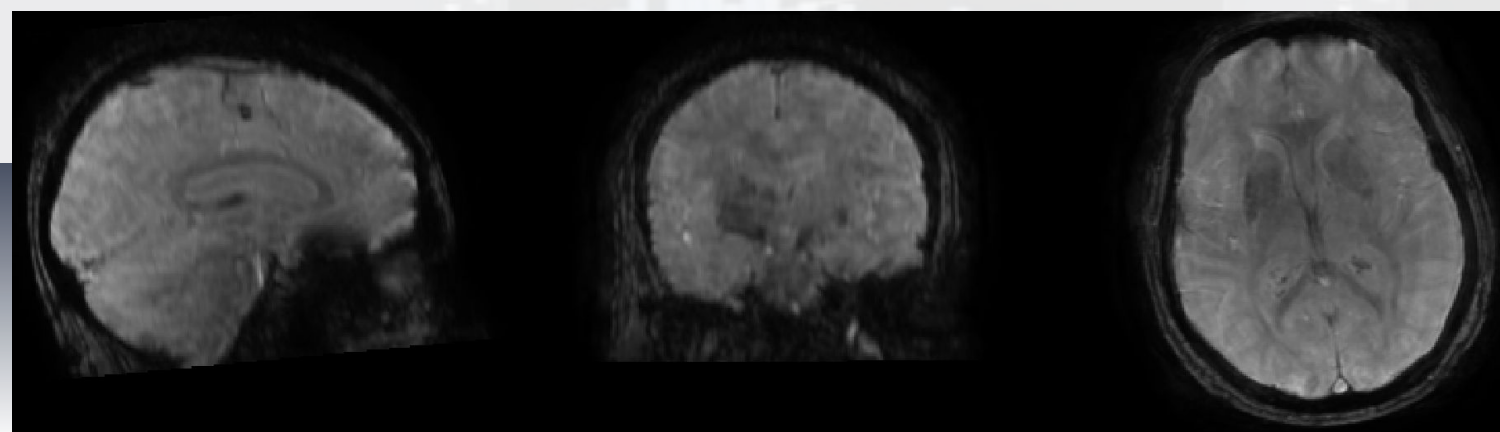
MRI APPARATUS
1.5 T MRI SCANNER
GE SIGNA XT

Diffusion Tensor Imaging (DTI) → Fractional Anisotropy (FA)



$b=0, 1000 \text{ s/mm}^2$
32 gradient directions
voxel size $3 \times 3 \times 3 \text{ mm}^3$

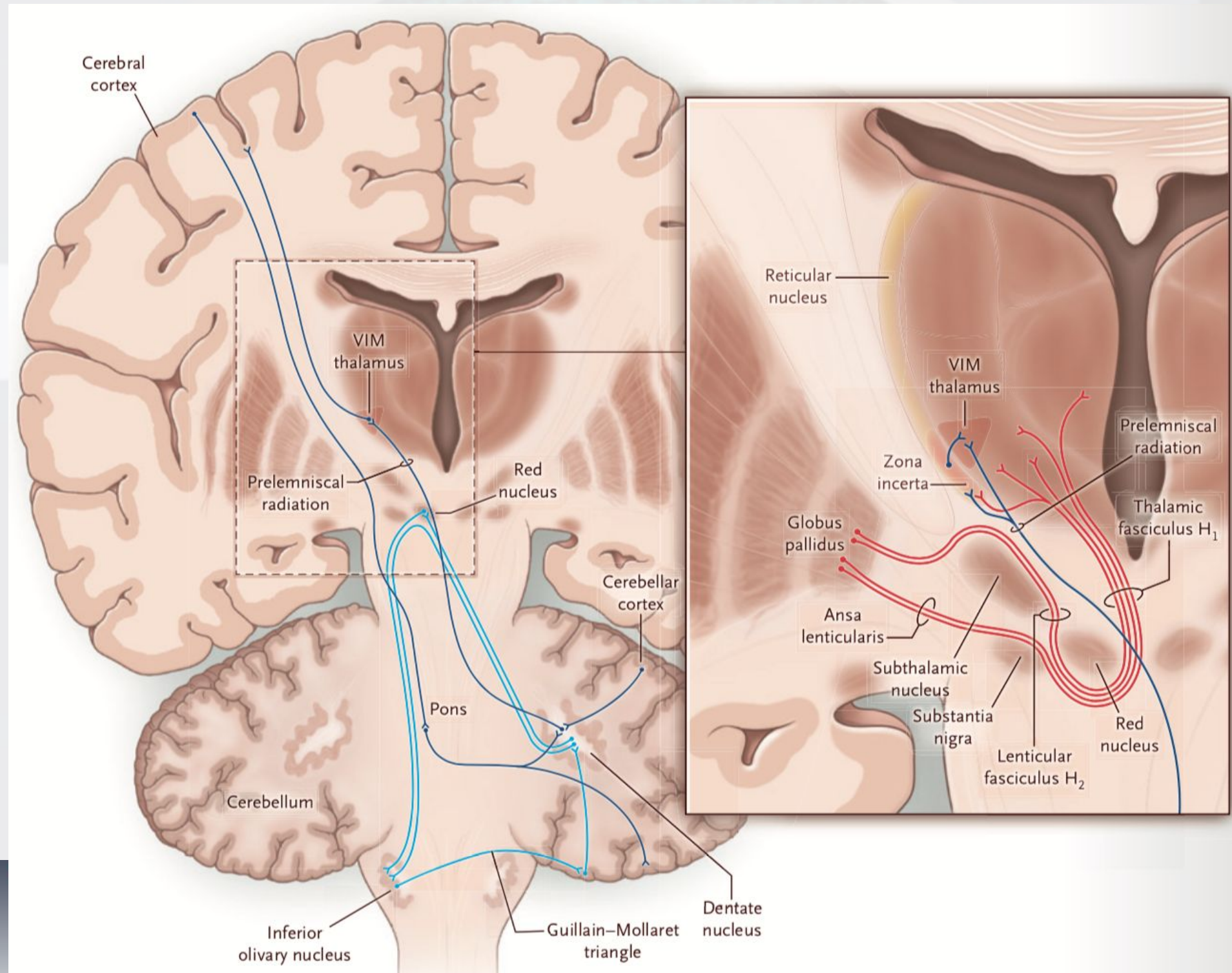
Susceptibility Weighted Imaging (SWI)



SWAN sequence



Regions of Interest (ROIs) identification

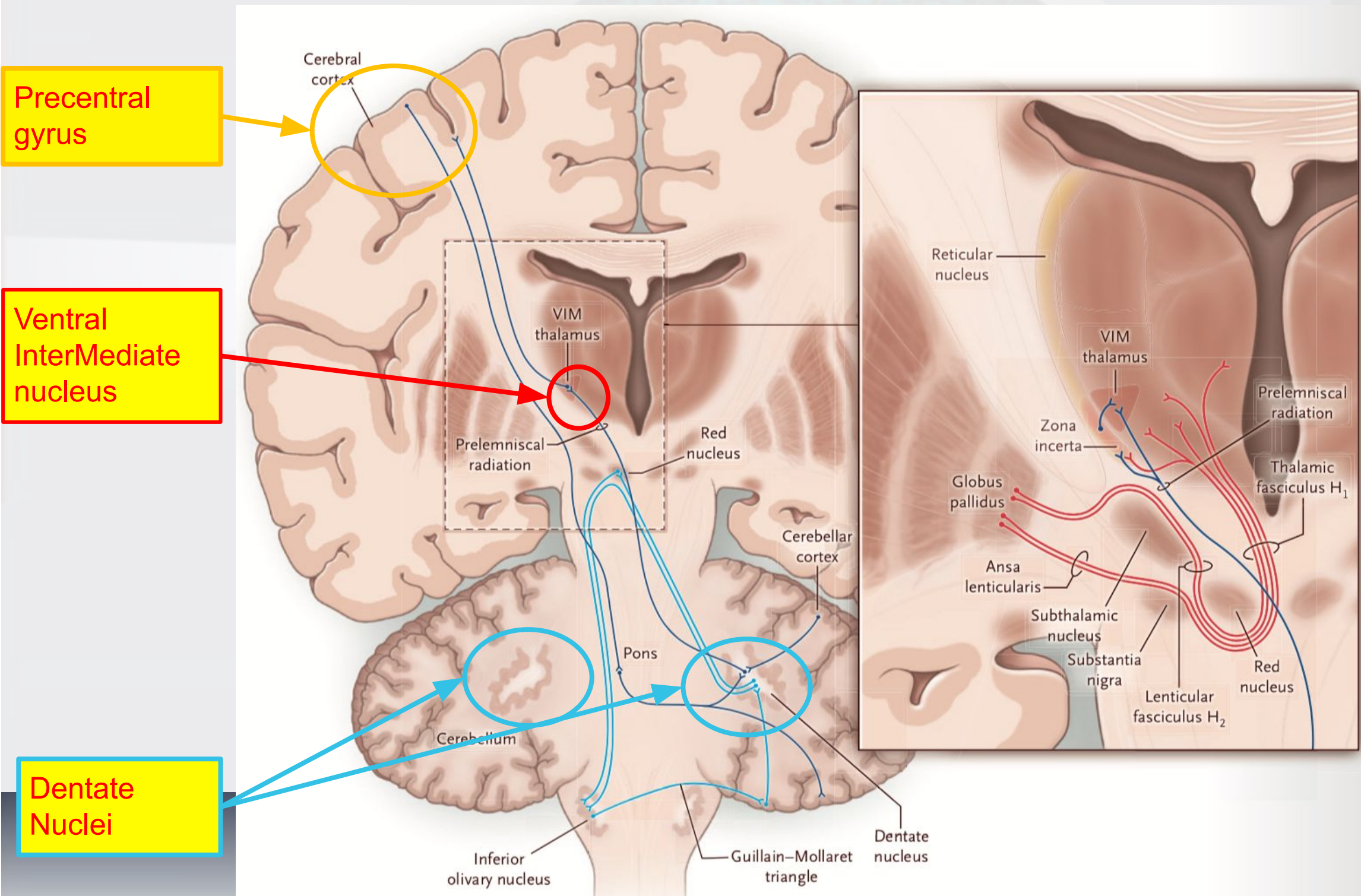


Essential Tremor. Haubenberger D, Hallett M. N Engl J Med. 2018 Aug 9;379(6):596-597. doi: 10.1056/NEJMc1807690.

nextAIM - Kickoff Meeting 17-18 February 2022



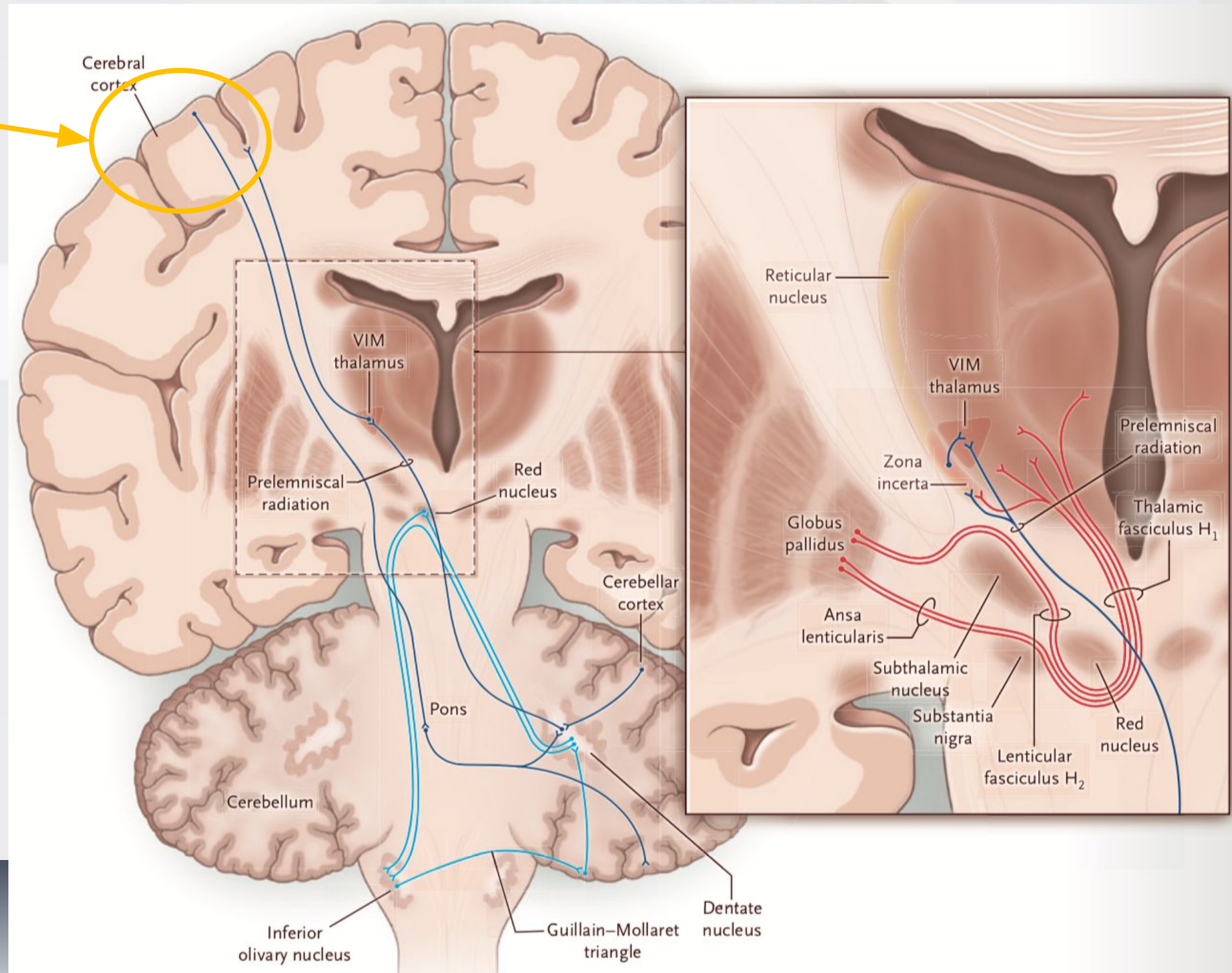
Regions of Interest (ROIs) identification





Regions of Interest - Precentral gyrus

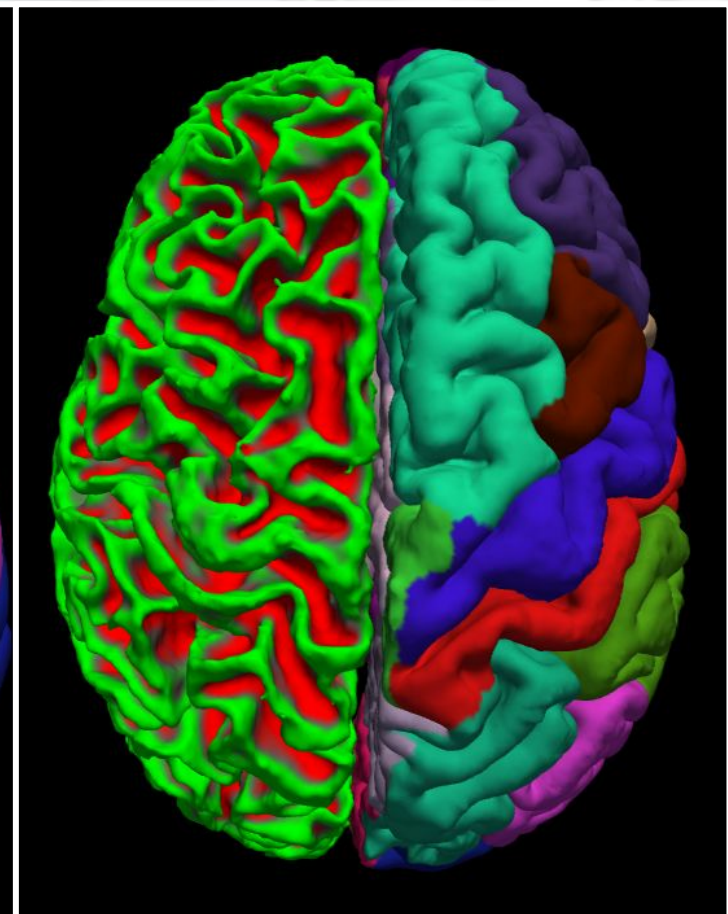
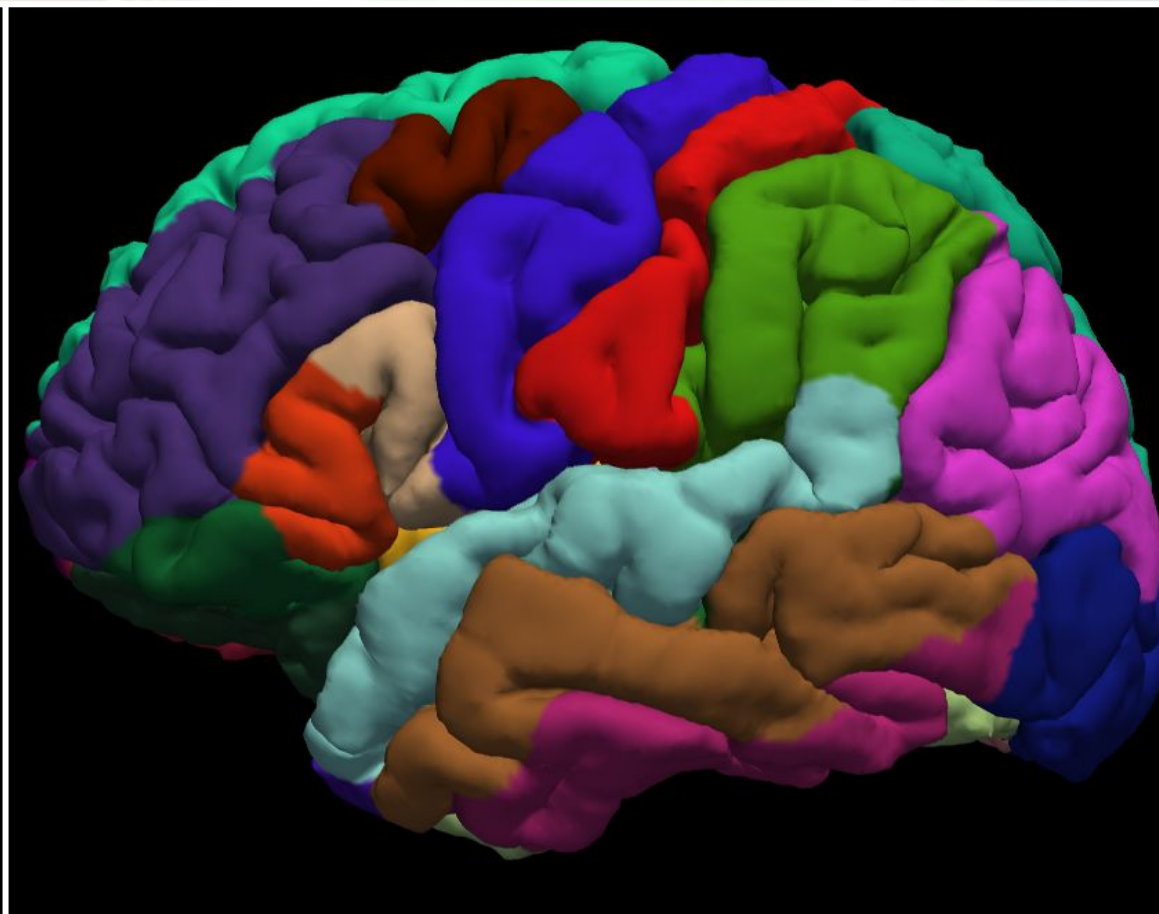
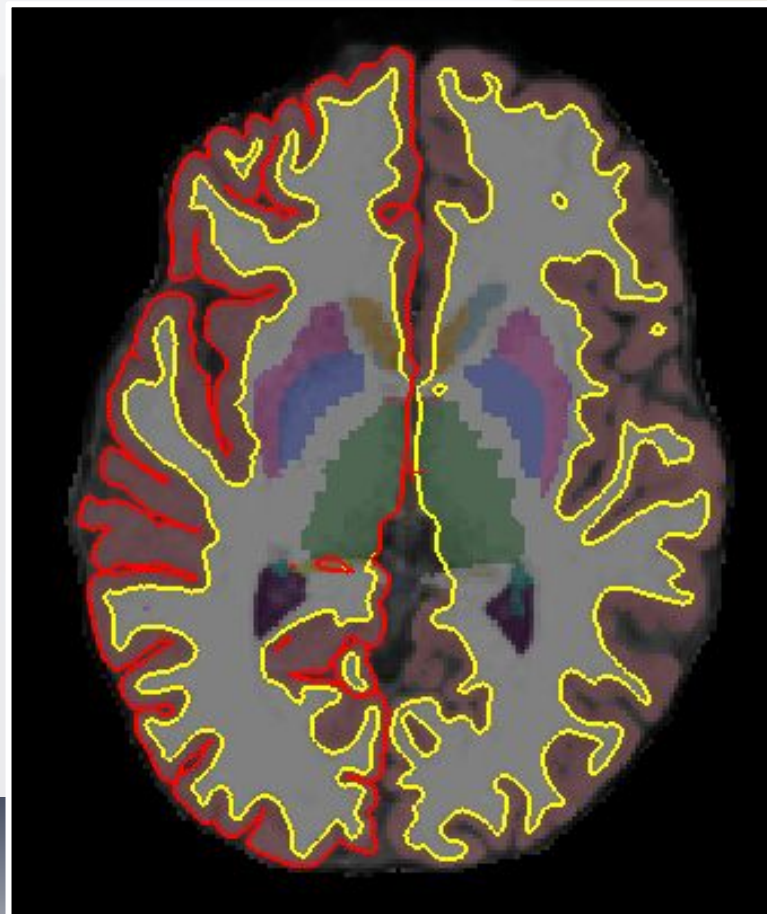
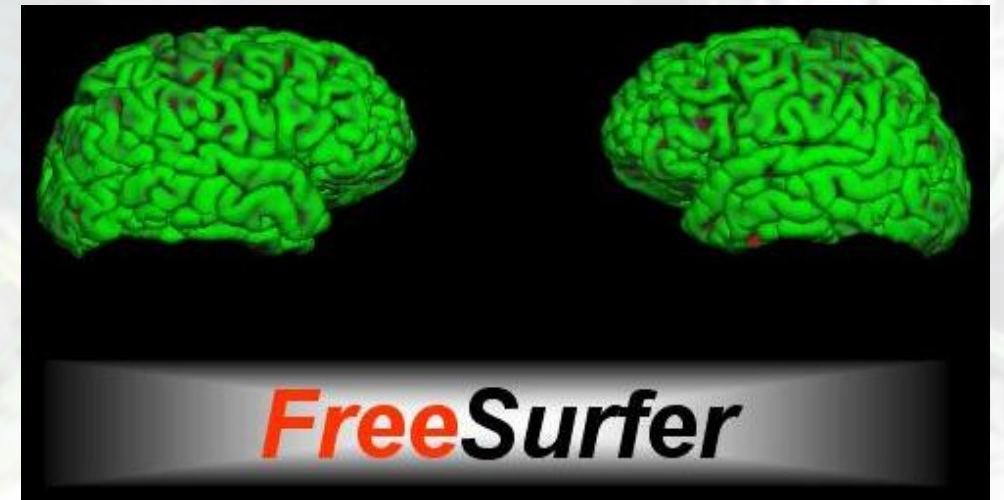
Precentral gyrus





CORTICAL SEGMENTATION

The T₁w BRAVO 3D datasets (1x1x1mm³) were used. The FreeSurfer 6.0 workflow was used to segment both the cortical and deep gray matter.



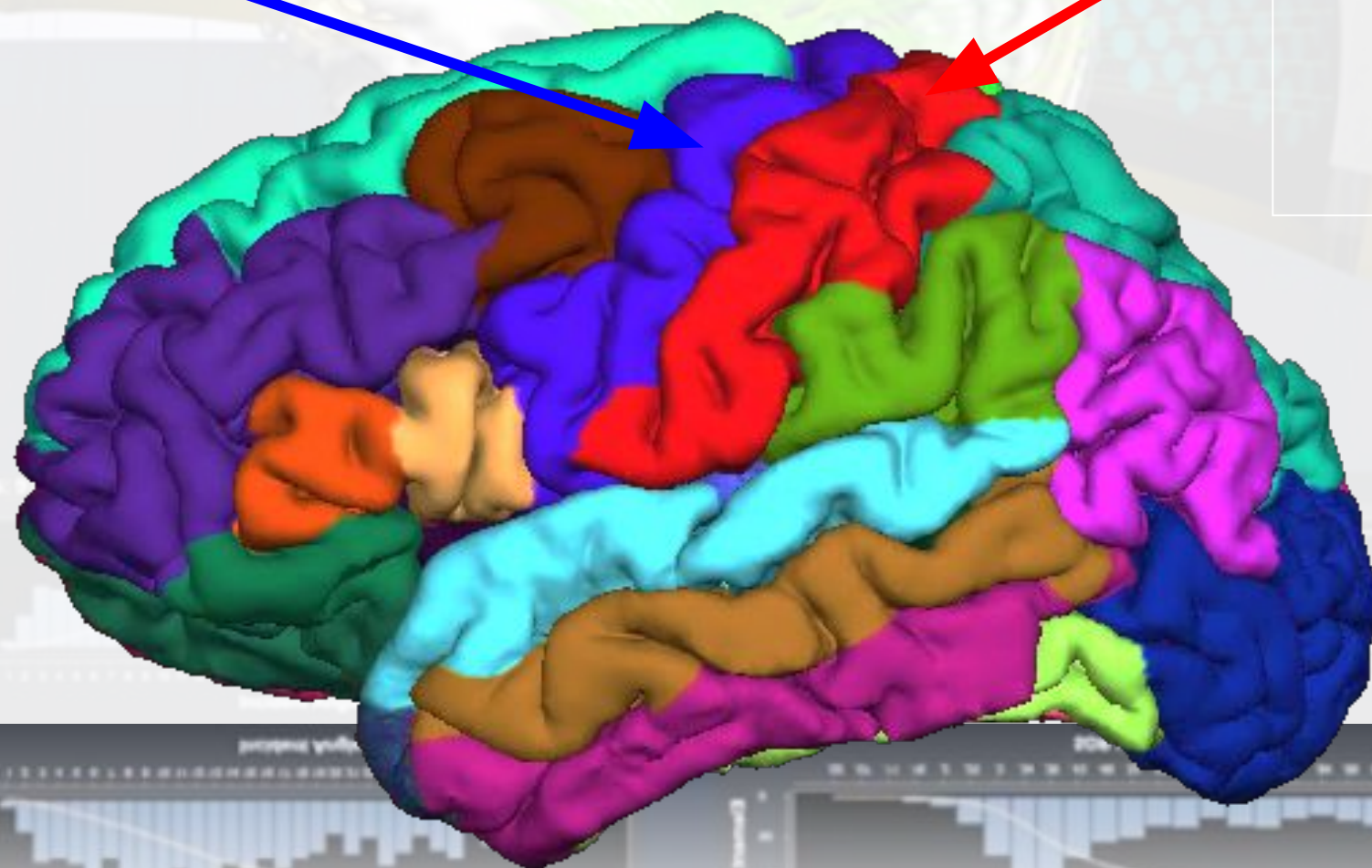


CORTICAL SEGMENTATION

Automatic Surface Parcellation:
Desikan/Killiany Atlas (35 ROI's)

Precentral
Gyrus

Postcentral
Gyrus



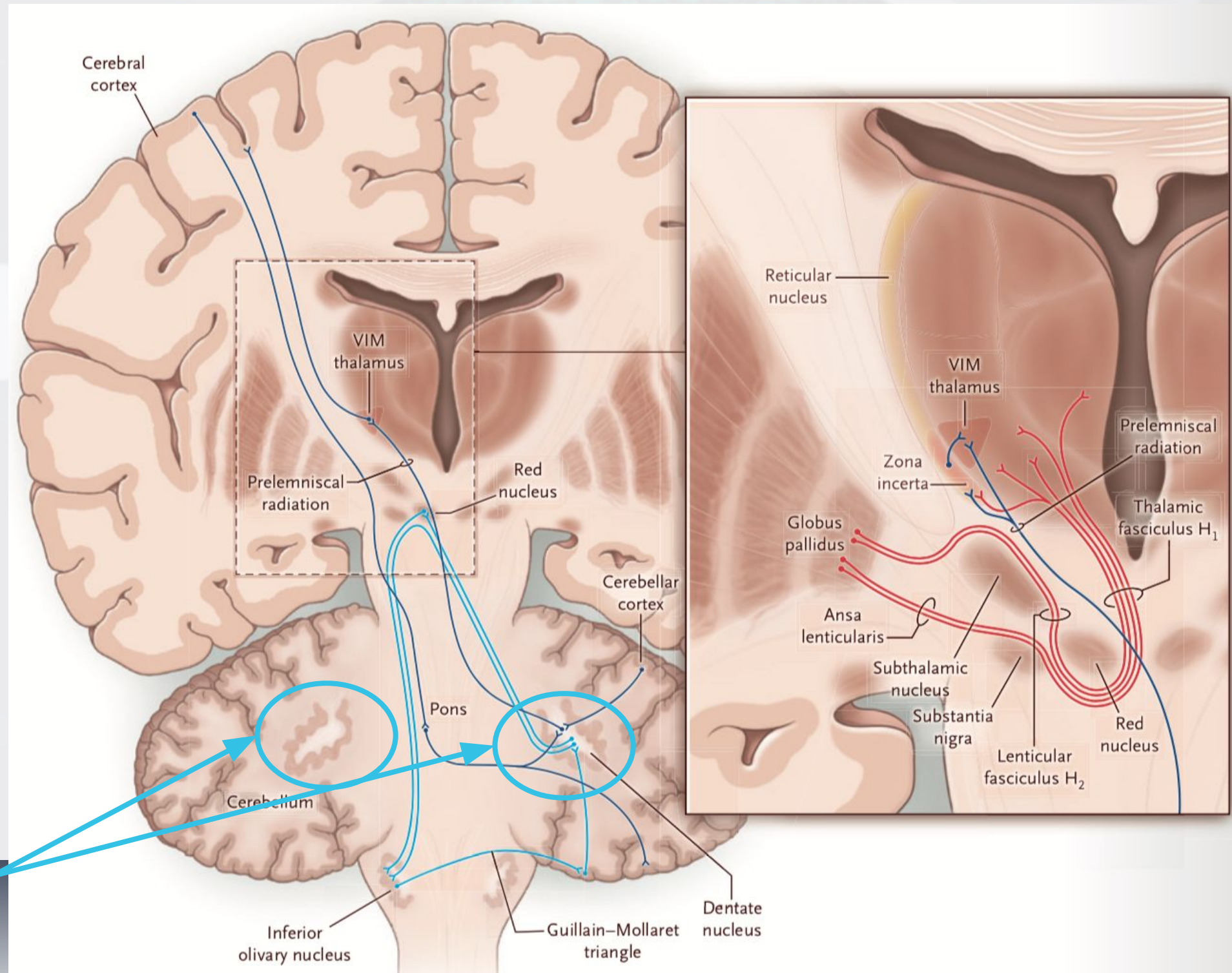


Regions of Interest - Precentral gyrus





Regions of Interest - Dentate

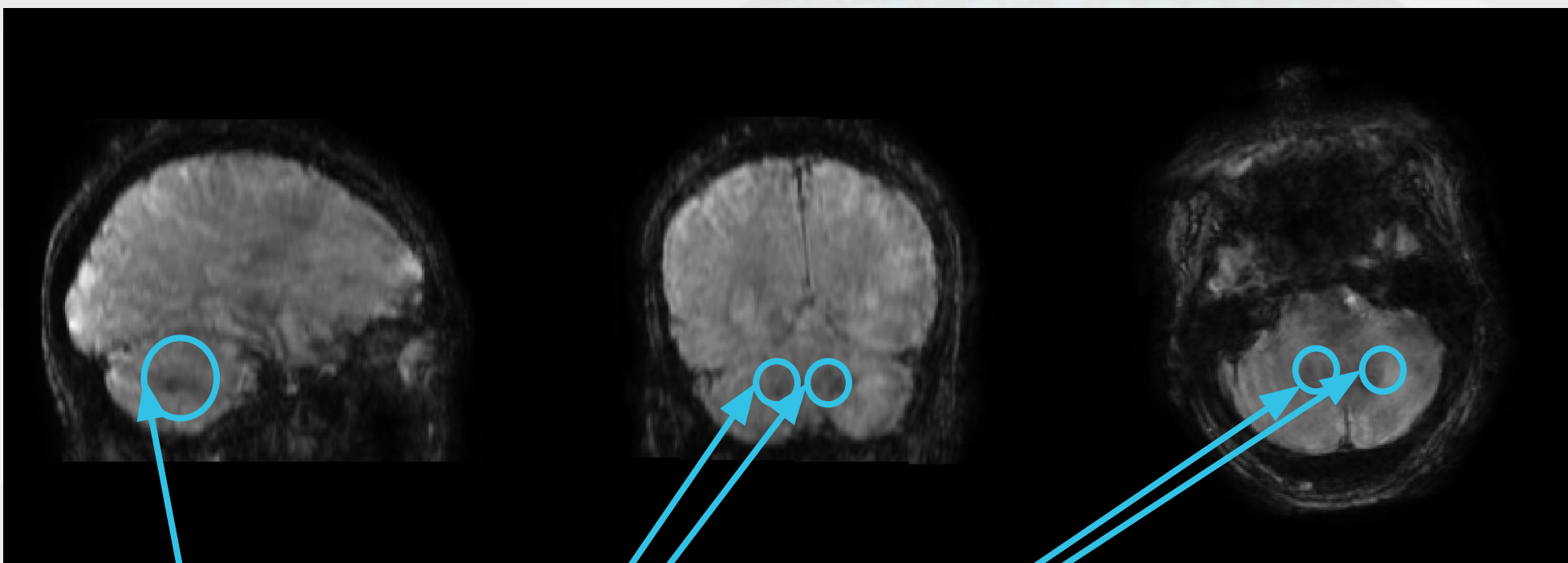


Dentate
Nuclei



Regions of Interest - Dentate

The dentate nucleus is the largest and most lateral of the cerebellar nuclei, located medially within each cerebellar hemisphere, just posterolateral to the fourth ventricle. It is rich in iron and it is hypo-intense in susceptibility weighted images (SWI)

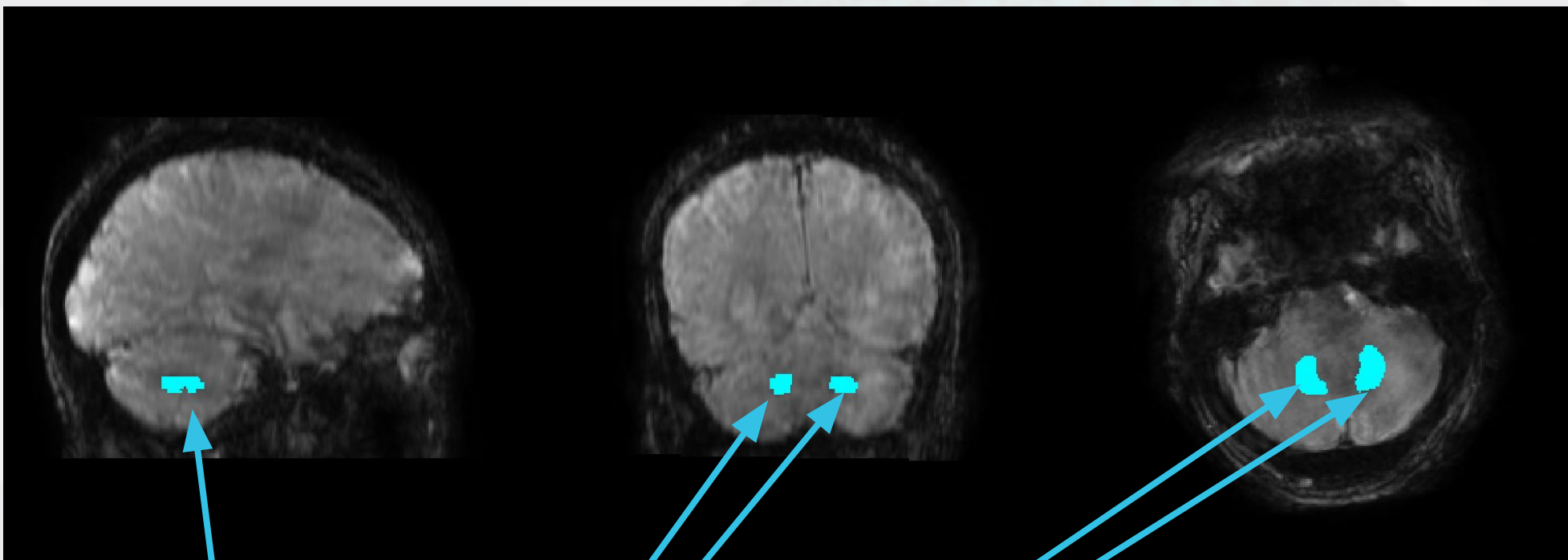


Dentate
Nuclei



Regions of Interest - Dentate

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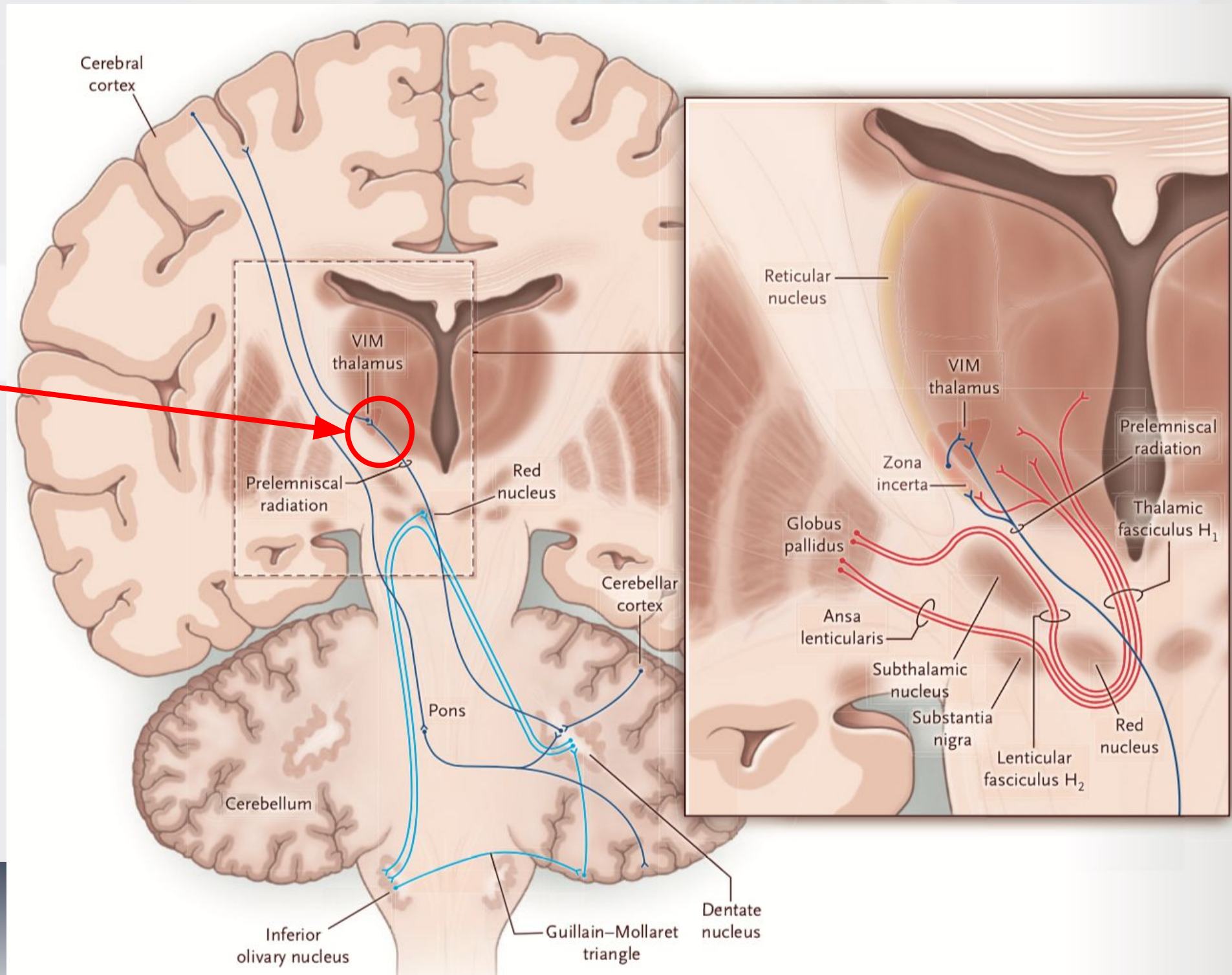
Manually segmented by a neuroradiologist and verified by another expert neuroradiologist

Dentate Nuclei



Region of Interest - Ventral Intermediate Nucleus

Ventral
InterMediate
nucleus



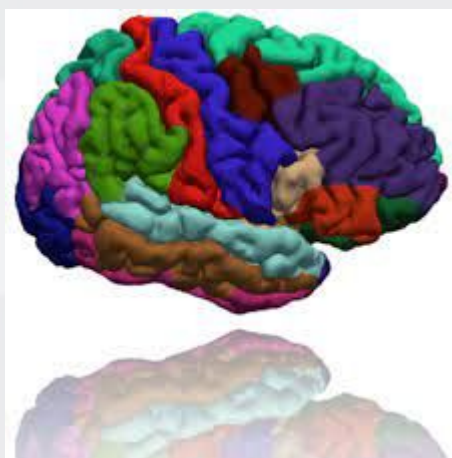
Essential Tremor. Haubenberger D, Hallett M. N Engl J Med. 2018 Aug 9;379(6):596-597. doi: 10.1056/NEJMc1807690.

nextAIM - Kickoff Meeting 17-18 February 2022



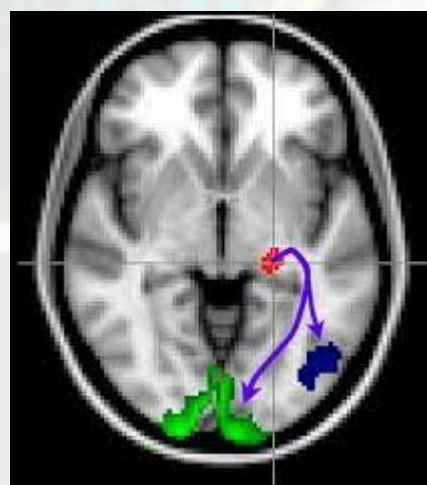
Region of Interest - Ventral Intermediate Nucleus

T1w-structural
images



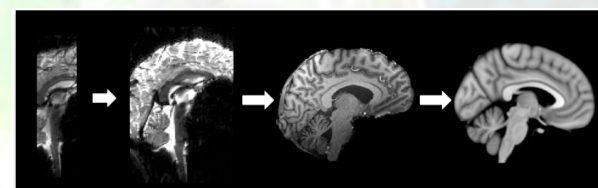
SEGMENTATION OF THE
BRAIN THROUGH
FREESURFER

DTI



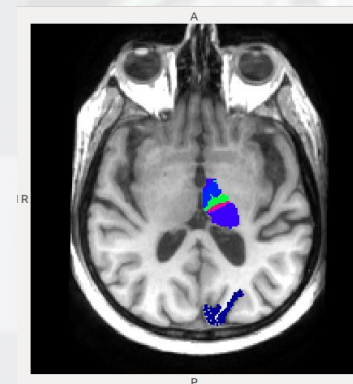
TRACTOGRAPHY THROUGH
BEDPOSTX AND PROBTRACKX
TOOLS OF FSL

REGISTRATION



REGISTRATION
THROUGH FSL

THALAMIC
PARCELLATION

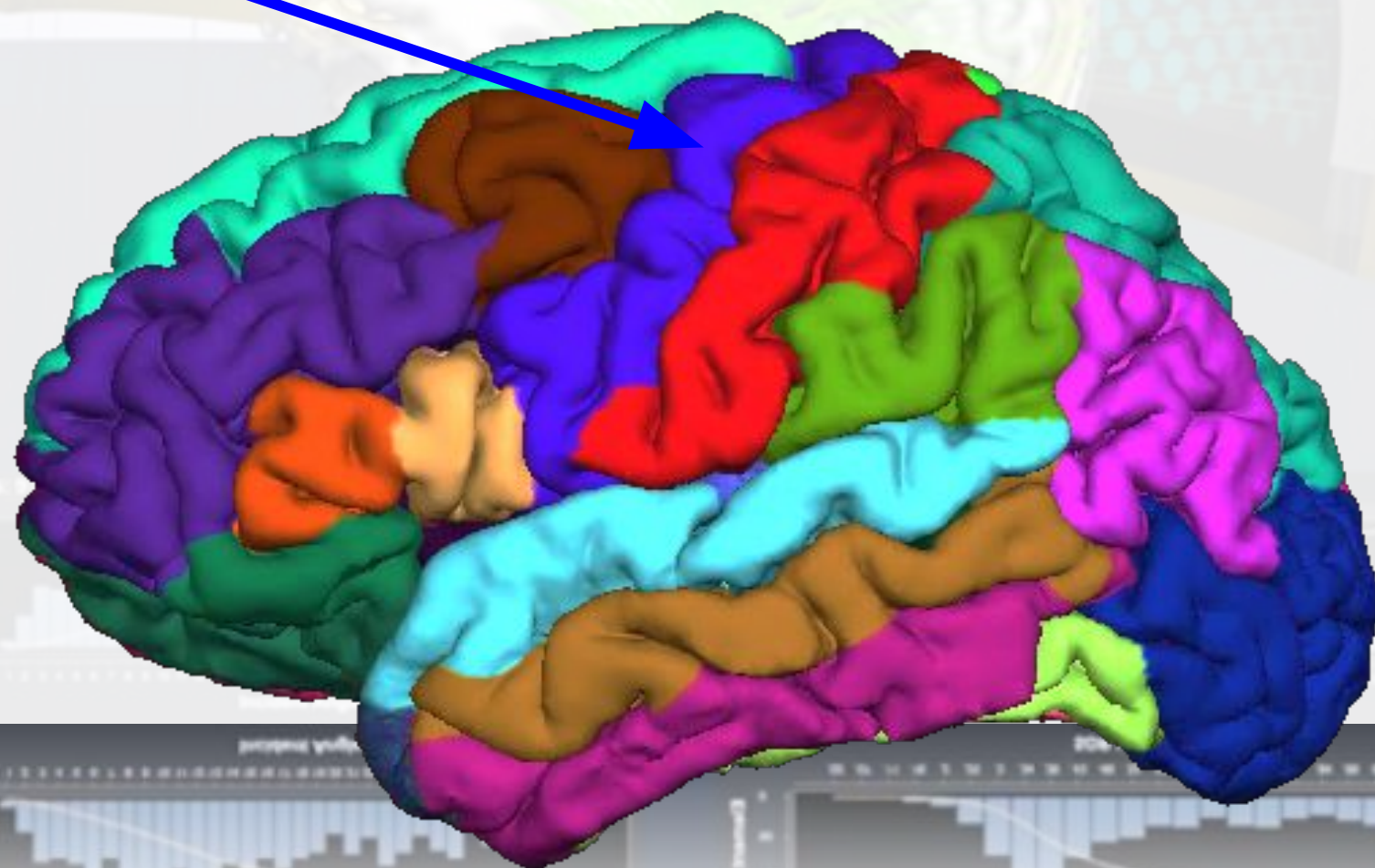




Region of Interest - Ventral Intermediate Nucleus

CORTICAL SEGMENTATION

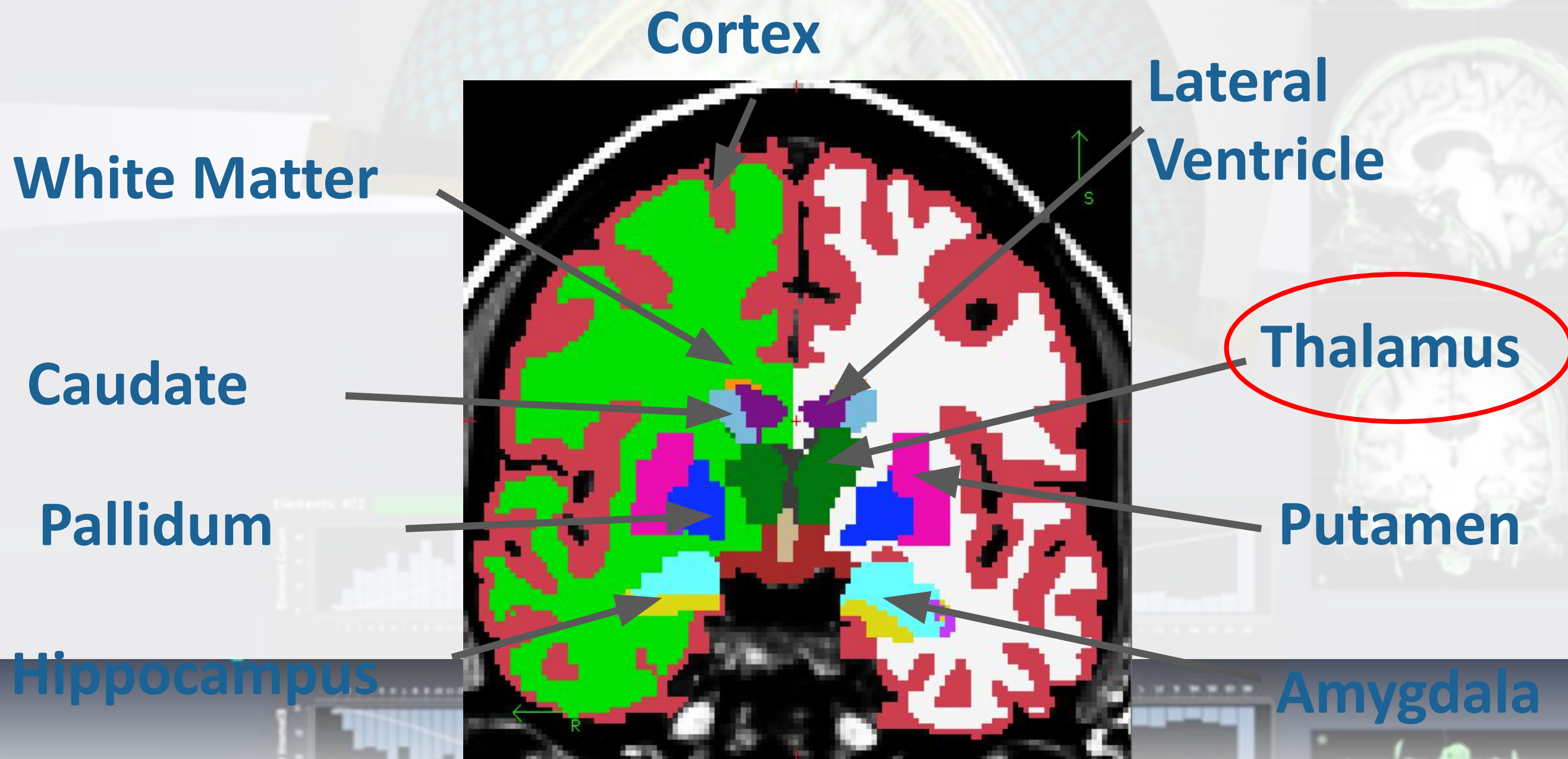
Precentral
Gyrus





Region of Interest - Ventral Intermediate Nucleus

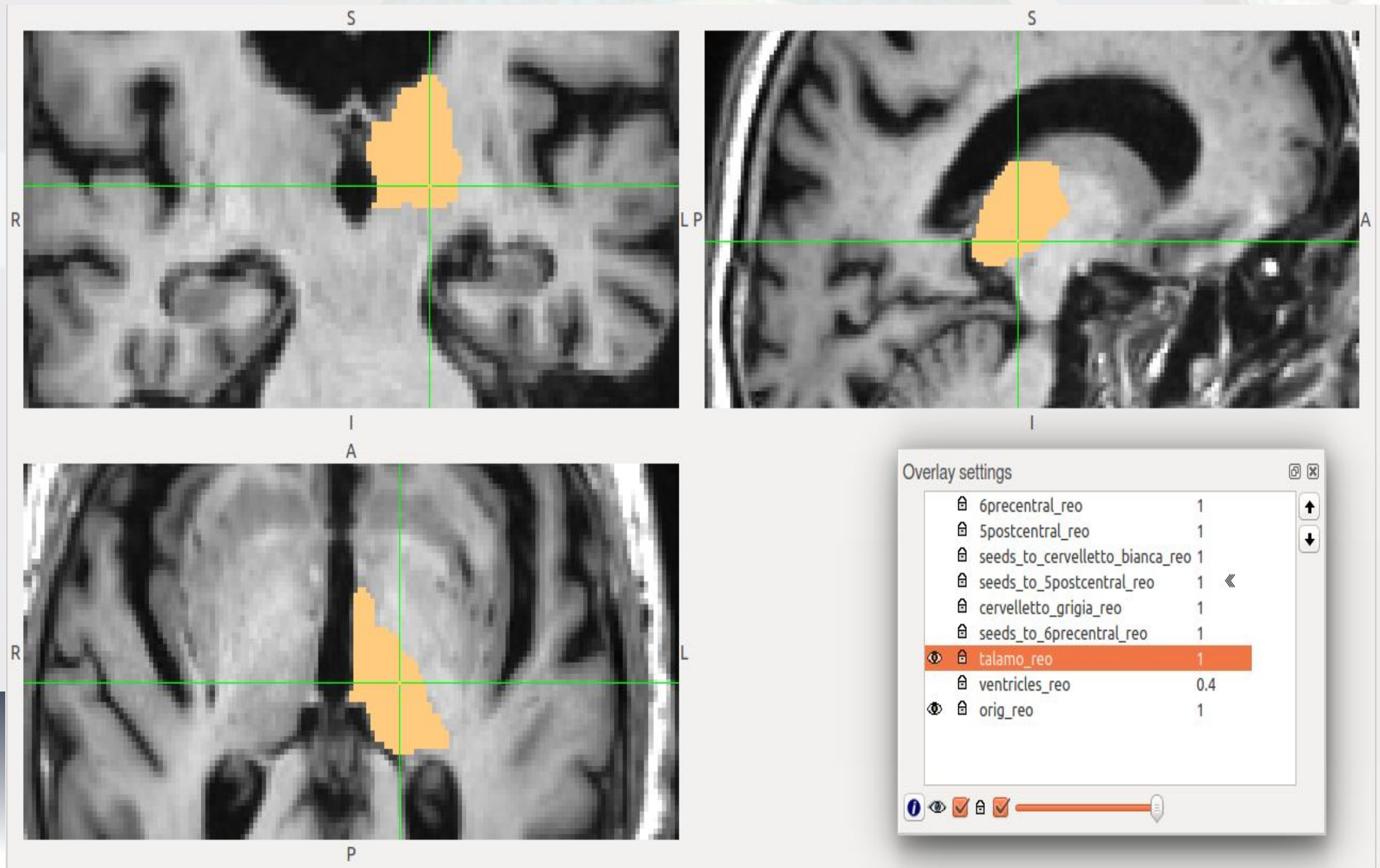
SUBCORTICAL SEGMENTATION





Region of Interest - Ventral Intermediate Nucleus

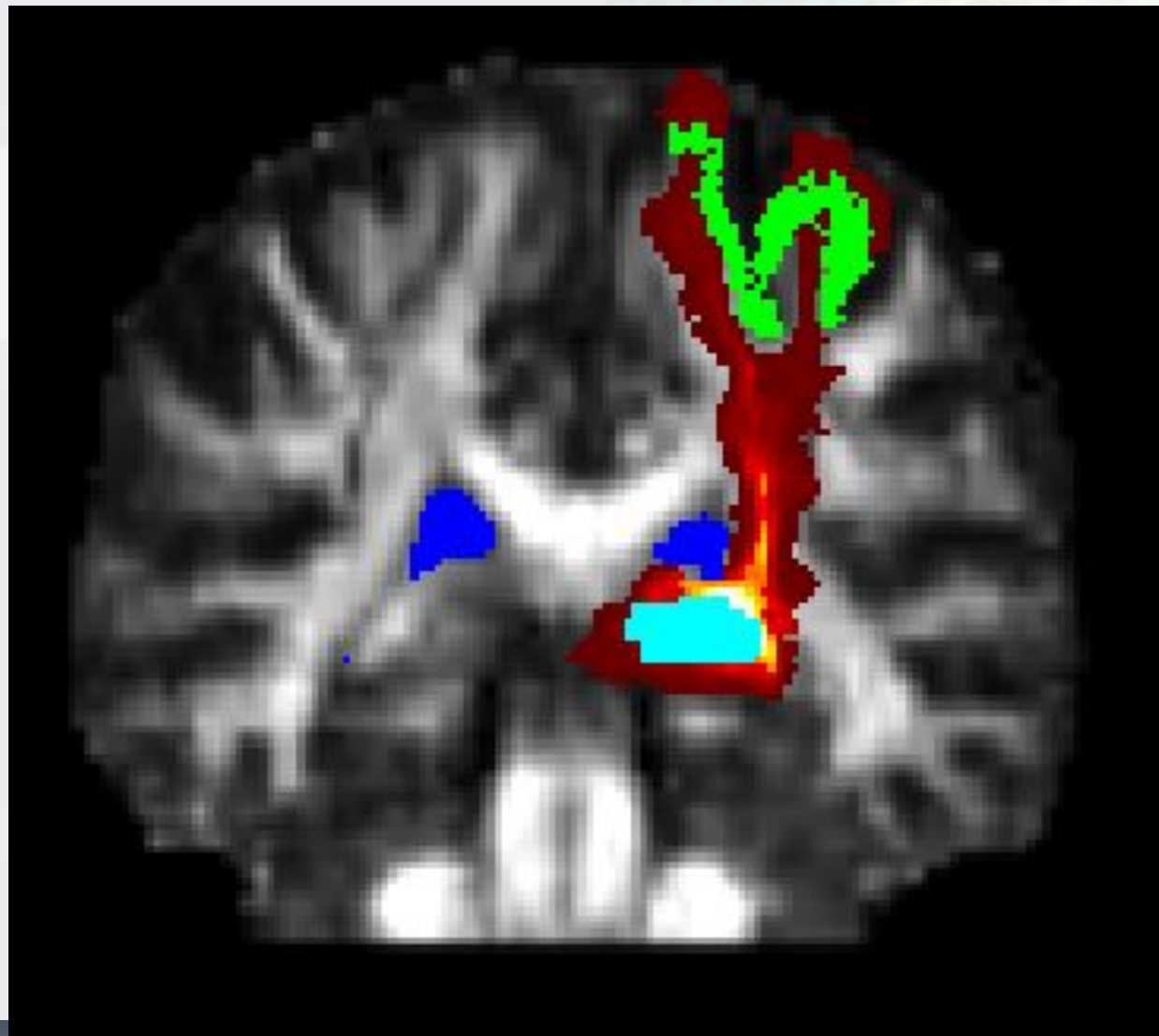
SUBCORTICAL SEGMENTATION





Region of Interest - Ventral Intermediate Nucleus

Probabilistic Tractography



- ❖ Fits the entire pathway, using diffusion orientation at all voxels along pathway length
- ❖ Constrained to connection of two specific end regions

Seeds

→ pre-central gyrus

Target

→ Thalamus
→ Cerebellum

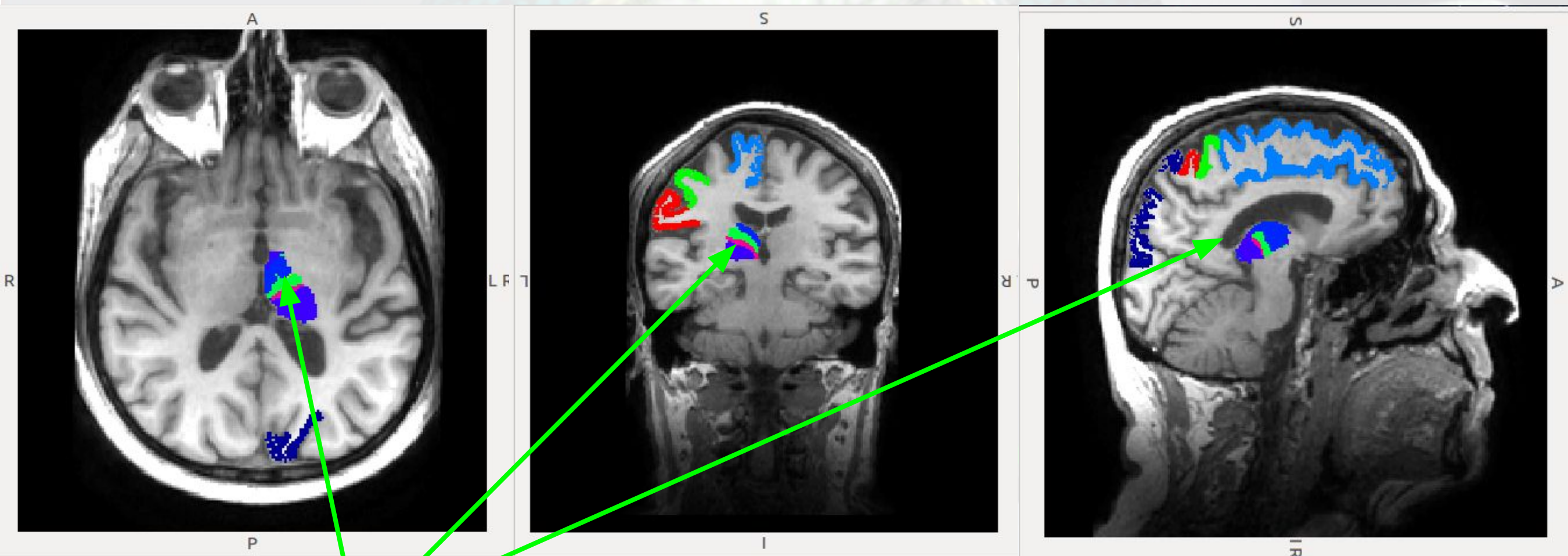
Regions excluded

→ Ventricles



Region of Interest - Ventral Intermediate Nucleus

Thalamic segmentation for the first patients

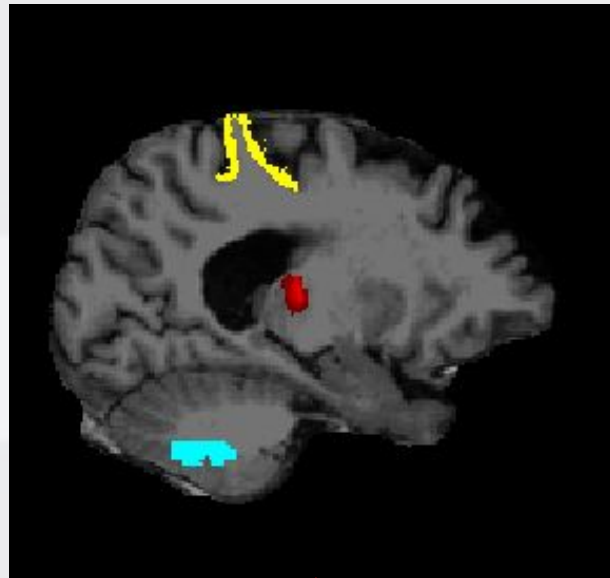


ROI RELATED TO THE PRECENTRAL GYRUS

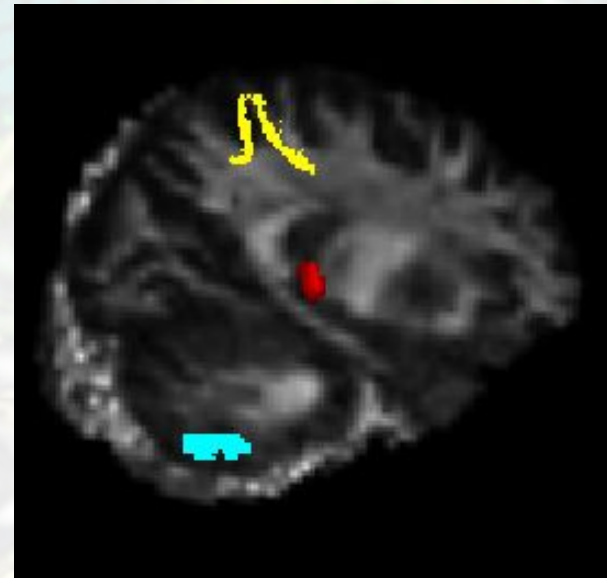


Radiomic Features extraction

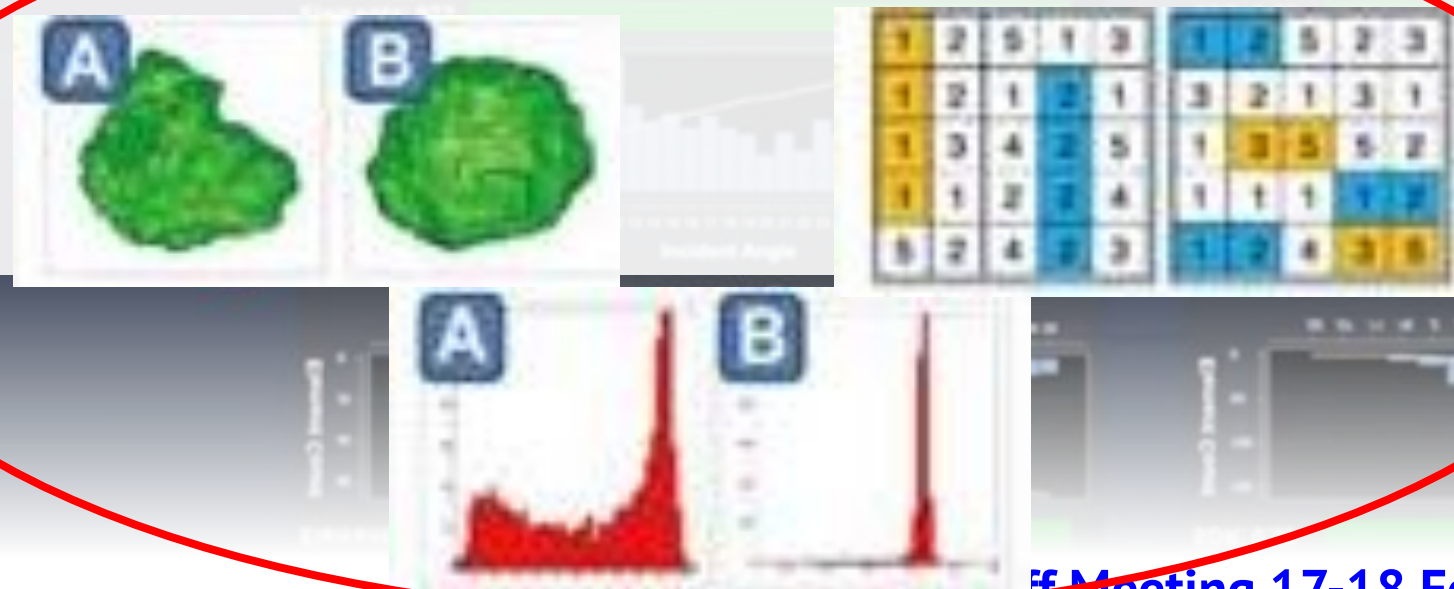
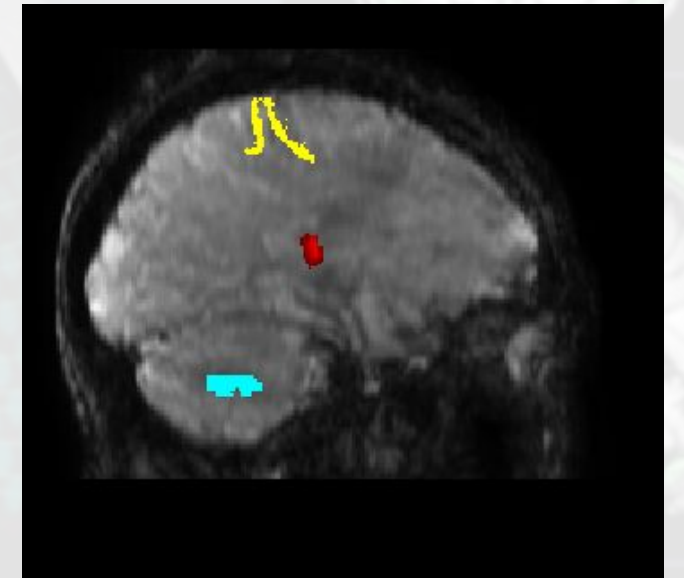
T_1 w-Structural MRI



FA



SWI



For each image type and for each ROI the radiomic features were extracted



Radiomic Features extraction



Shape-based features which are external representations of a region that characterize the shape, size, and surface information of the ROIs

Shape-based (3D) (16 features)

Shape-based (2D) (10 features)



First-order features (e.g., mean, median) describe the overall intensity and variation of the ROI

First Order Statistics (19 features)



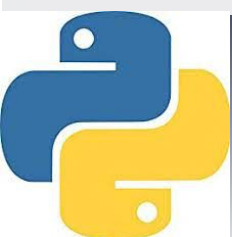
Second-order (texture) features in contrast can provide inter-relationships among voxels.

Gray Level Cooccurrence Matrix (24 features)

Gray Level Run Length Matrix (16 features)

Gray Level Size Zone Matrix (16 features)

Gray Level Dependence Matrix (14 features)



Nibabel - Neuroimaging in Python





Patients characteristics and clinical data considered:

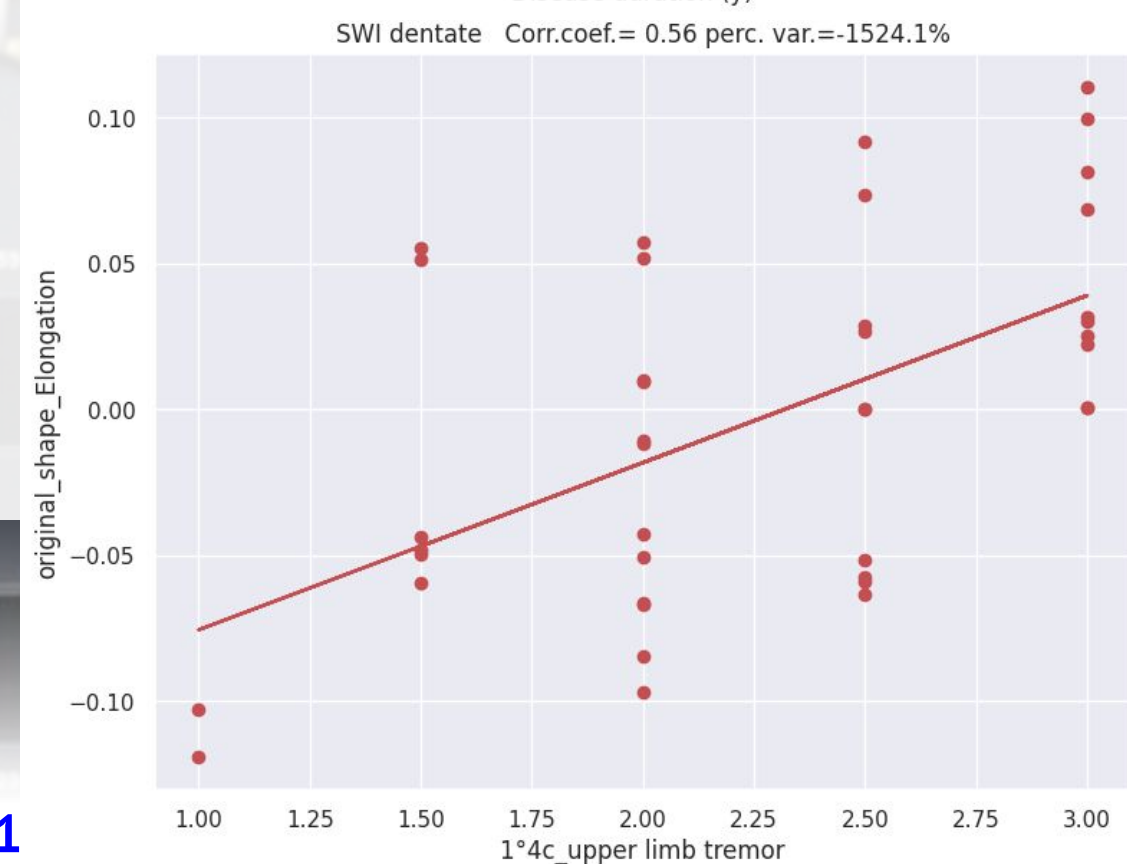
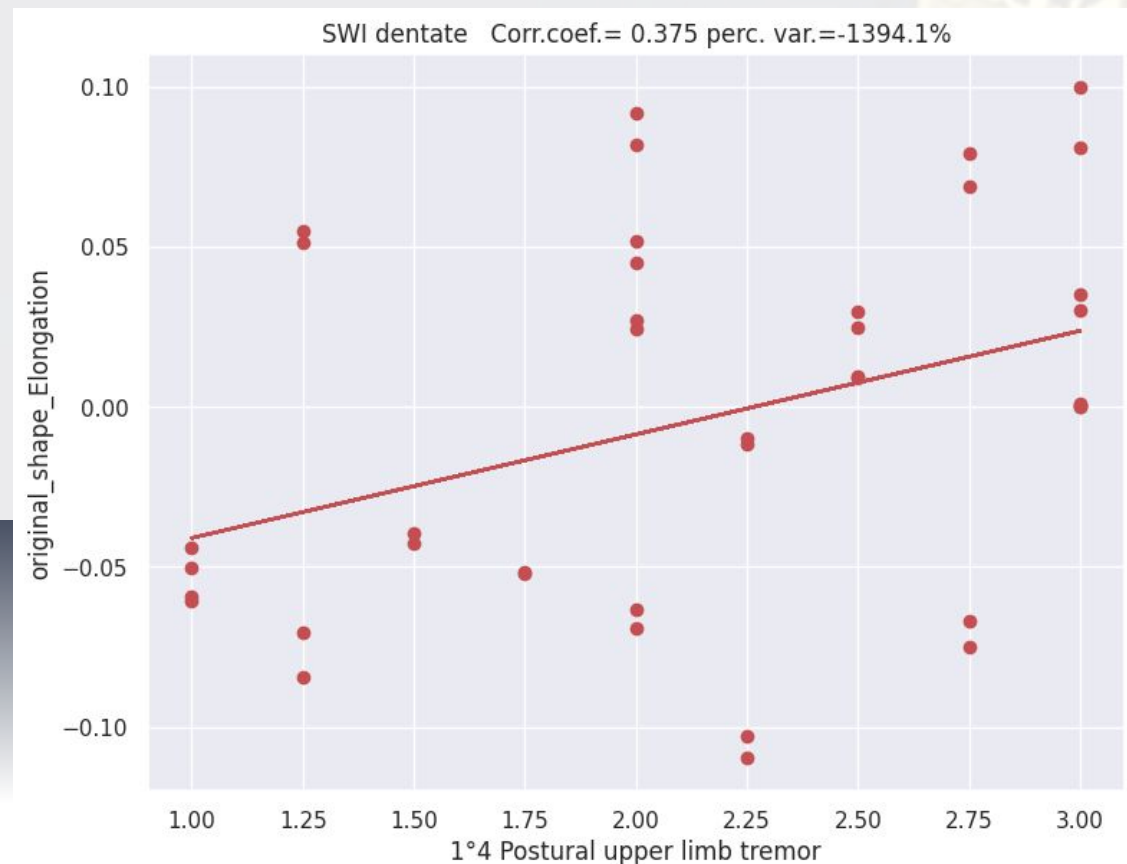
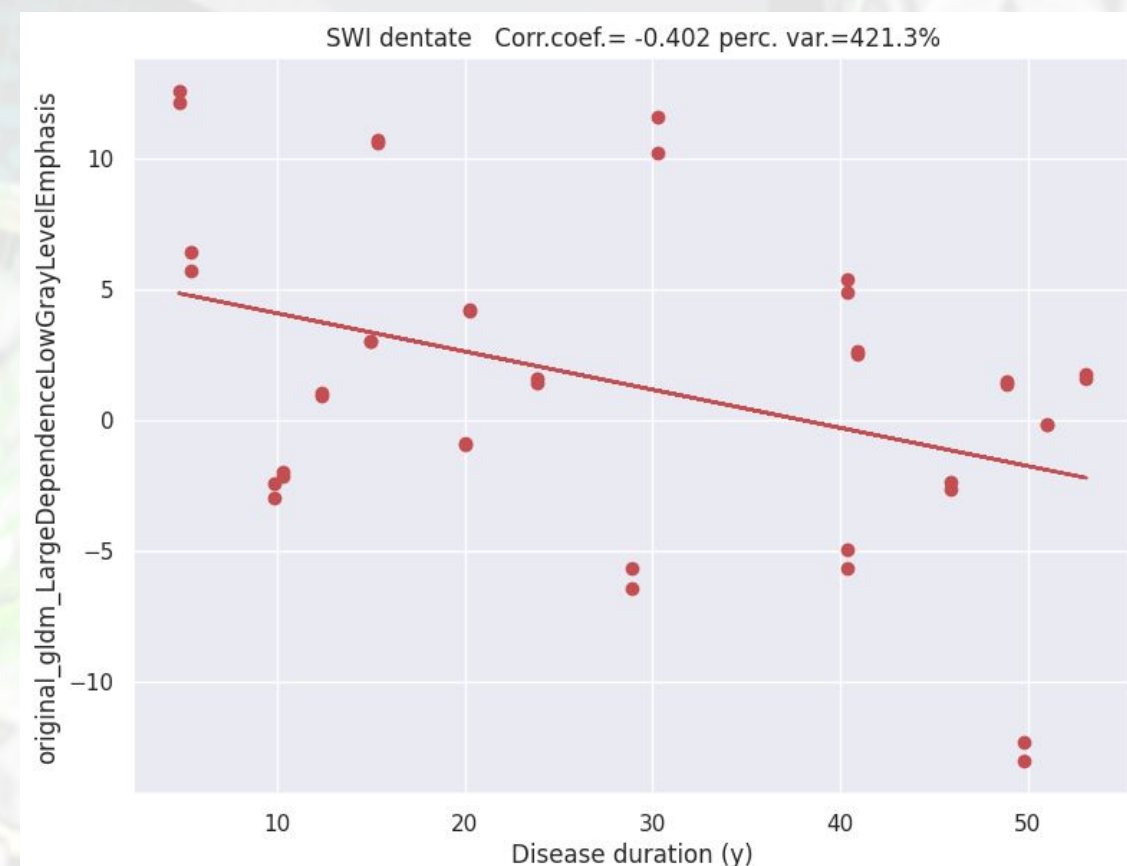
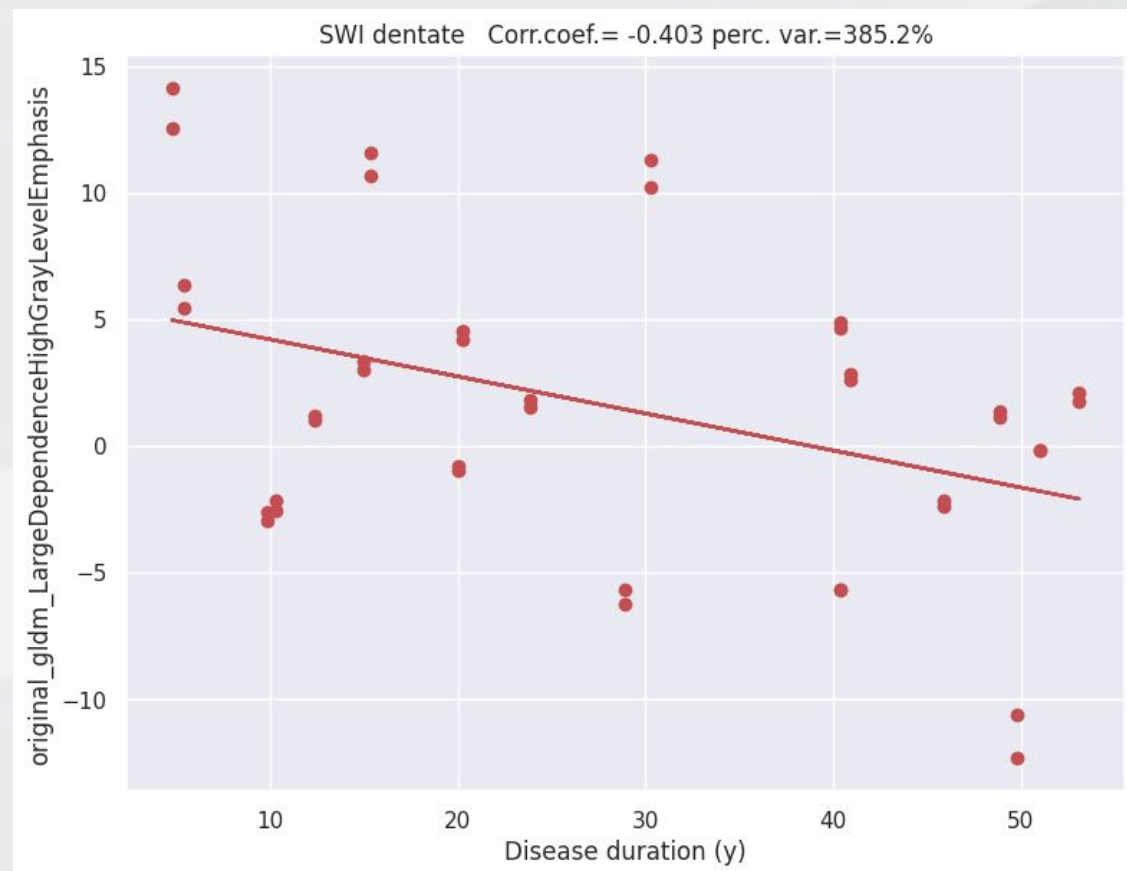
- Age
- Disease duration (years from the beginning of tremor)
- Kinetic tremor - occurs during voluntary movement, such as holding a glass to your mouth
- Postural tremor - occurs during voluntary holding of a position against gravity, such as reaching or extending an arm

TARGET: IDENTIFICATION OF FEATURES THAT ARE RELATED TO THESE PATIENTS CHARACTERISTICS OR CLINICAL DATA

DISCRIMINATION BETWEEN PREVALENT AND NON-PREVALENT SIDE



CORRELATION COEFFICIENT ANALYSIS





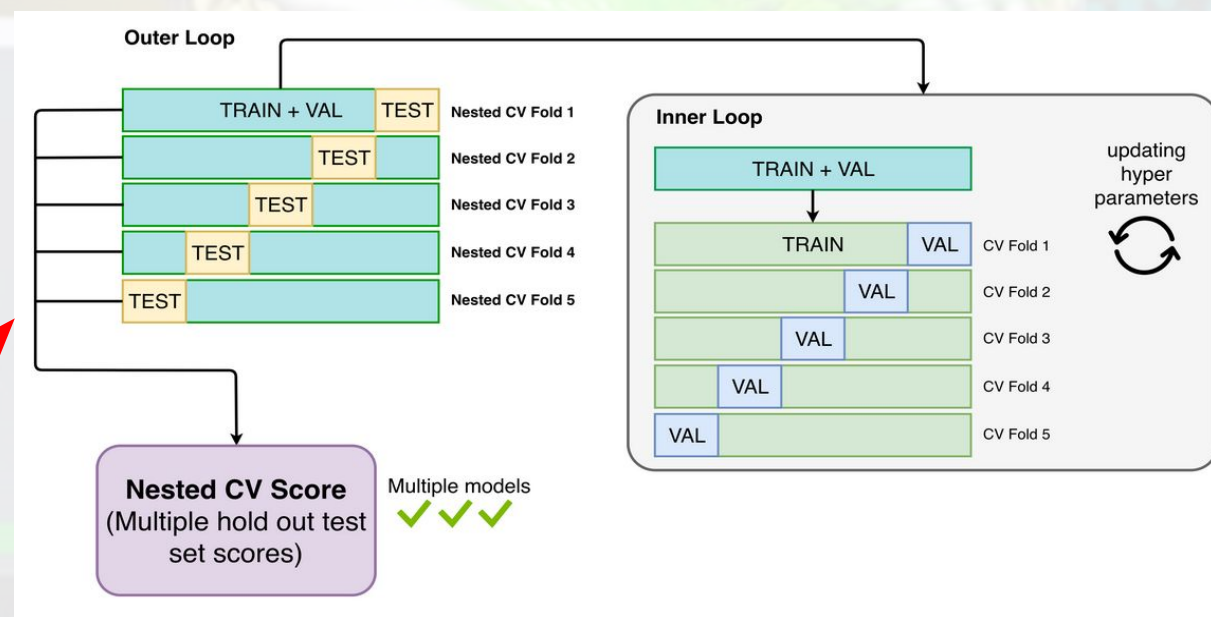
ML CLASSIFICATION

Numerical indexes (such as for kinetic and postural tremor) were **binarized** by using as threshold the **median** values in such a way to have two **almost equal sets** for each of above characteristics or clinical data

Feature scaling

Nested CV

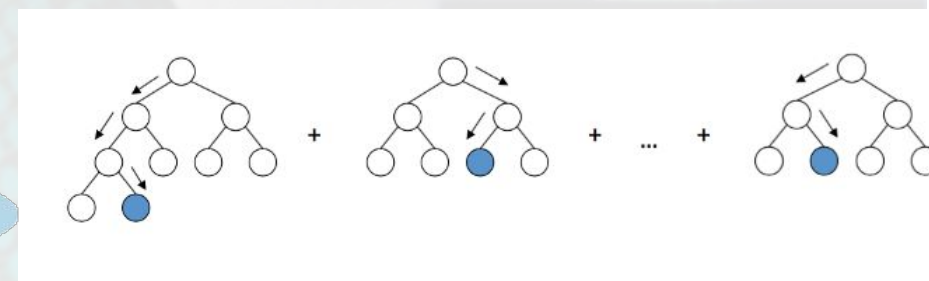
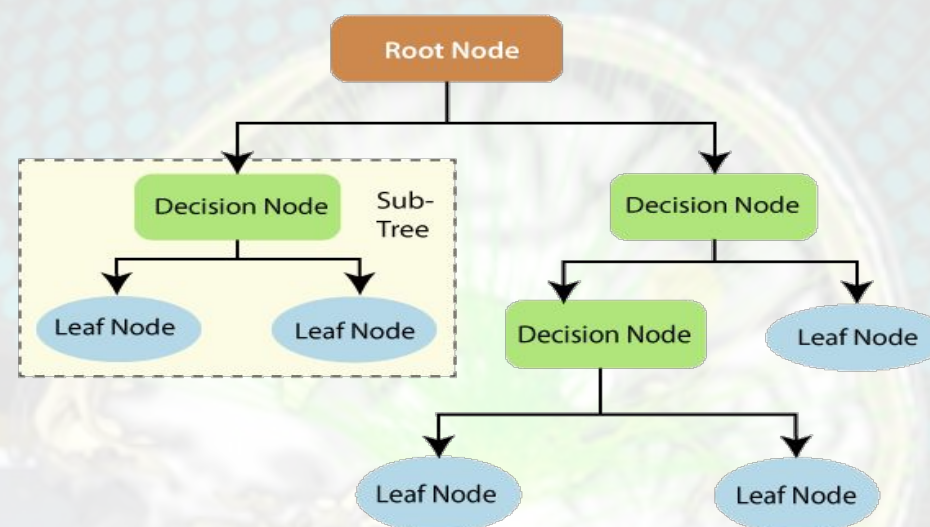
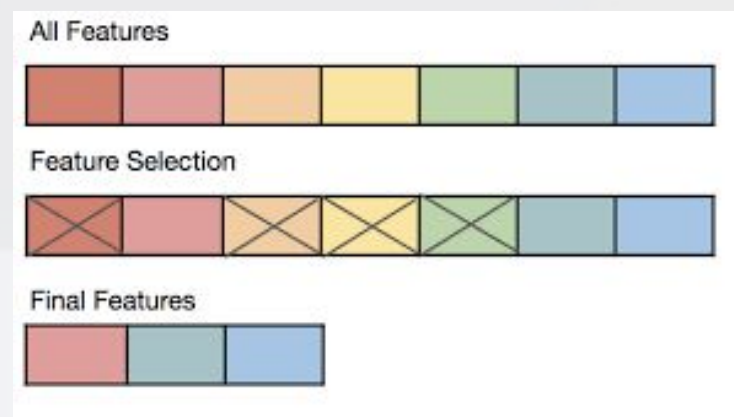
Features selection or dimension reduction



Hyperparameter optimization and score evaluation

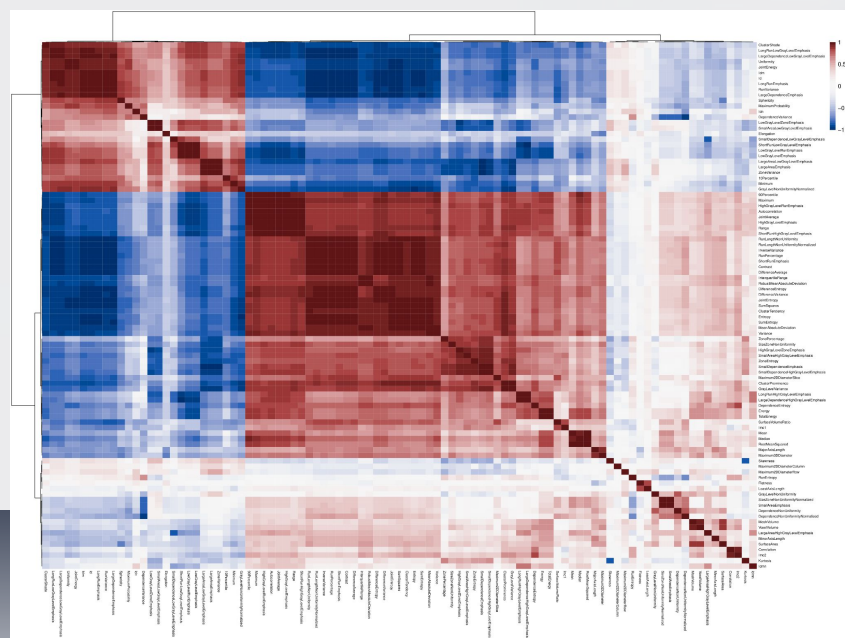


Features selection and dimension reduction

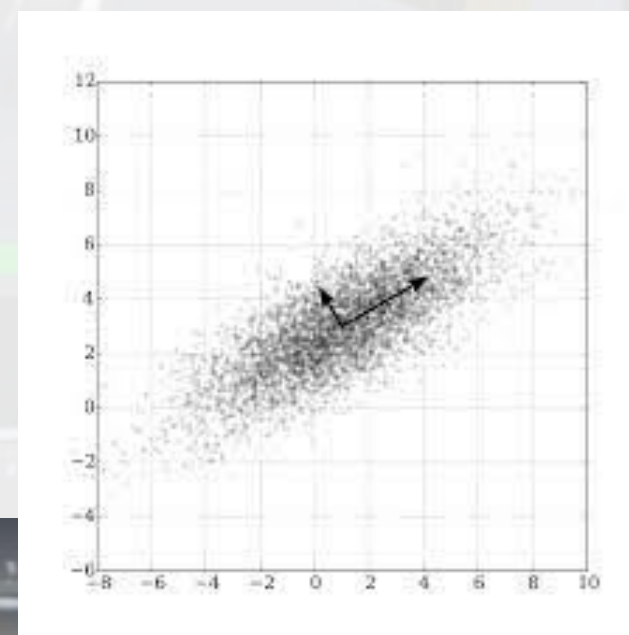


Random forest

Gradient Boosting



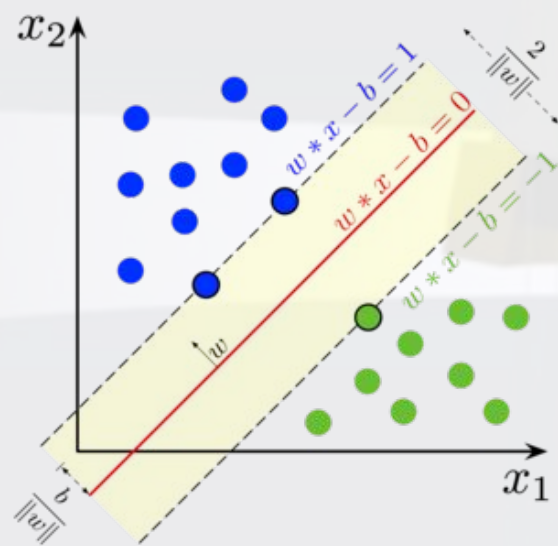
Dimension reduction using correlation matrix



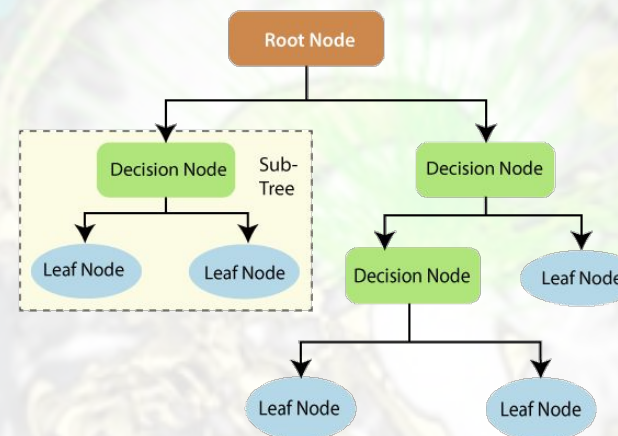
Dimension reduction using principal component analysis



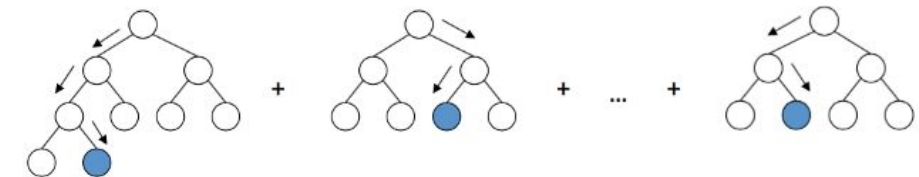
Classifiers adopted



Support vector machine



Random forest



Gradient Boosting



Pictures taken from <https://en.wikipedia.org>, <https://www.tutorialandexample.com>, <http://arogozhnikov.github.io>



Results for ML classification

Values of the Area Under Curve (AUC)

Postural tremor

SWI

Dentate

| | SVM | Random Forest | Gradient Boosting |
|-------------------------|-----------------|-----------------|-------------------|
| Nested Cross Validation | 0.76 ± 0.15 | 0.78 ± 0.10 | 0.78 ± 0.16 |

Kinetic tremor

SWI

Dentate

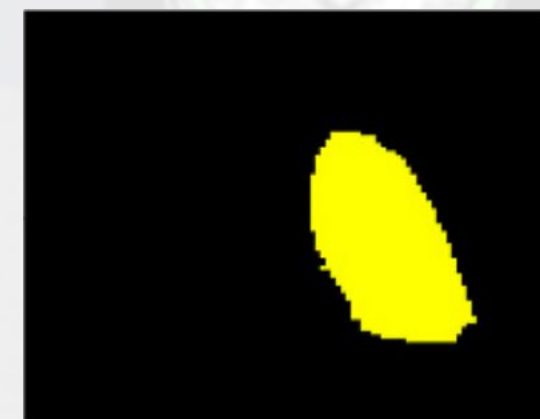
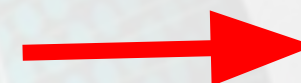
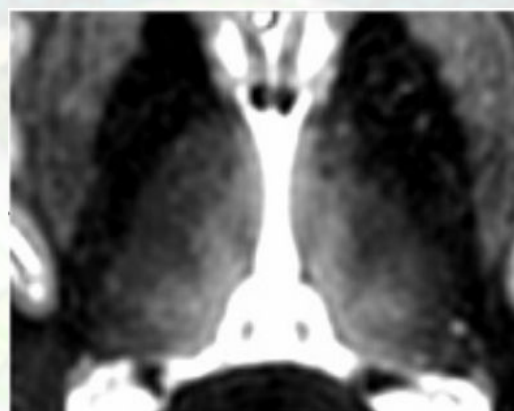
| | SVM | Random Forest | Gradient Boosting |
|-------------------------|-----------------|-----------------|-------------------|
| Nested Cross Validation | 0.80 ± 0.15 | 0.85 ± 0.08 | 0.82 ± 0.10 |



DL for thalamic parcellation for target identification

2D Convolutional neural networks have been used for

- segmentation thalamus



- Segmentation of thalamus nuclei



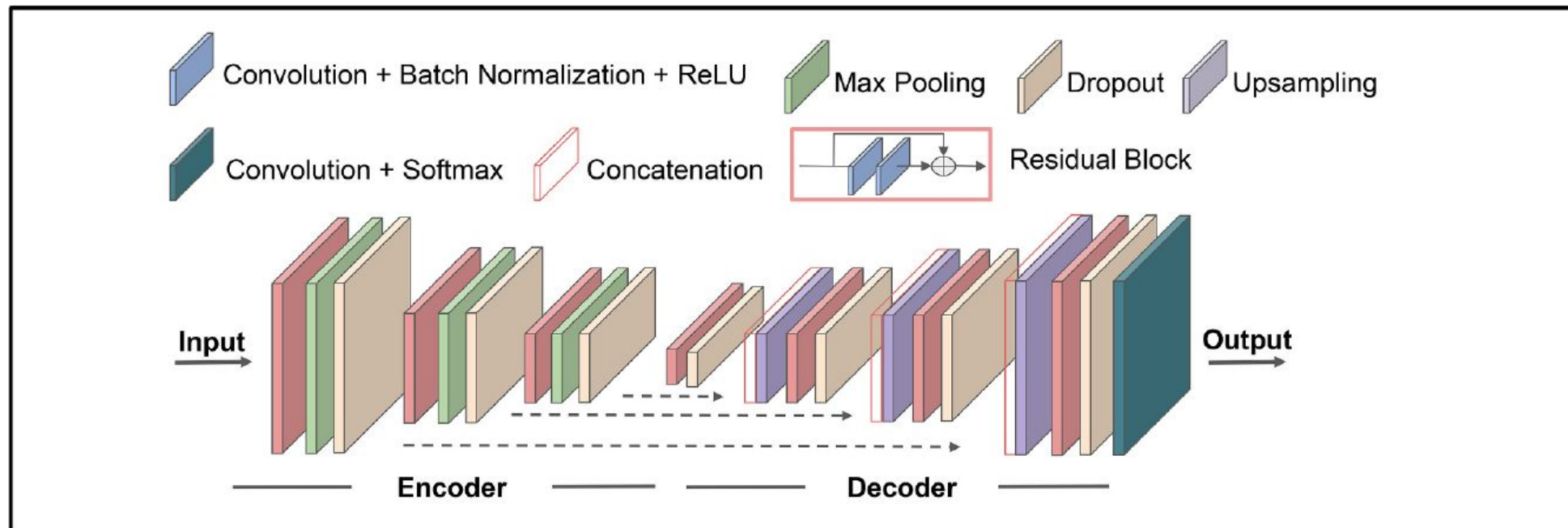
According to Morel model

Majdi et al. Magnetic Resonance Imaging 73 (2020) 45–54



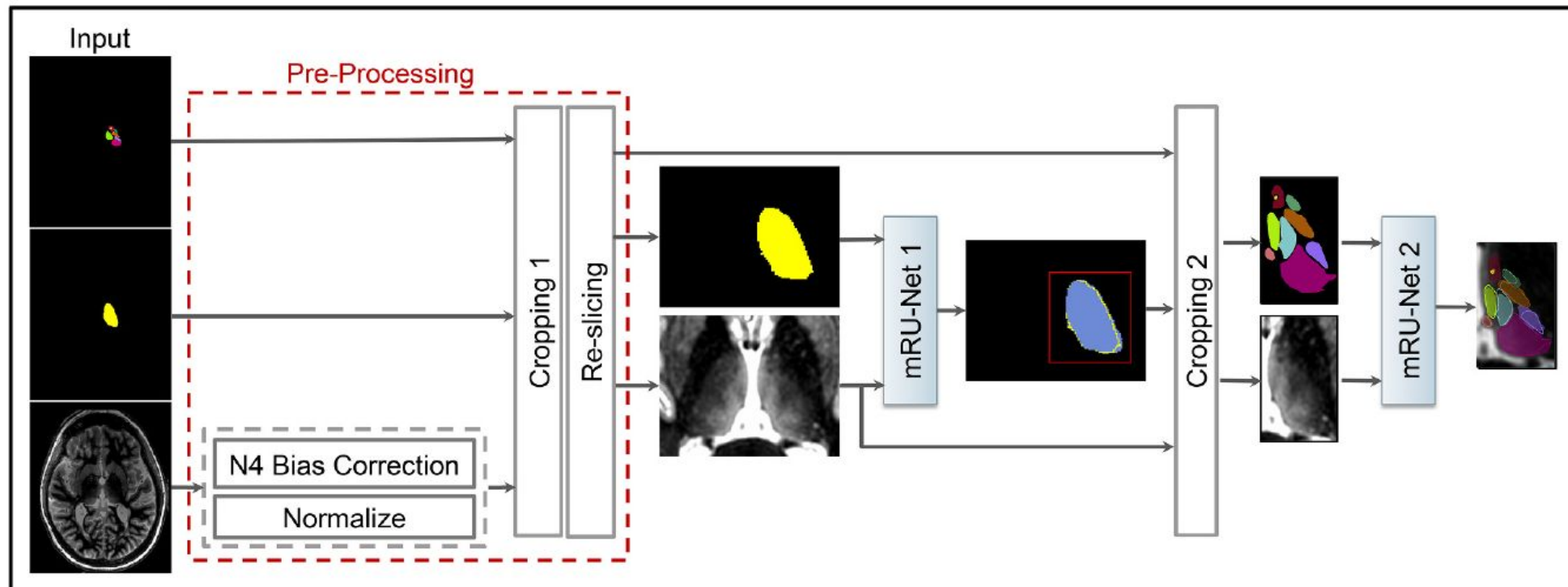
Modified residual U-Net architecture (mRU-Net)

mRU-Net Architecture



Training:
ADAM optimizer
300 epochs
Batch size: 100
Learning rate ≤ 0.001

Cascaded Network



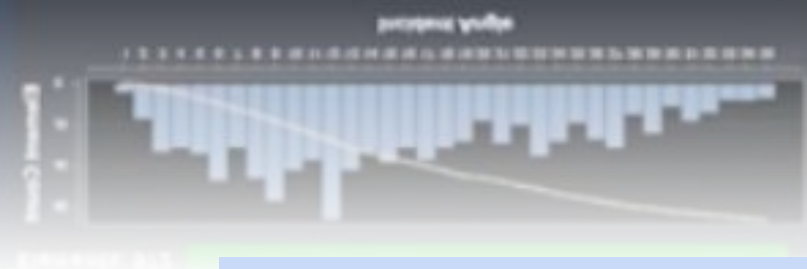
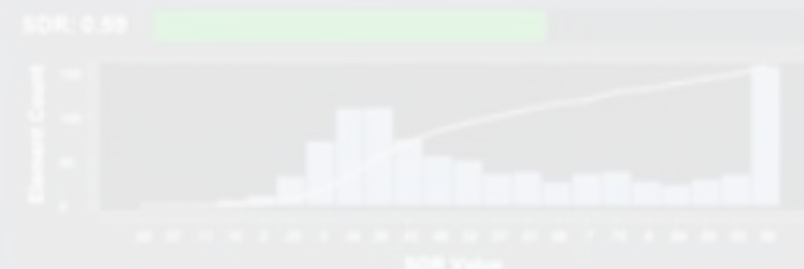


MR Datasets

40 subjects (13 healthy subjects, 15 patients with Multiple Sclerosis, and 12 patients with Essential Tremor) acquired on a 7 T scanner.

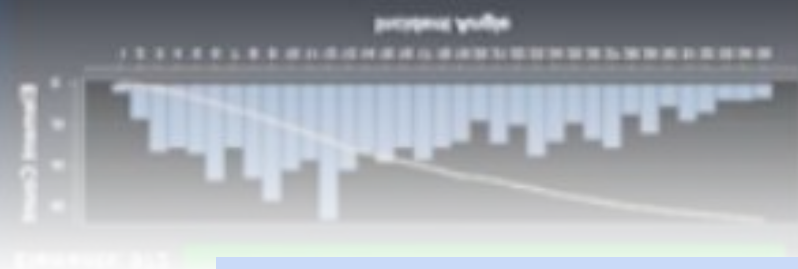
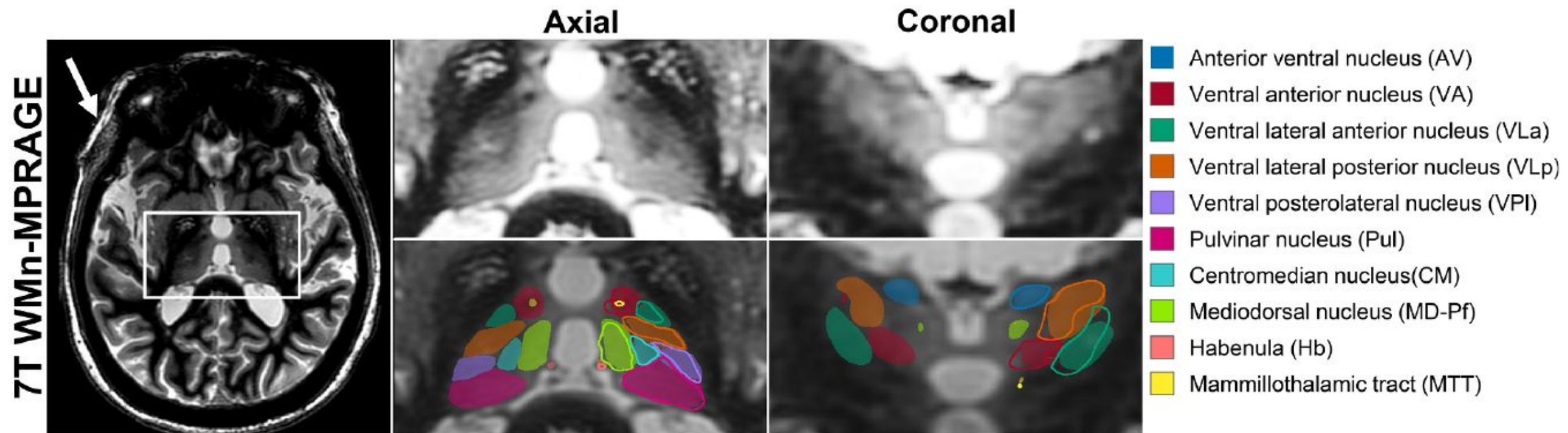
The thalamic nuclei in these dataset were labeled by an expert radiologist.

3D-CNN cannot be trained because the small number of labeled datasets available.





Comparison of the results with the ground truth





Conclusions and Perspectives

- Radiomics features were extracted from various brain regions (precentral gyrus, thalamus and dentate nuclei)
- Feature selection was performed on basis of patients' characteristics and clinical data

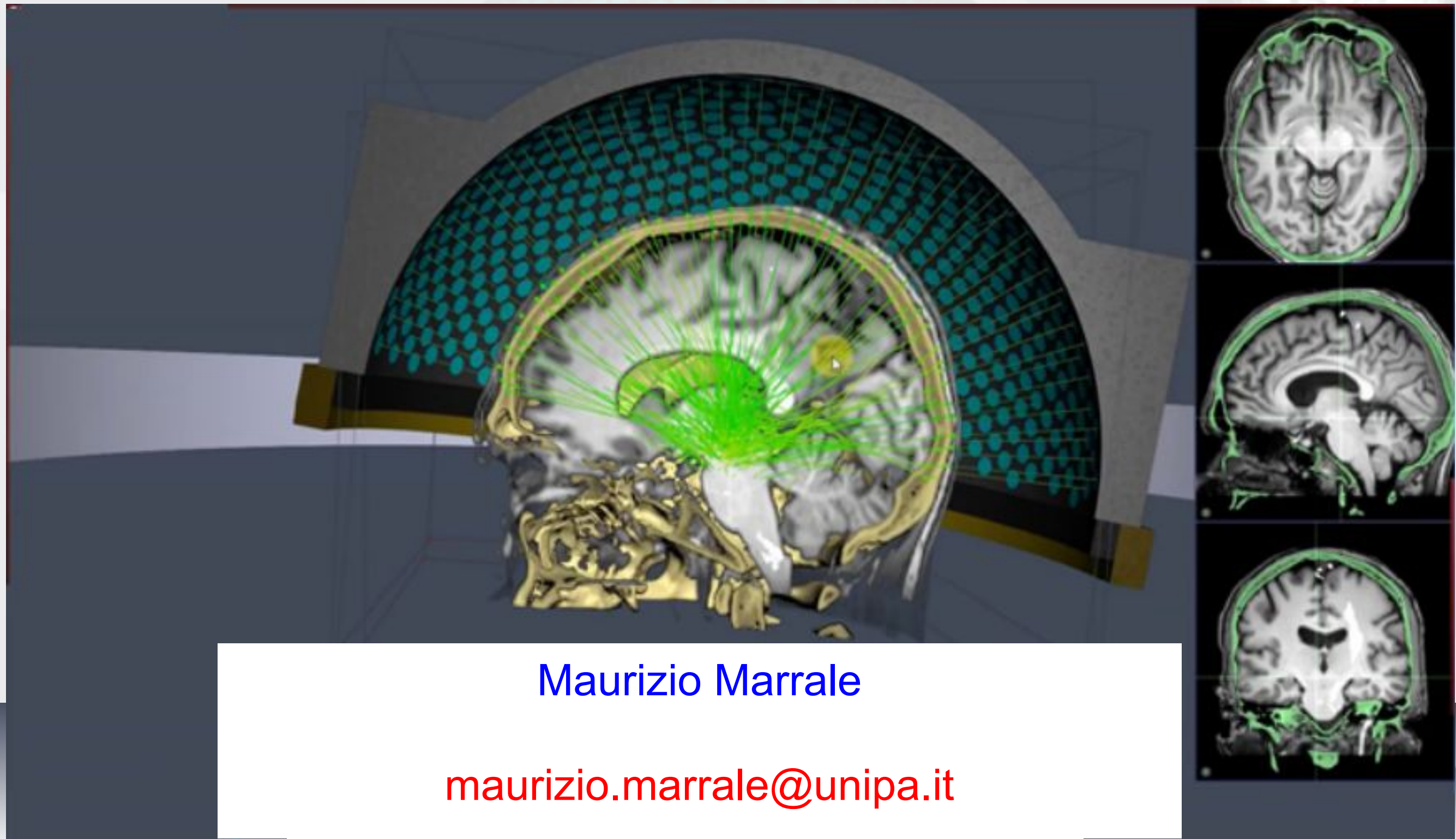
What's next?

- These analyses will be performed on a larger number of patients
- Radiomic analyses will be applied for evaluating changes after tcMRgFUS treatment and for evaluating the treatment success.
- DL segmentation of thalamus for target identification





THANK YOU FOR YOUR KIND ATTENTION!



Maurizio Marrale

maurizio.marrale@unipa.it