107° CONGRESSO NAZIONALE
della SOCIETÀ ITALIANA DI FISICA

Target identification in functional neurosurgery: A preliminary assessment of the variability of the Ventral Intermediate Nucleus through MR structural connectivity analysis from Human Connectome Project

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Transcranial Magnetic Resonance-guided Focused Ultrasound Surgery (tcMRgFUS) at 1.5T

Surgical therapy using magnetic resonance-guided focused ultrasound (Magnetic Resonance guided Focused Ultrasounds Surgery MRgFUS) is a modern and non-invasive ablative technique

Recent technological developments enabled MRI-guided therapeutic application of HI-FU to the brain (transcranial MRgFUS - tcMRgFUS)

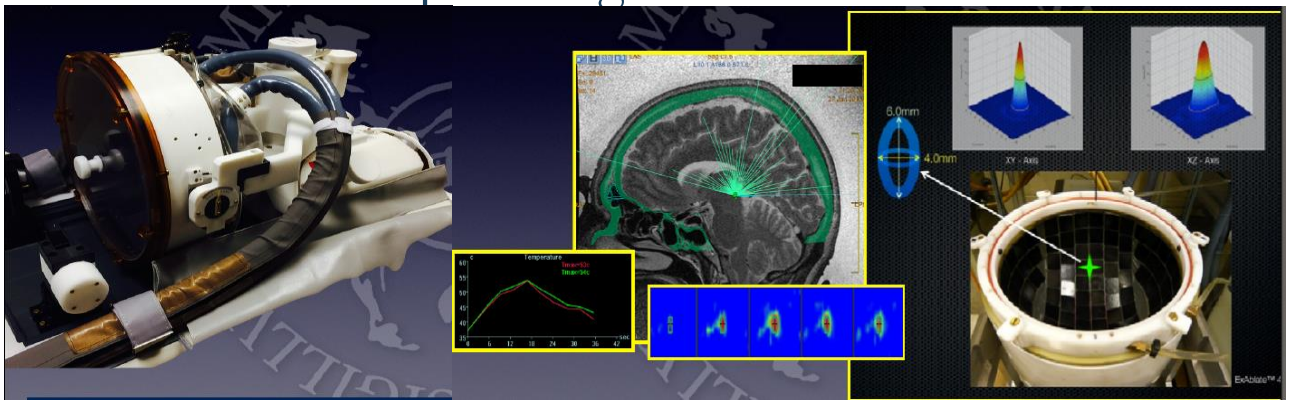
tcMRgFUS at 1.5T

This Focused Ultrasound (FUS) equipment

(ExAblate 4000, InSightec Ltd. - Haifa, Israel)

consists of an hemispheric 1024-element phased-array transducer

operating at 650 kHz



Essential Tremor

Essential Tremor interfers with main daily activities like:

- Eating
- Drinking
- Writing
- Typing
- Personal Hygiene

Treatment of ET

General principles

- Treat only if bothersome
- The longer the tremor has been there the more difficult treatment will be
- Limb tremor responds much better than head/neck to oral tremor

Pharmacologic

- Mainly for not heavy tremors

Surgery

- Stereotactic Radiation Surgery (SRS)
- Radiofrequency ablation (RFA)
- Deep Brain Stimulation (DBS)
- Magnetic Resonance guided Focused Ultrasounds Surgery (MRgFUS)

tcMRgFUS

tcMRgFUS offers an **incisionless** approach to treat movement disorders

tcMRgFUS

tcMRgFUS offers an **incisionless** approach to treat movement disorders

The **v**entral **i**nter**m**ediate **n**ucleus (**VIM**) of the thalamus is an established **surgical target** for these diseases

tcMRgFUS

tcMRgFUS offers an **incisionless** approach to treat movement disorders

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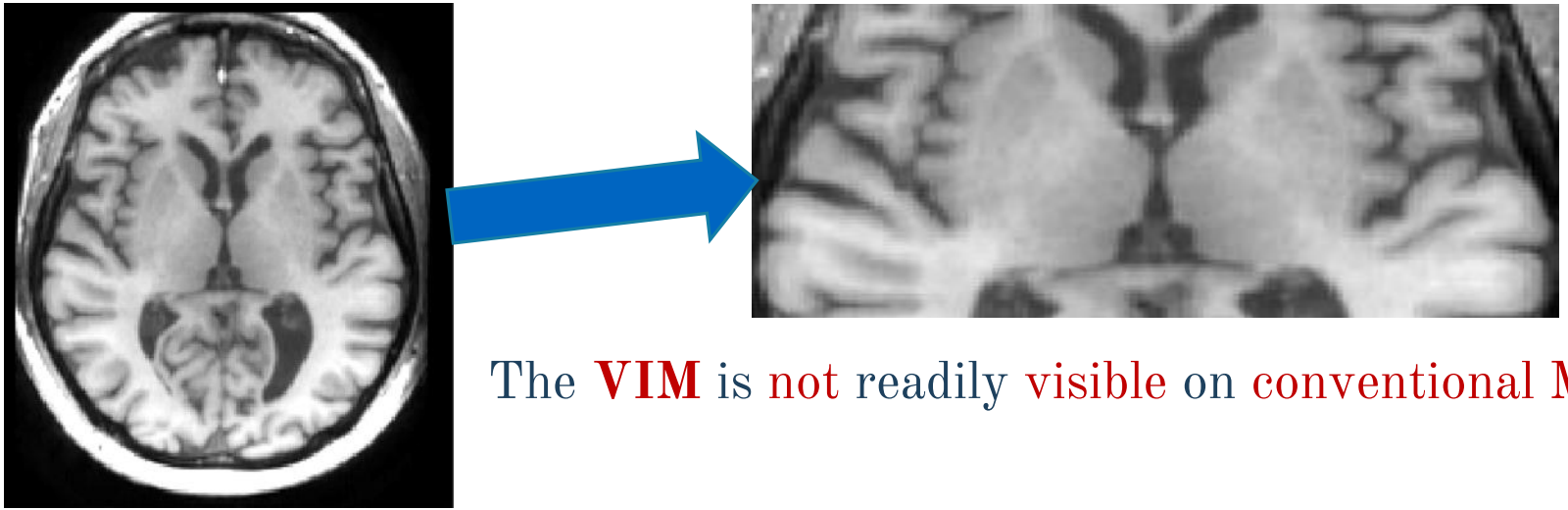

The **VIM** is not readily visible on conventional MR imaging

tcMRgFUS

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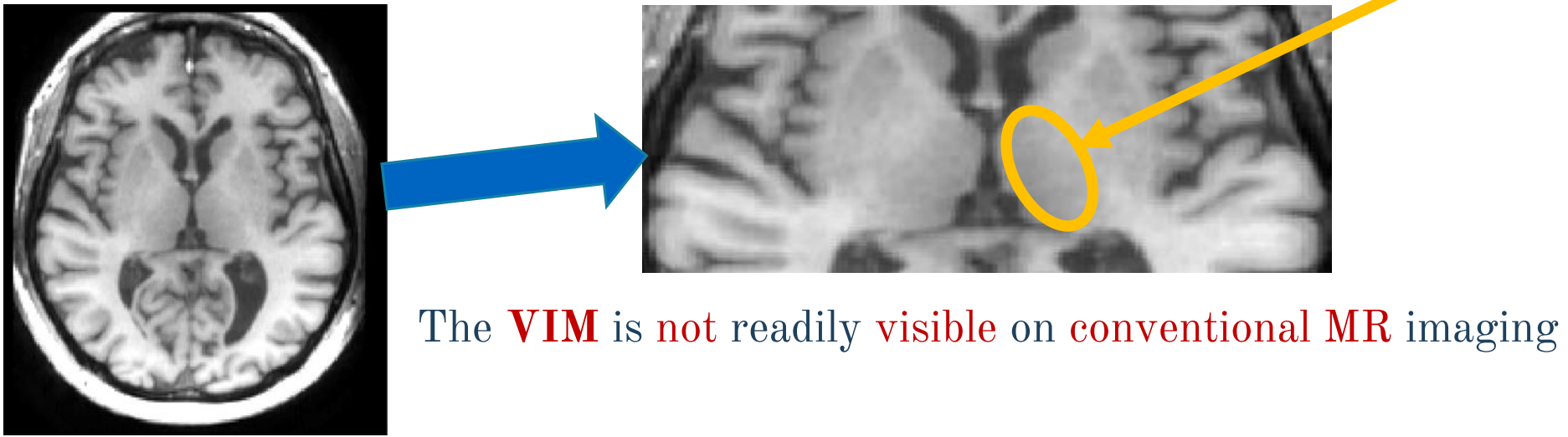
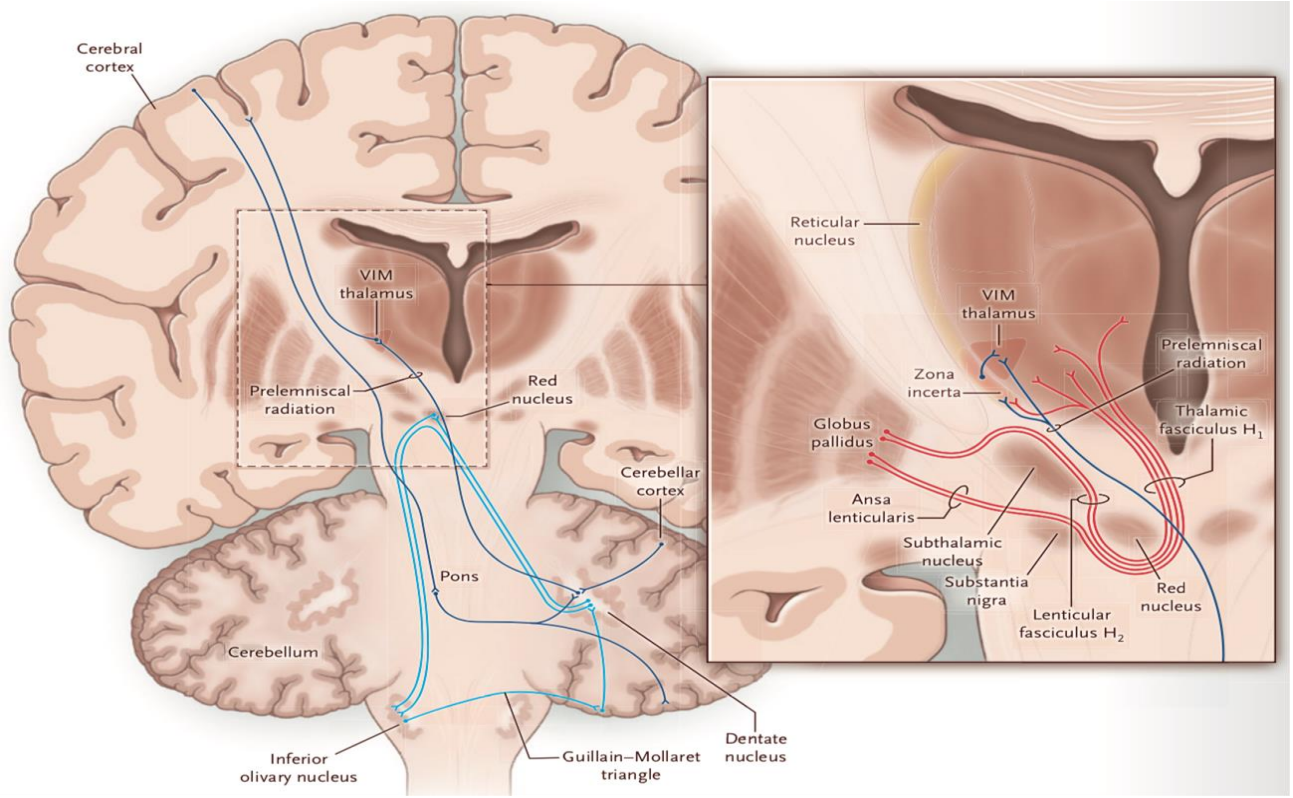


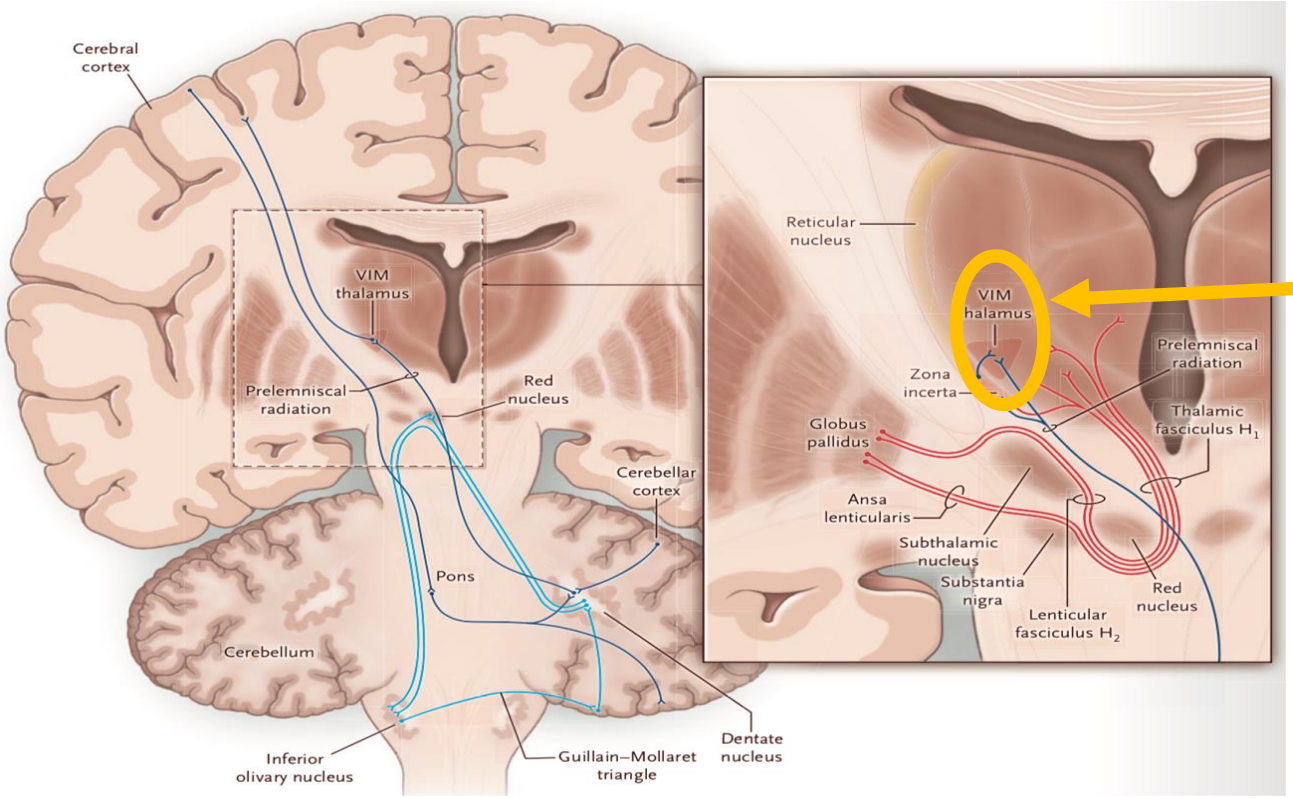
The **VIM** is not readily visible on conventional MR imaging

Cerebellar-thalamo-cortical tract



(Calzavara et al., 2005; Darian-Smith et al., 1990; Dum 56 and Strick, 2003; Gallay et al., 2008)

Cerebellar-thalamo-cortical tract



VIM

tcMRgFUS

tcMRgFUS allows to carry out a real neurofunctional exploration to confirm and optimize the lesion target before inducing a permanent brain injury

The choice of treatment target is based on stereotaxic coordinates

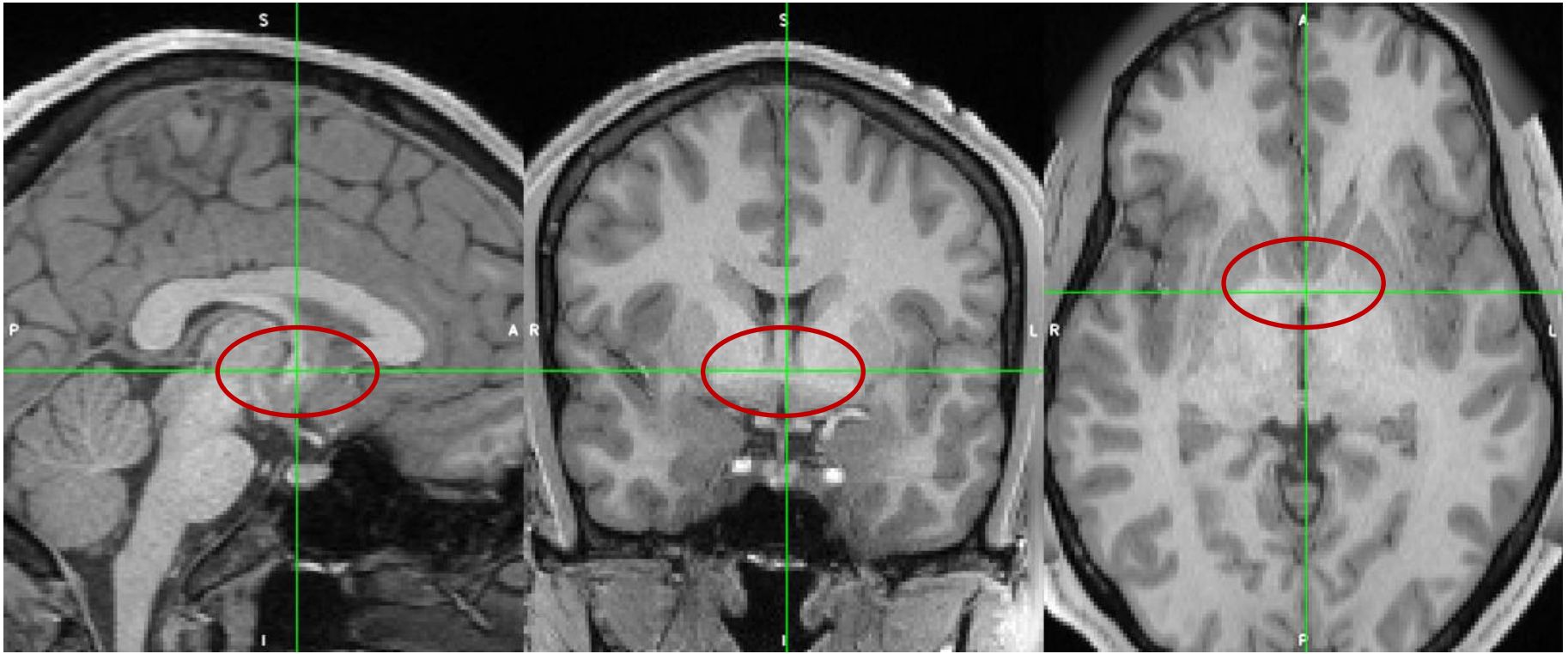
STEREOTAXIC COORDINATES

- AP direction = (AC-PC length)/3 – 2 mm anterior to PC
- ML direction = Midline ± 12 to 14 mm; (12.5mm used in this study)
- SI direction = 0 mm

Akram et al., 2018

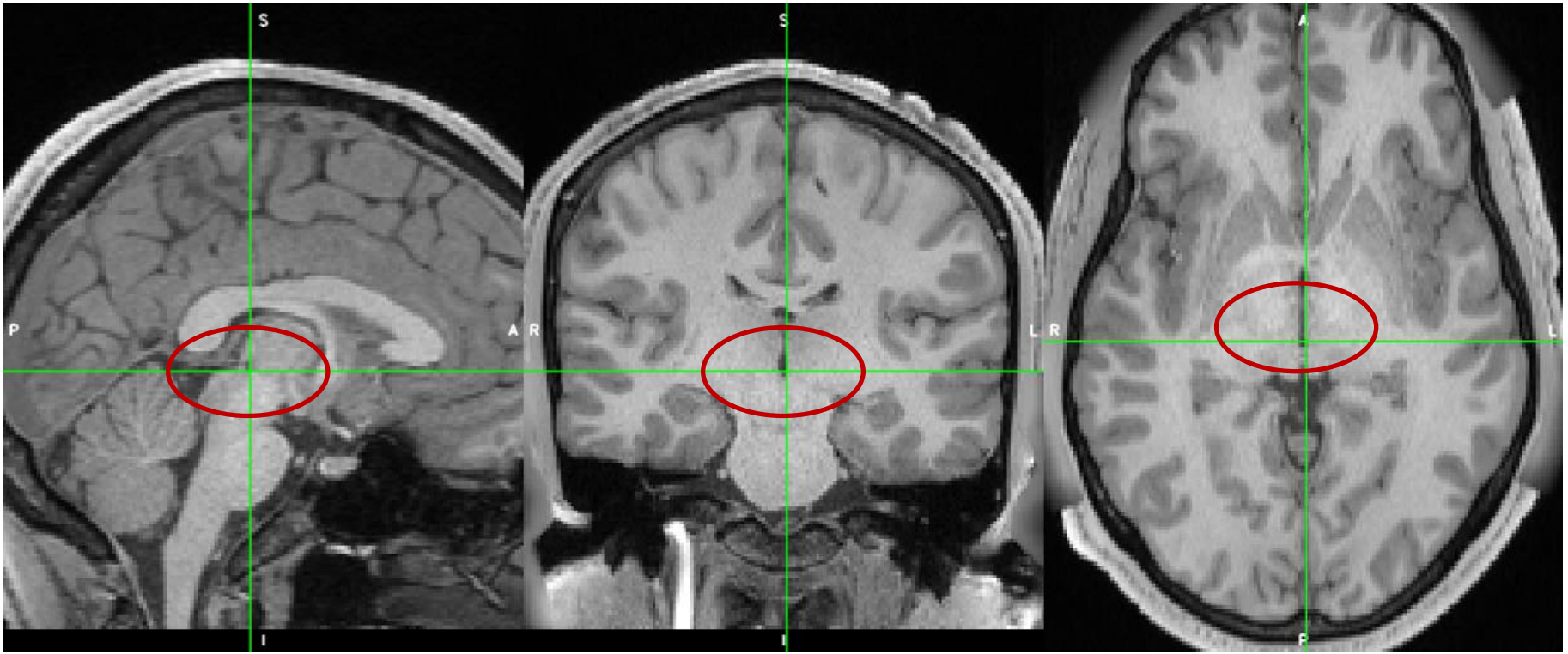
CLASSIC TARGETING

AC COORDINATES



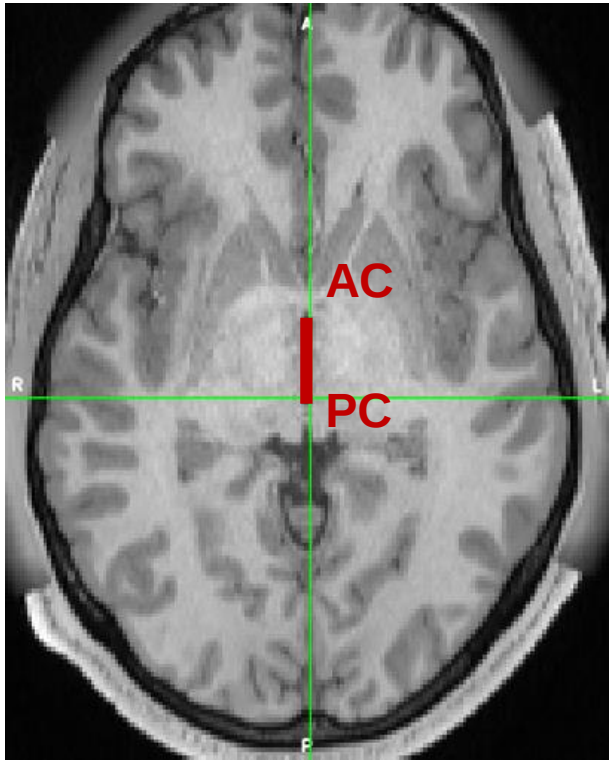
CLASSIC TARGETING

PC COORDINATES

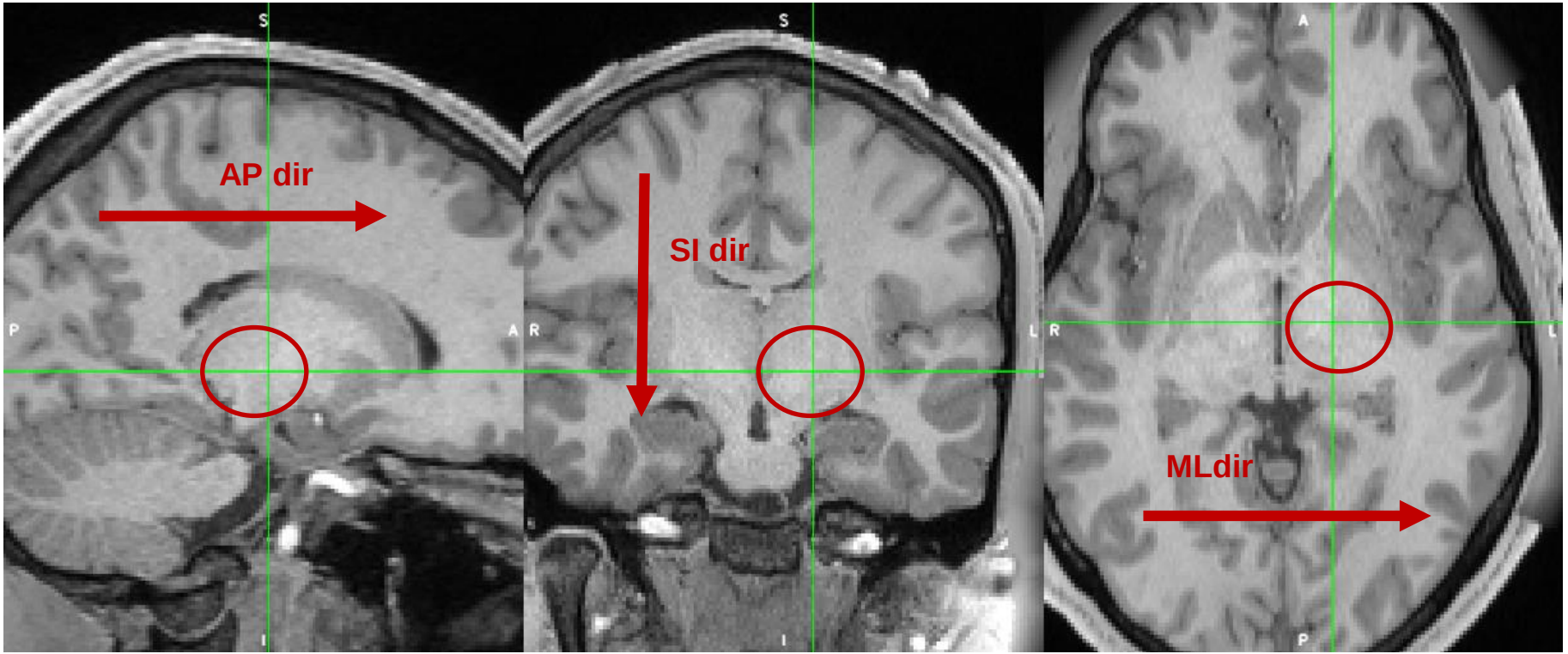


CLASSIC TARGETING

AC-PC LINE

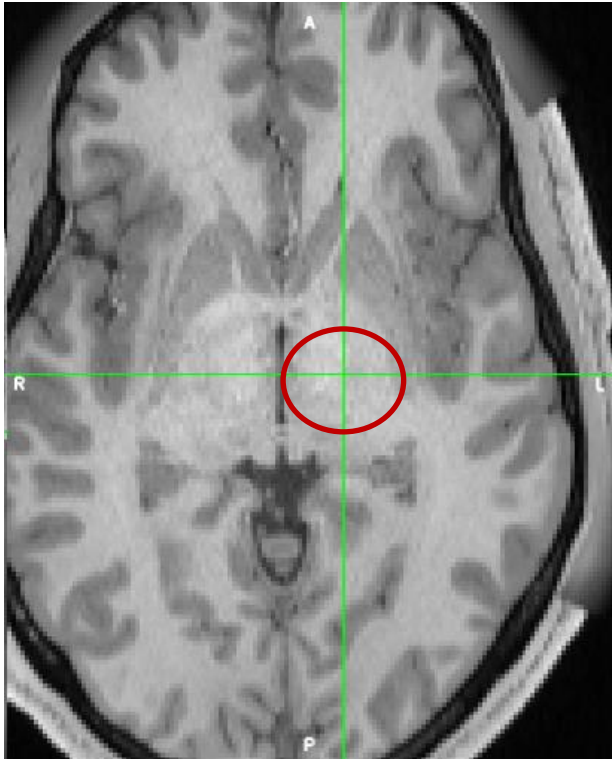


STEREOTAXIC COORDINATES



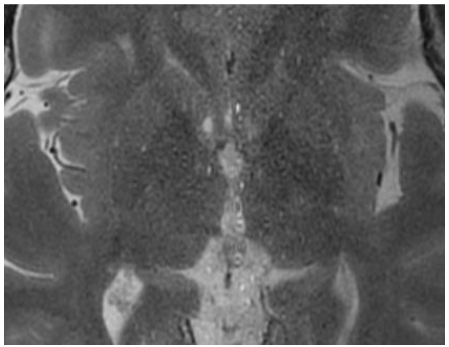
THALAMIC PARCELLATION

STEREOTAXIC COORDINATES

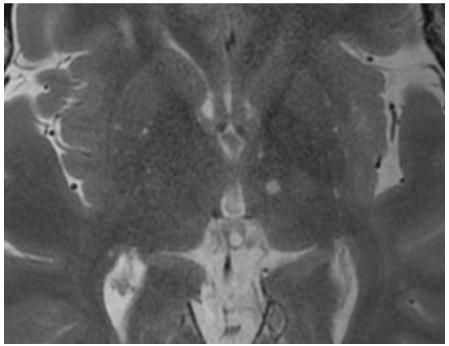


tcMRgFUS - “live” MR imaging

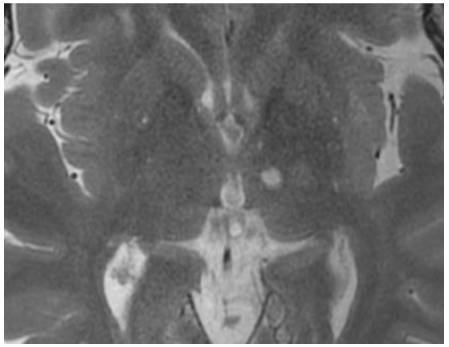
The optimization of the treatment target is carried out based on the patient's feedback during the procedure itself



First MRI Scan



13th sonication



16th sonication

Many low power sonications

Optimization of the treatment target on patient's feedback

NO PERMANENT LESION

Few sonications at high power

PERMANENT LESION

tcMRgFUS at 1.5T

As conventional magnetic resonance imaging (**MRI**) **lacks of intrinsic contrast** to identify **VIM**, interest towards **advanced MRI techniques** for personalized targeting is currently growing

The aim of this study is to identify the **VIM** with a more accurate method

(Boutet et al., 2019; Fenoy and Schiess, 2018; Shah et al., 2020; Cacciola et al., 2019b; da Silva 63 et al., 2017; Middlebrooks et al., 2018b; Plantinga et al., 2018; Pouratian et al., 2011)

Dataset from the Human Connectome Project

The **Human Connectome Project** aims to provide an unparalleled compilation of **neural data**, an interface to **graphically navigate** this data and the opportunity to achieve never before realized conclusions about the **living human brain**

Diffusion and **anatomical** neuroimaging data from the Human Connectome Project are **openly available** to the **scientific community for examination and exploration**. These include brain image and results volumes obtained from the advanced **Siemens 3T Connectom imaging system**.

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- SEGMENTATION OF THE CEREBRAL CORTEX
- PROBABILISTIC TRACTOGRAPHY
- THALAMIC PARCELLATION
- STUDY OF VARIABILITY OF THE VENTRAL INTERMEDIATE NUCLEUS

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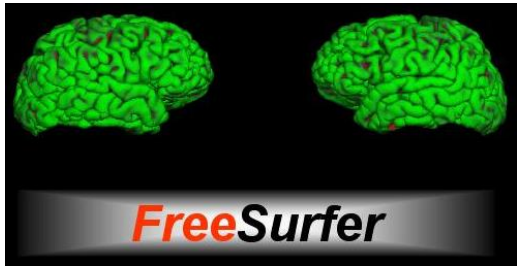
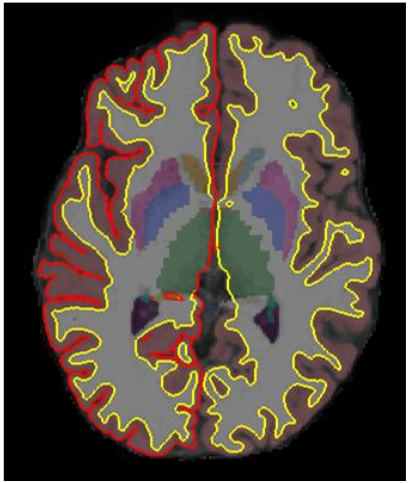
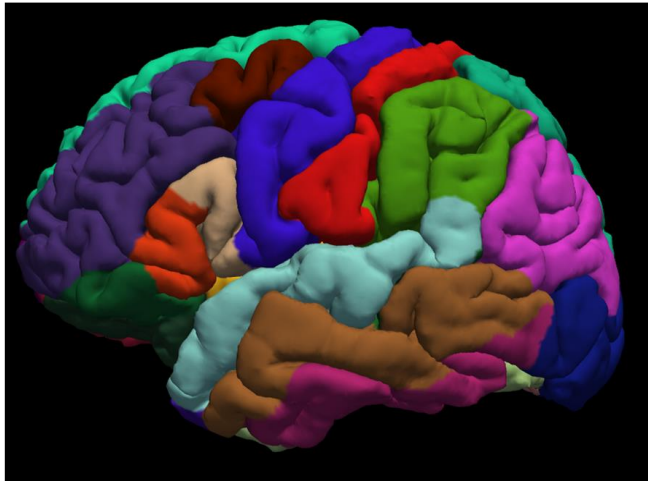
SEGMENTATION

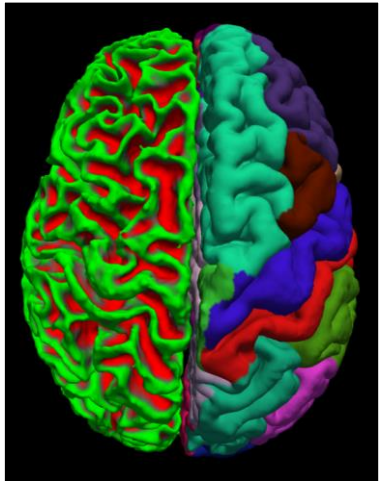
The **T_1w FSPGR 3D** datasets ($1x1x1mm^3$) were used

The **FreeSurfer 6.0** workflow was used to segment both the cortical and deep gray matter

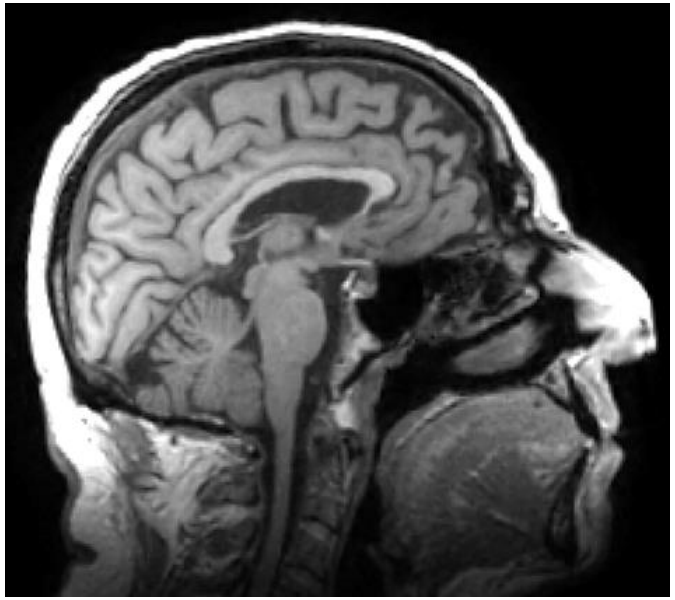








CORTICAL SEGMENTATION



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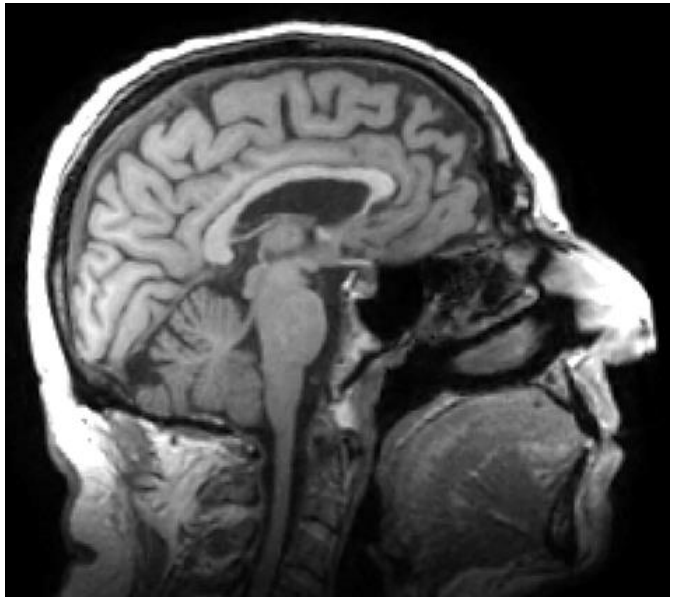
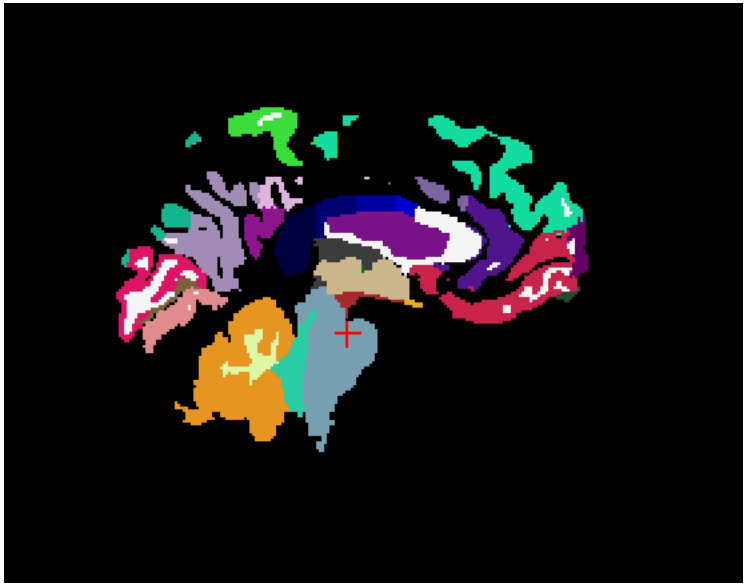
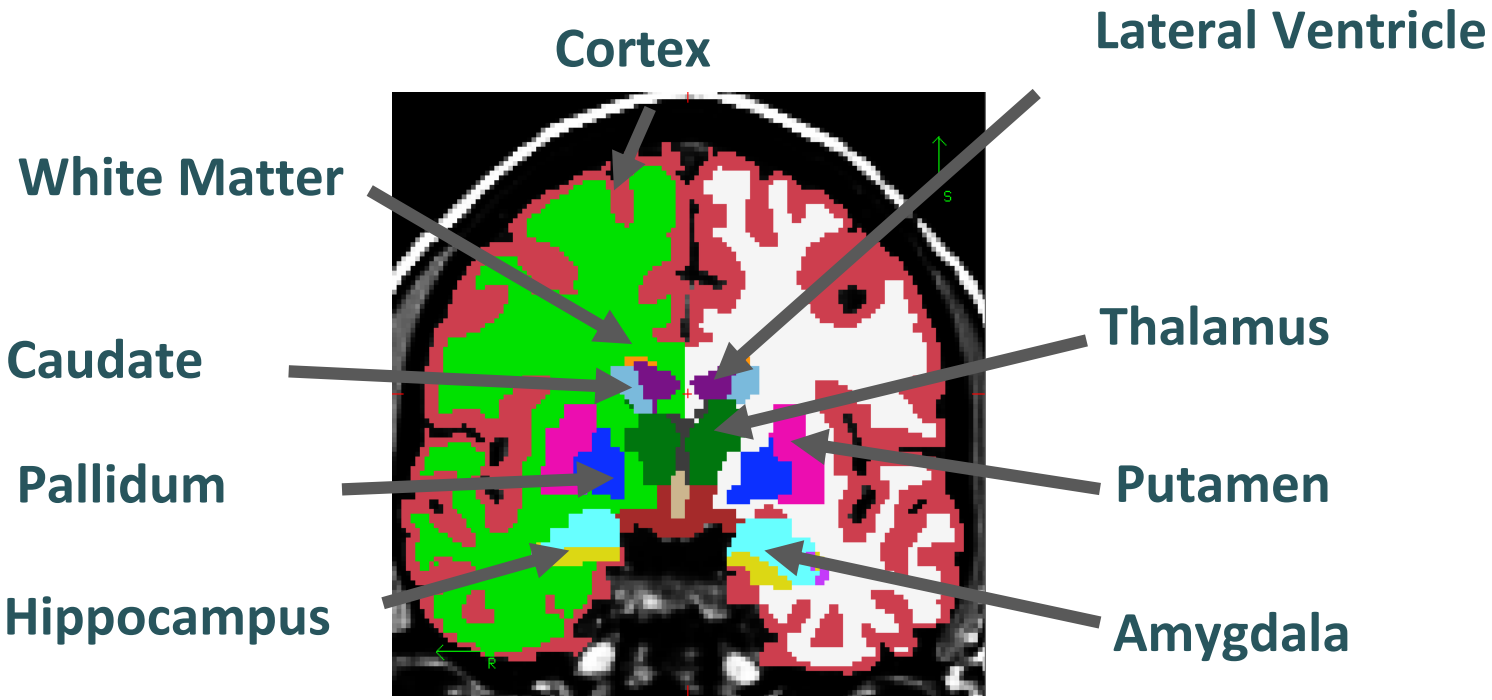




SUBCORTICAL SEGMENTATION



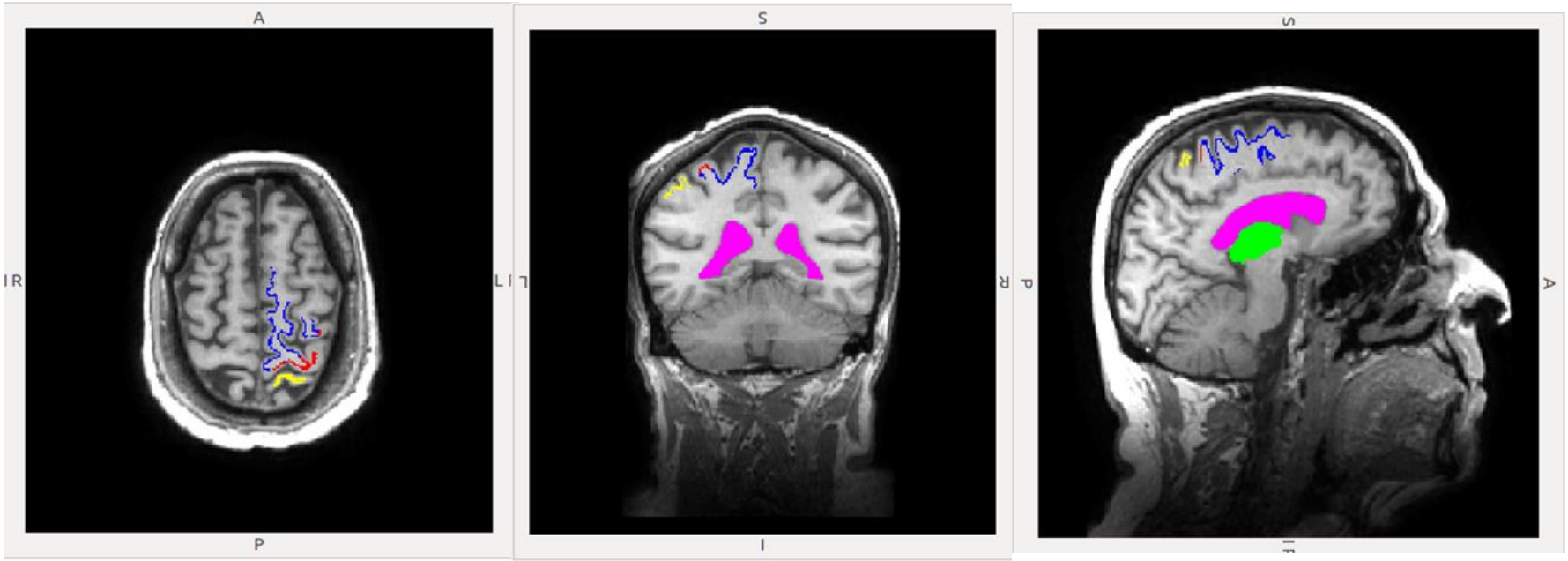
SEGMENTATION

Creation of masks using Python scripts of:

- thalamus
- ventricles
- precentral gyrus
- postcentral gyrus
- Brodman area 6
- Cerebellar cortex

Nibabel - Neuroimaging in Python

SEGMENTATION



VENTRICLES RIGHT THALAMUS BRODMAN AREA 6

PRECENTRAL GYRUS POSTCENTRAL GYRUS

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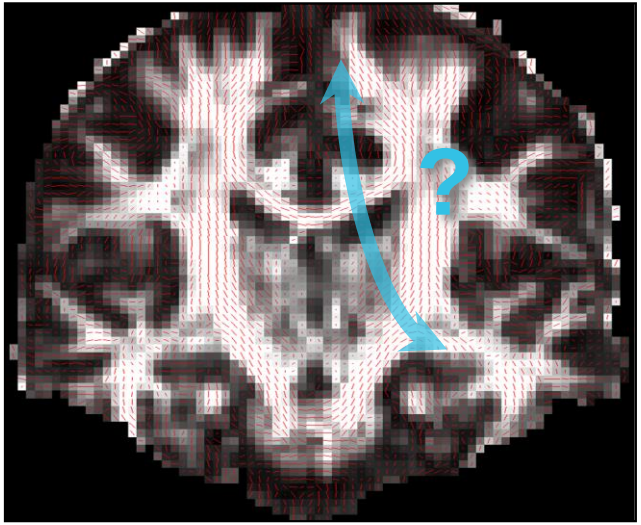
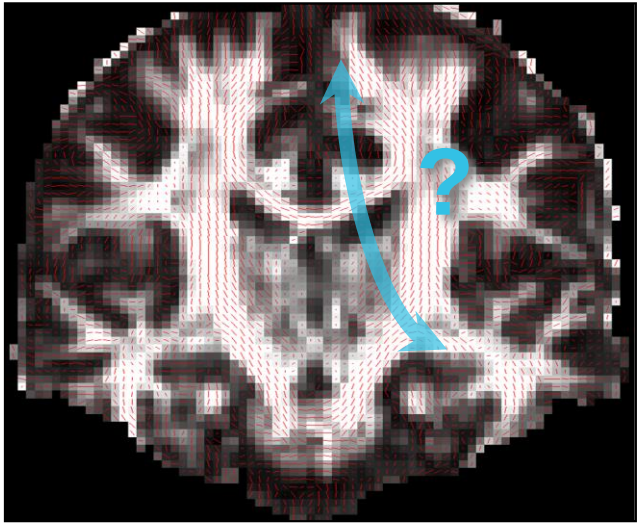
TRACTOGRAPHY

- Use at each voxel **local diffusion orientation** to determine **pathway** between distant brain regions



TRACTOGRAPHY

- Use at each voxel **local diffusion orientation** to determine **pathway** between distant brain regions
- Local orientation comes from diffusion model fit (**tensor, ball-and-stick**, etc.)



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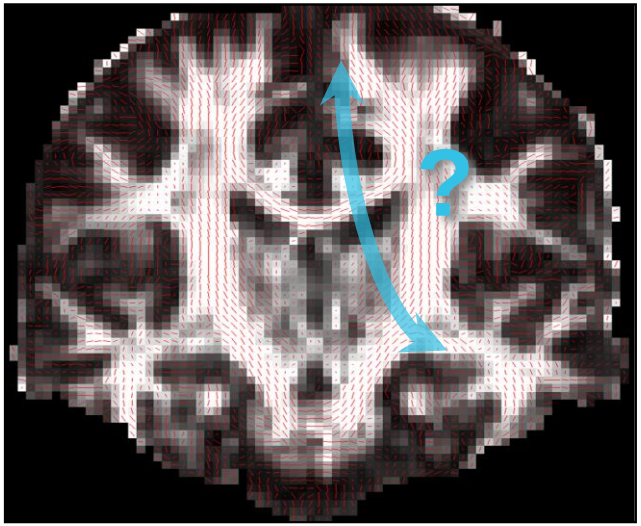


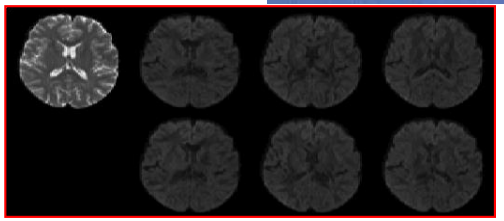
- Use at each voxel **local diffusion orientation** to determine **pathway** between distant brain regions
- Local orientation comes from diffusion model fit (**tensor, ball-and-stick**, etc.)
- **Deterministic** vs. **probabilistic tractography**:

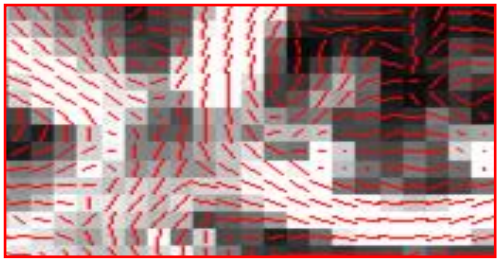
  -**Deterministic** assumes a single orientation at each voxel

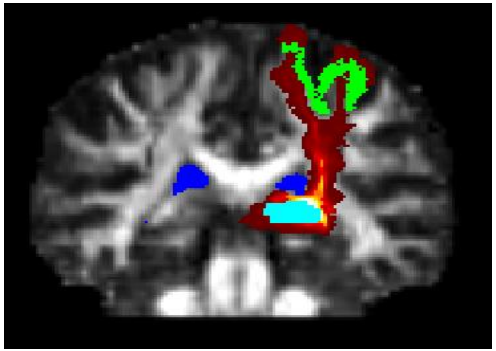
  -**Probabilistic** assumes a distribution of orientations

Data analysis steps

- **Pre-processing of images**
  FSL: eddy-correct, rotate-bvecs
- **Fitting adiffusion model at every voxel**
  FSL: Ball-and-stick (bedpostx)
- **Reconstructing pathways**
  FSL: Probabilistic tractography (probtracx)
  using ball-and-stick model

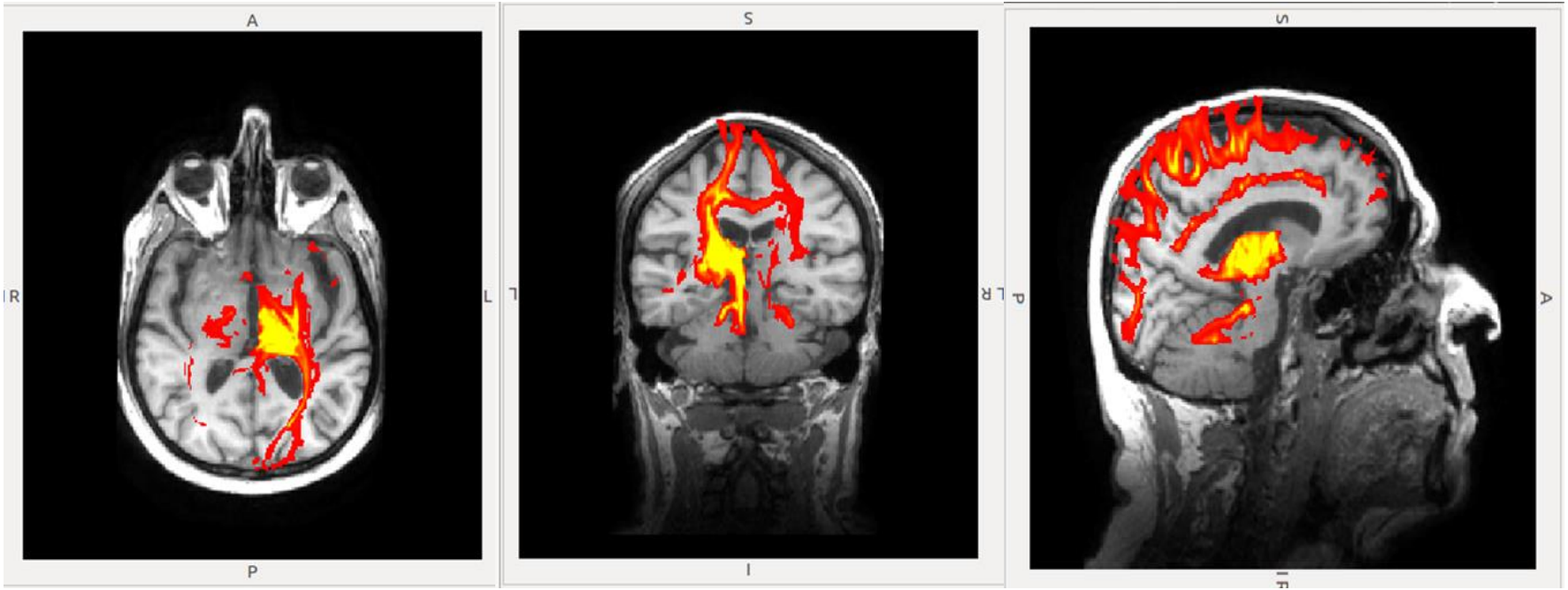






FSL: www.fmrib.ox.ac.uk/fsl

PROBABILISTIC TRACTOGRAPHY



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THALAMIC PARCELLATION

Constrained to connection of **two** specific end **regions**

Seeds:

➔Thalamus

Target:

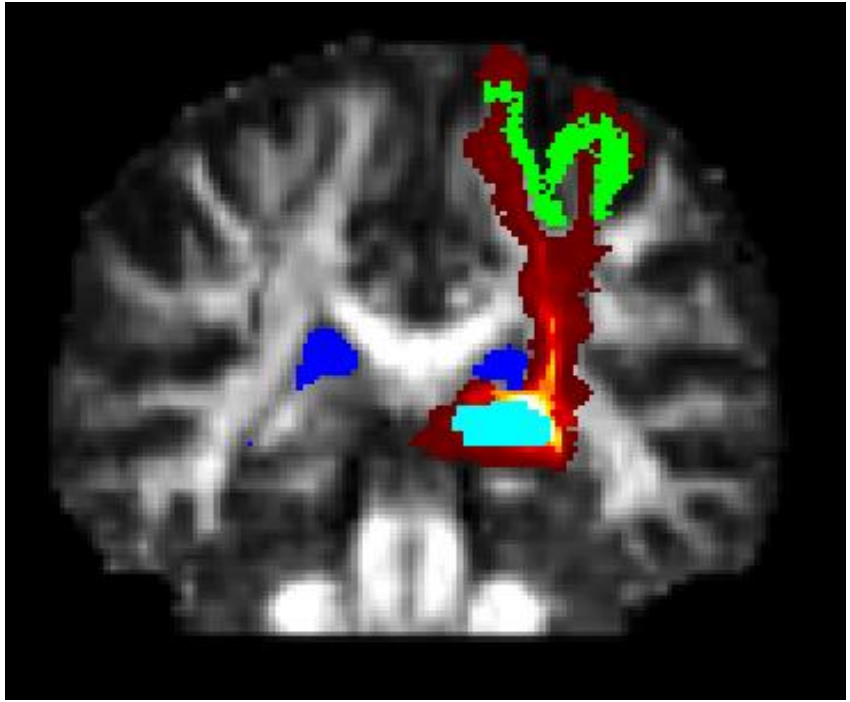
➔pre-central gyrus

➔post-central gyrus

➔Cerebellar cortex

Regions excluded:

➔Ventricles



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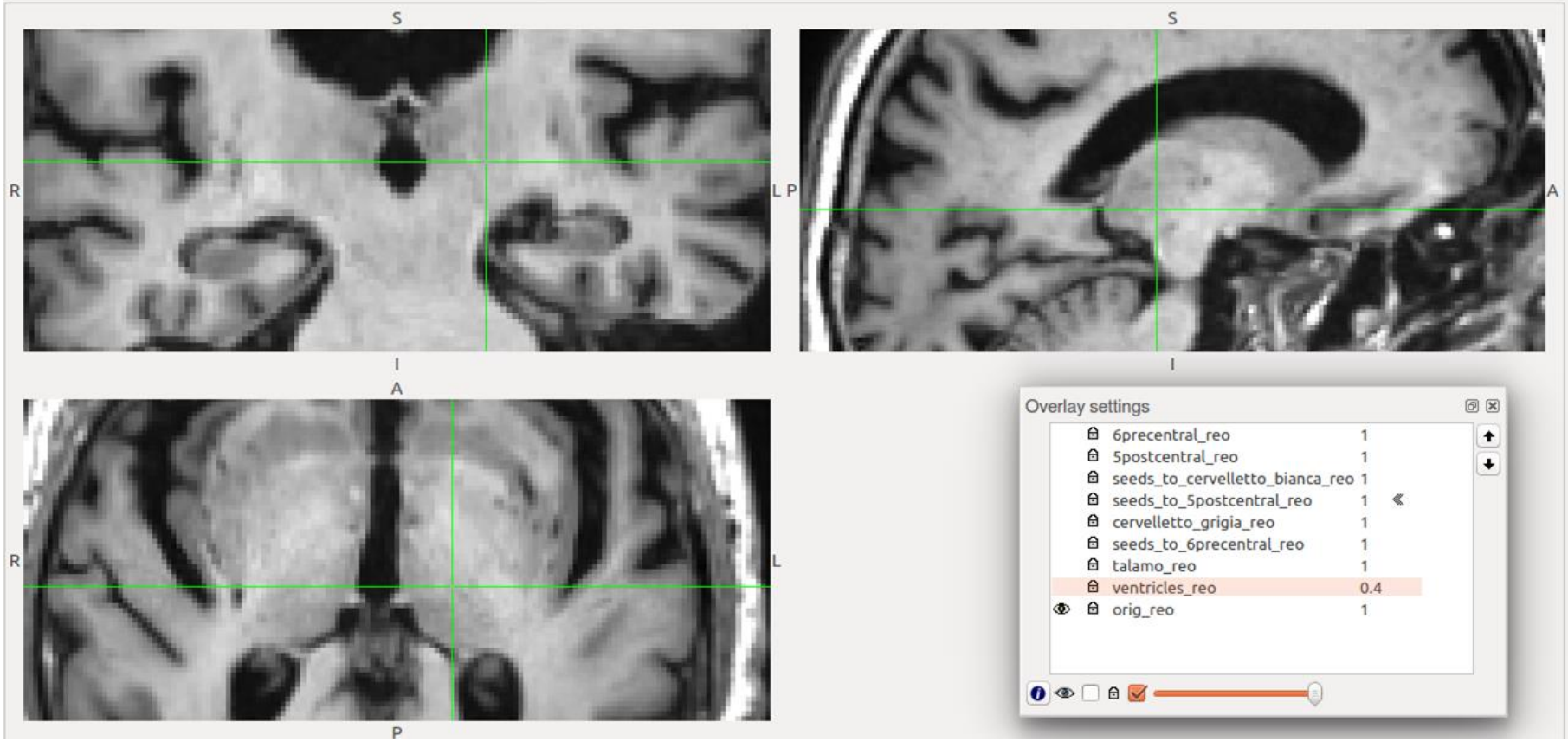

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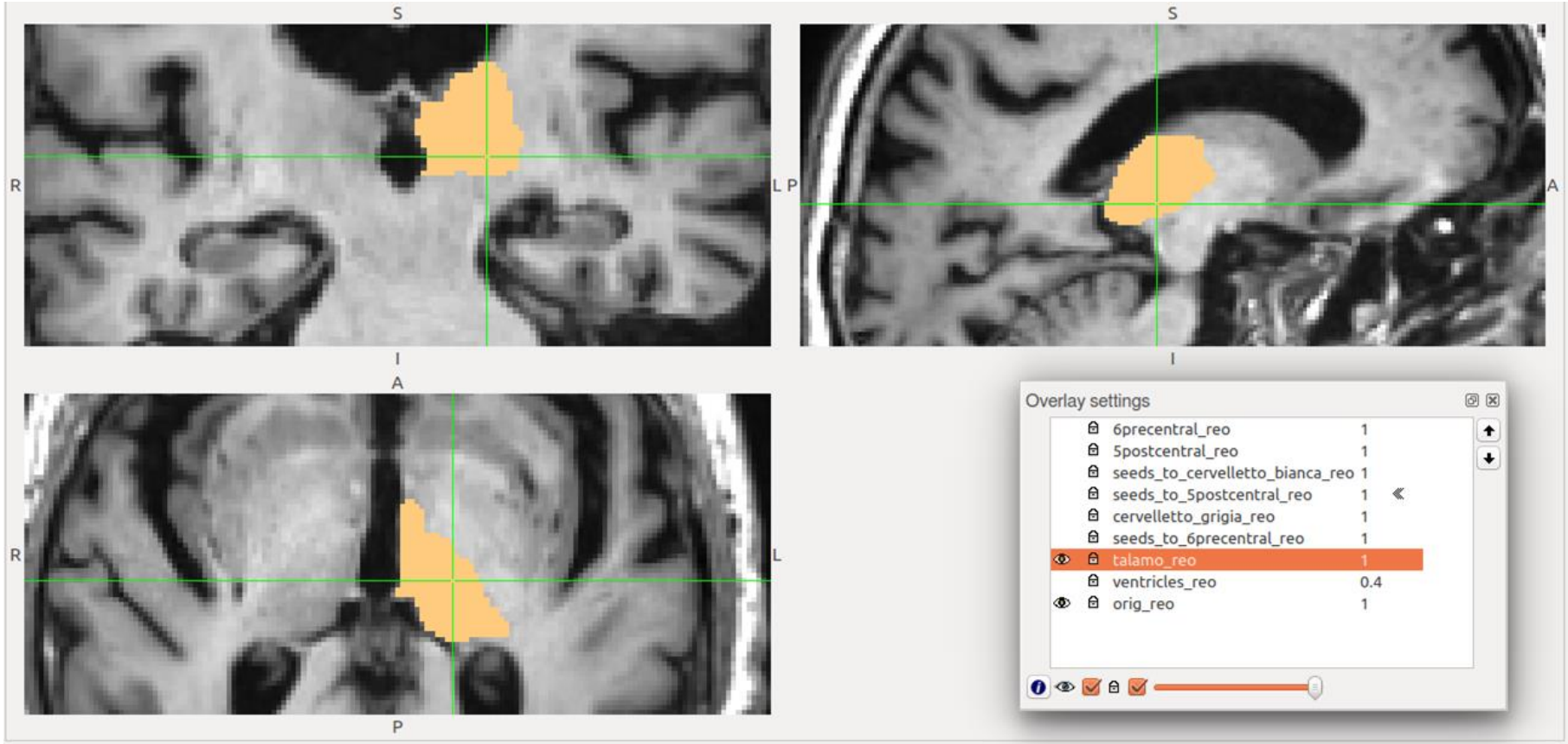

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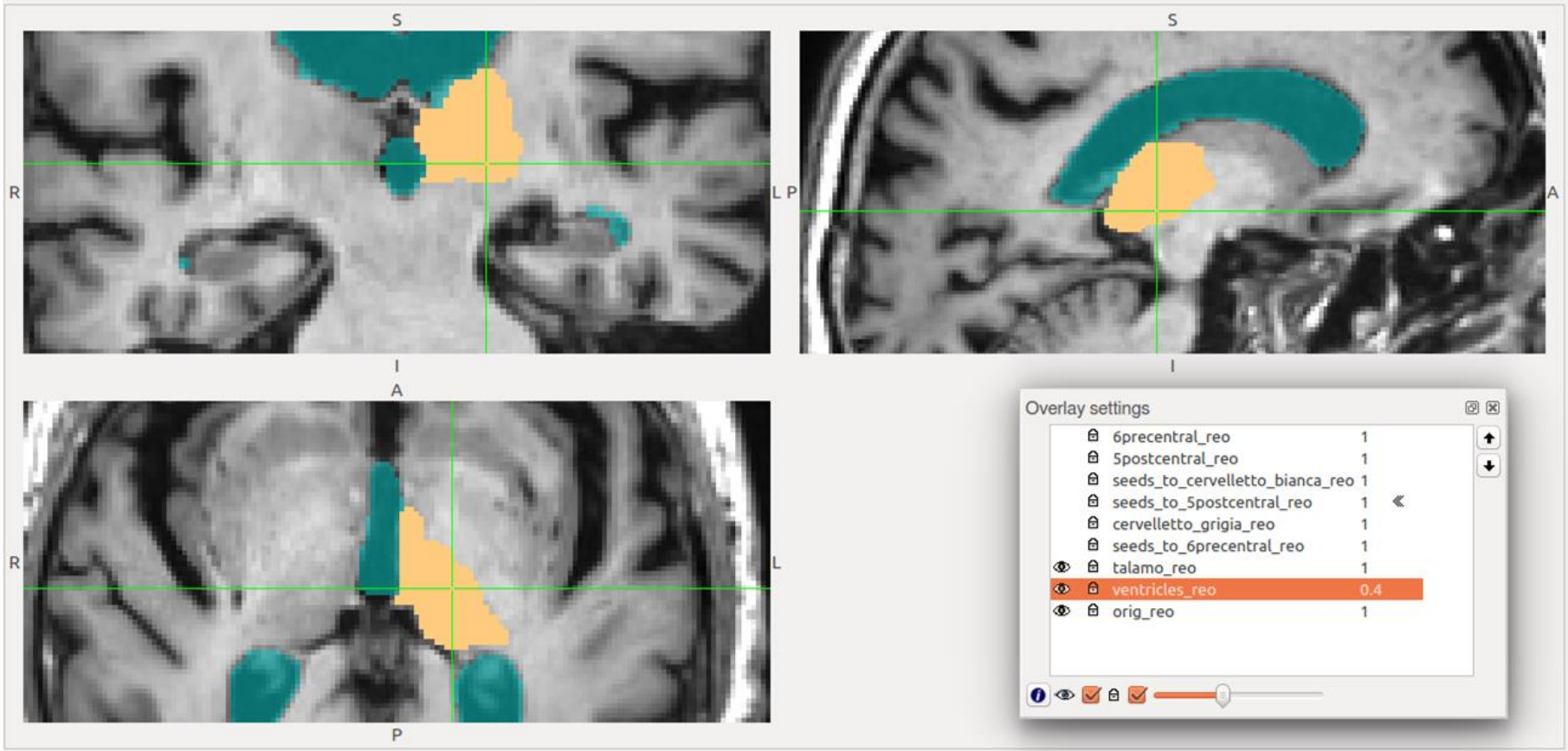

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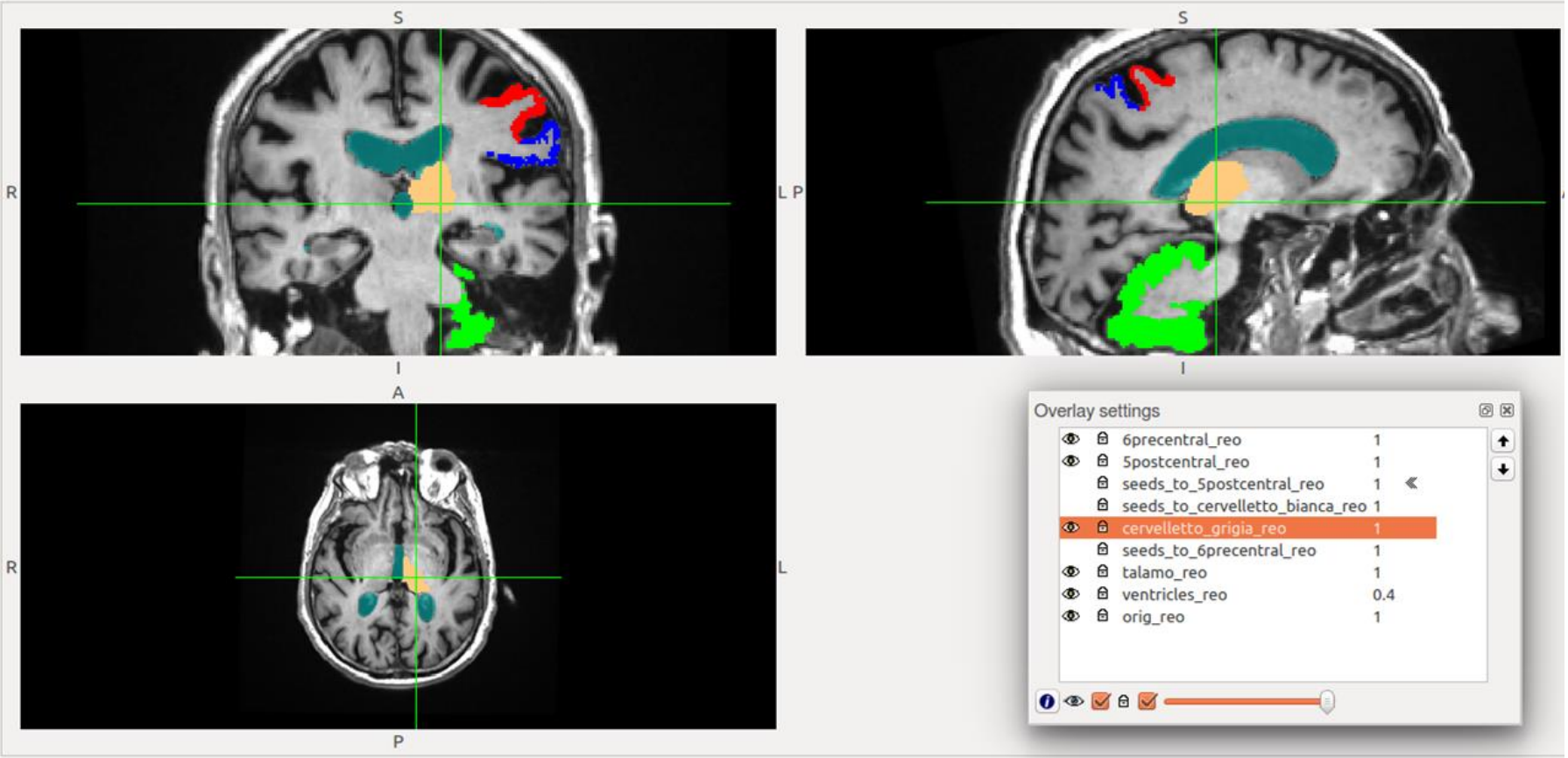

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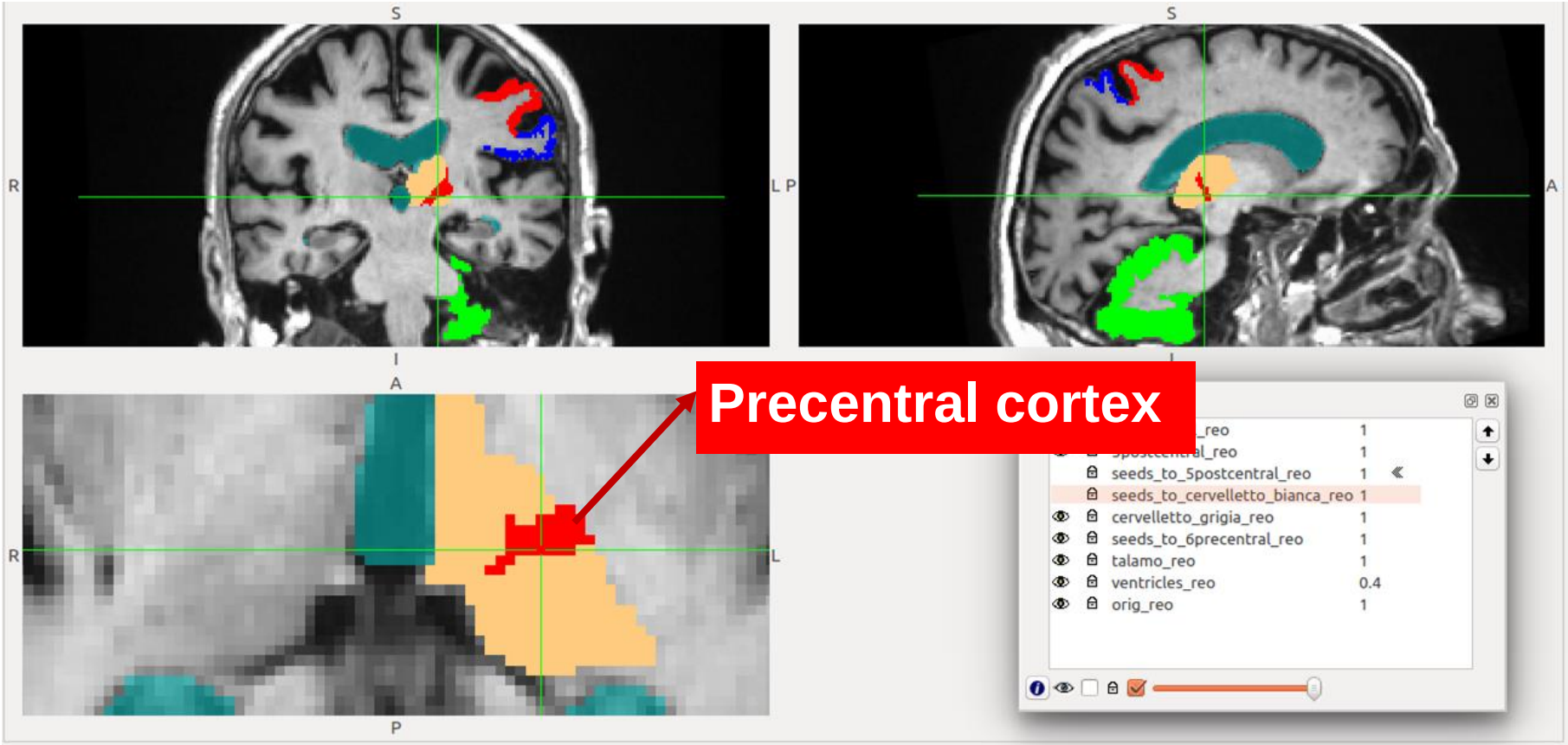

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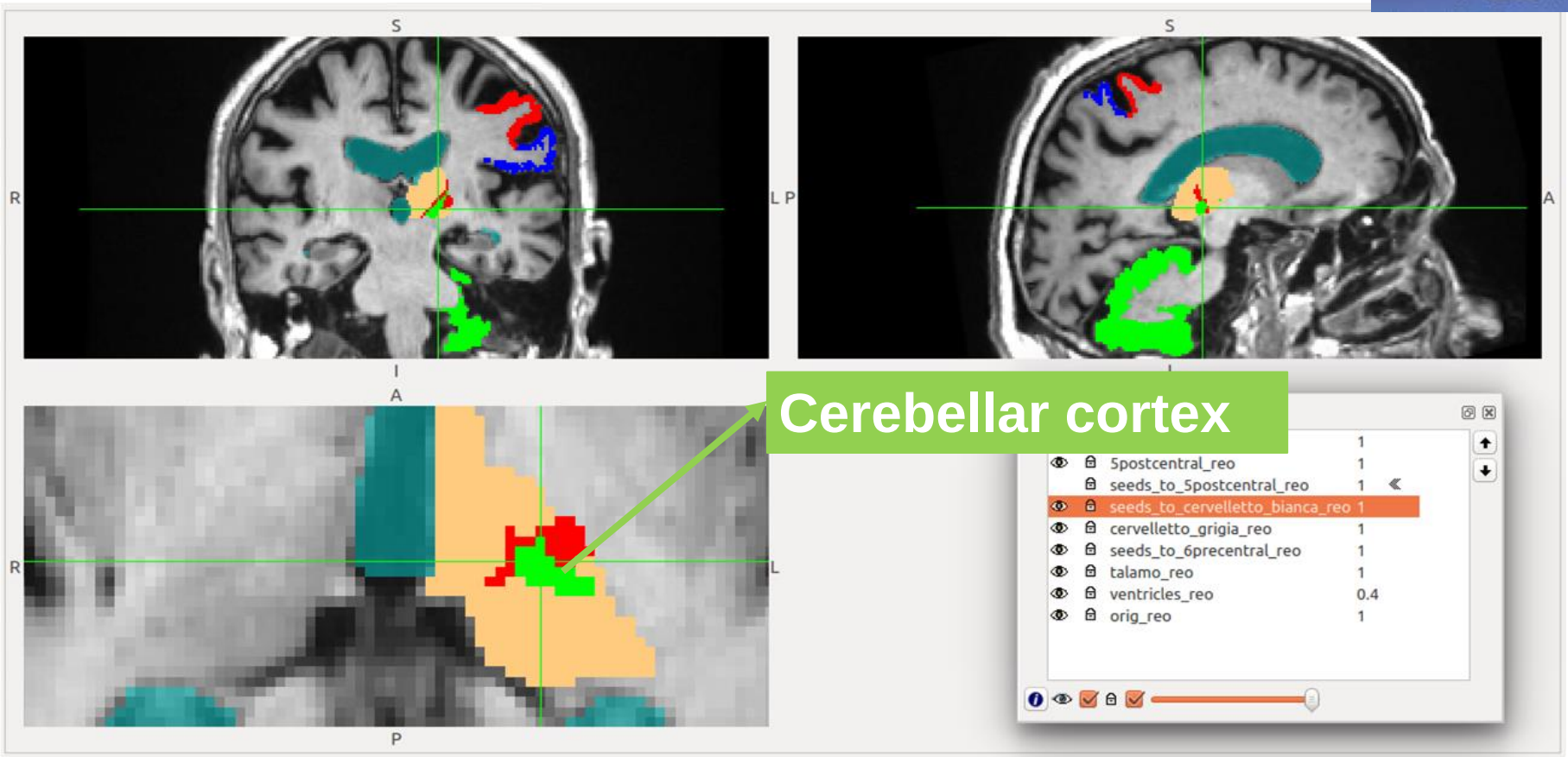
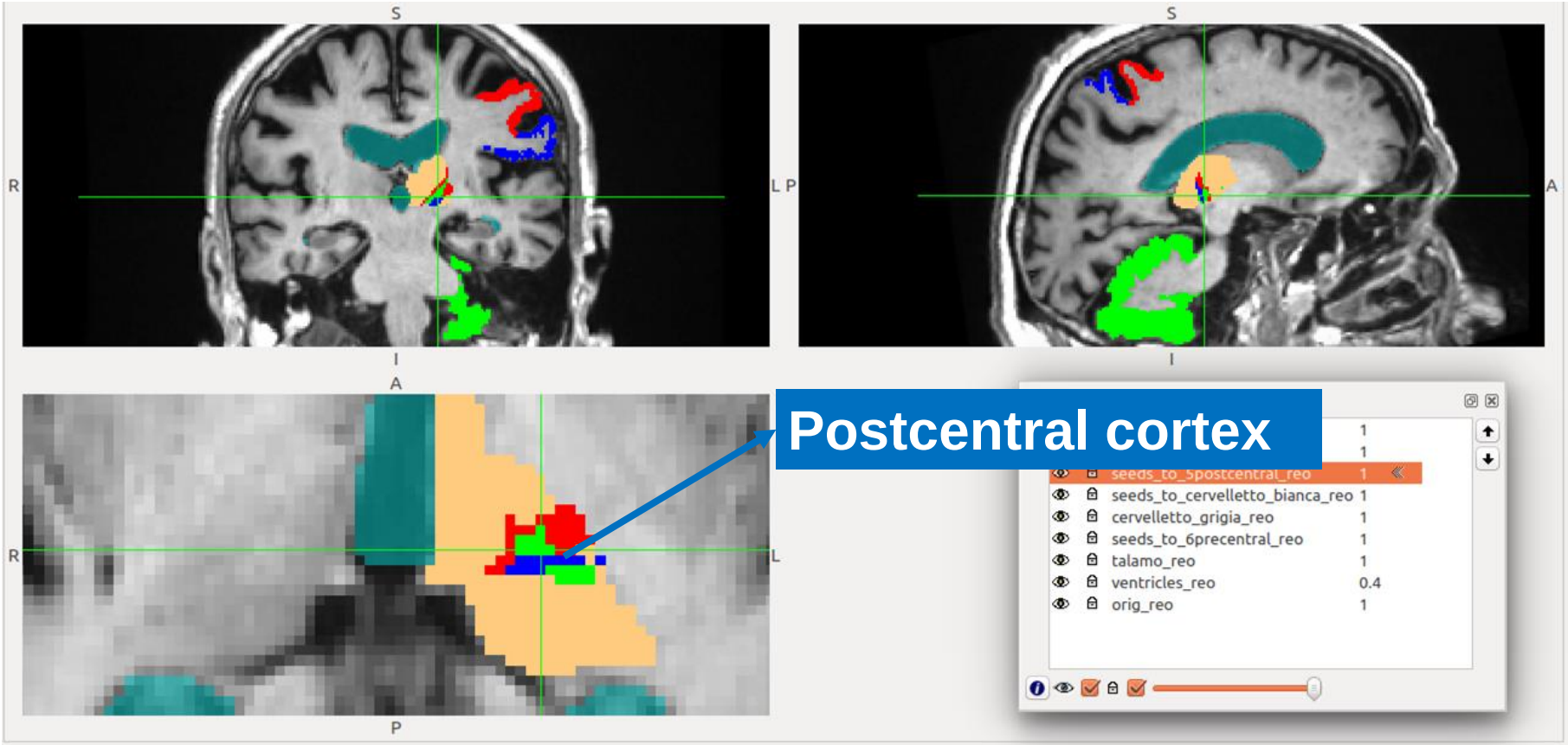
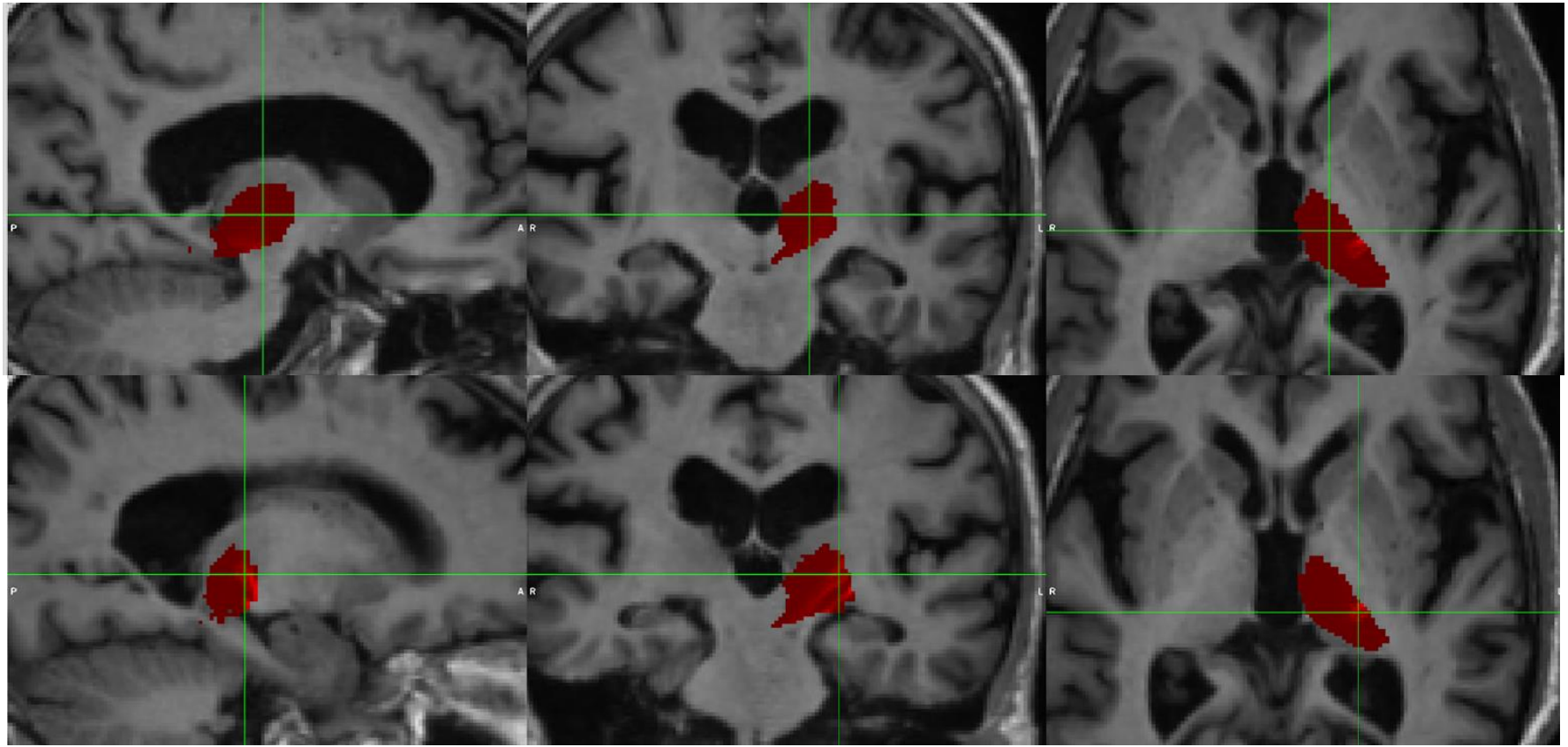


THALAMIC PARCELLATION



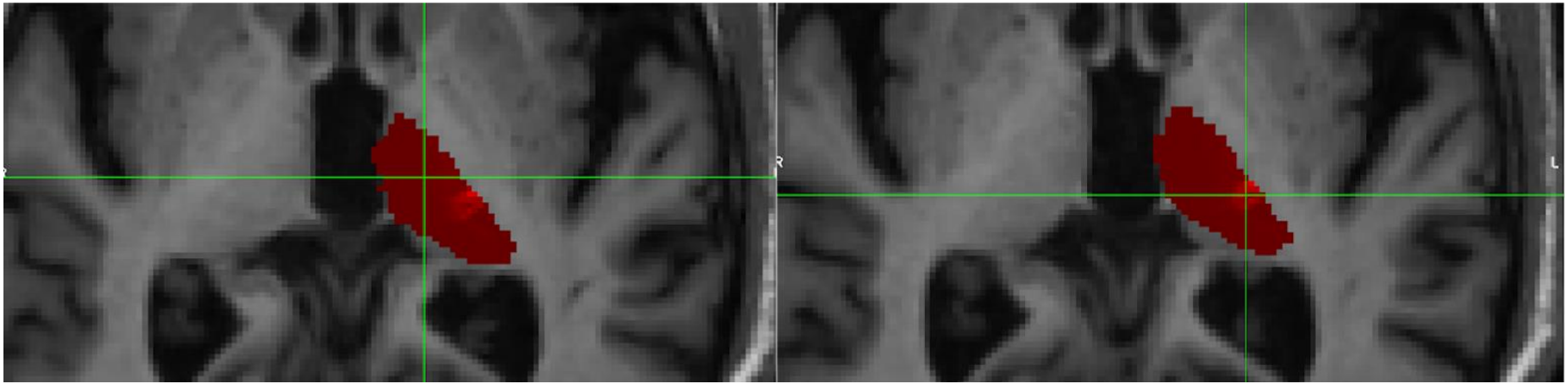
THALAMIC PARCELLATION vs CLASSIC TARGETING



THALAMIC PARCELLATION vs CLASSIC TARGETING

CLASSIC TARGETING

THALAMIC PARCELLATION



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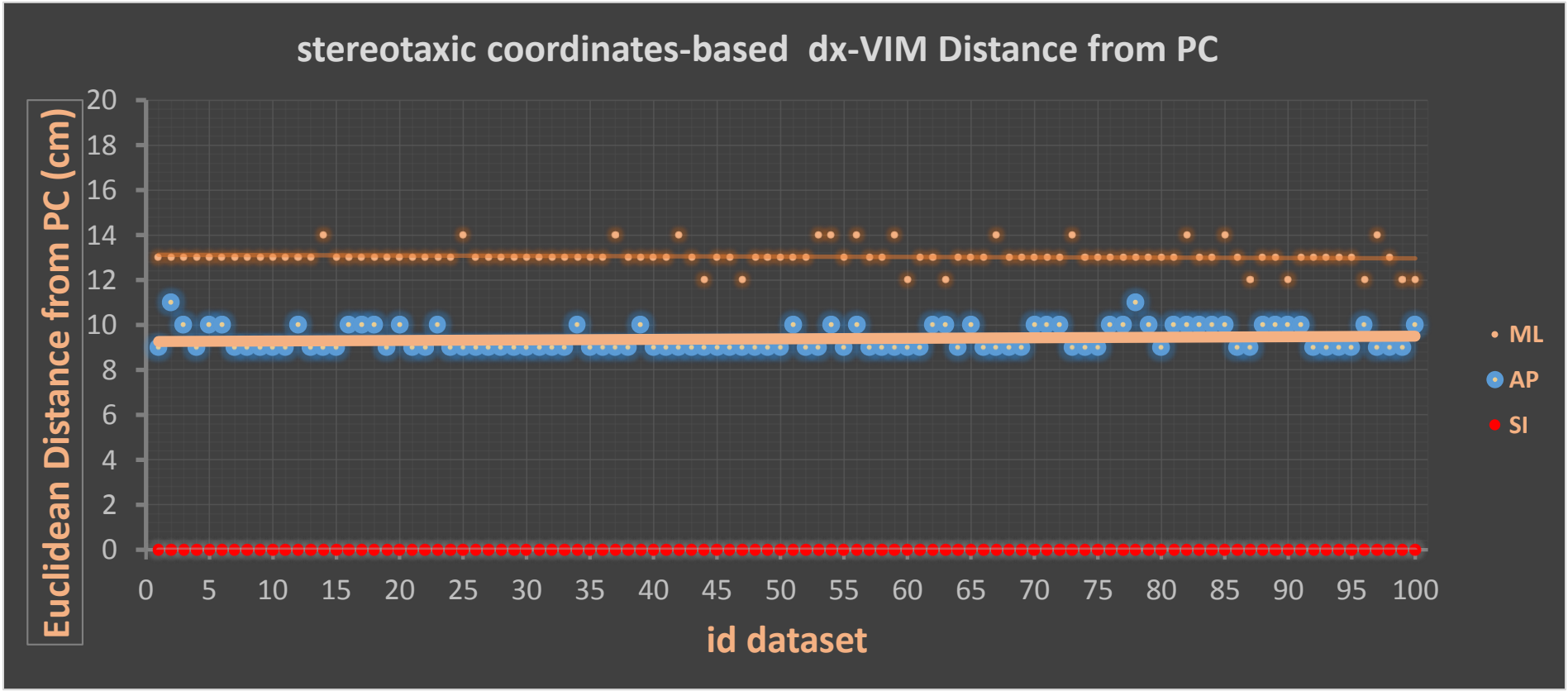
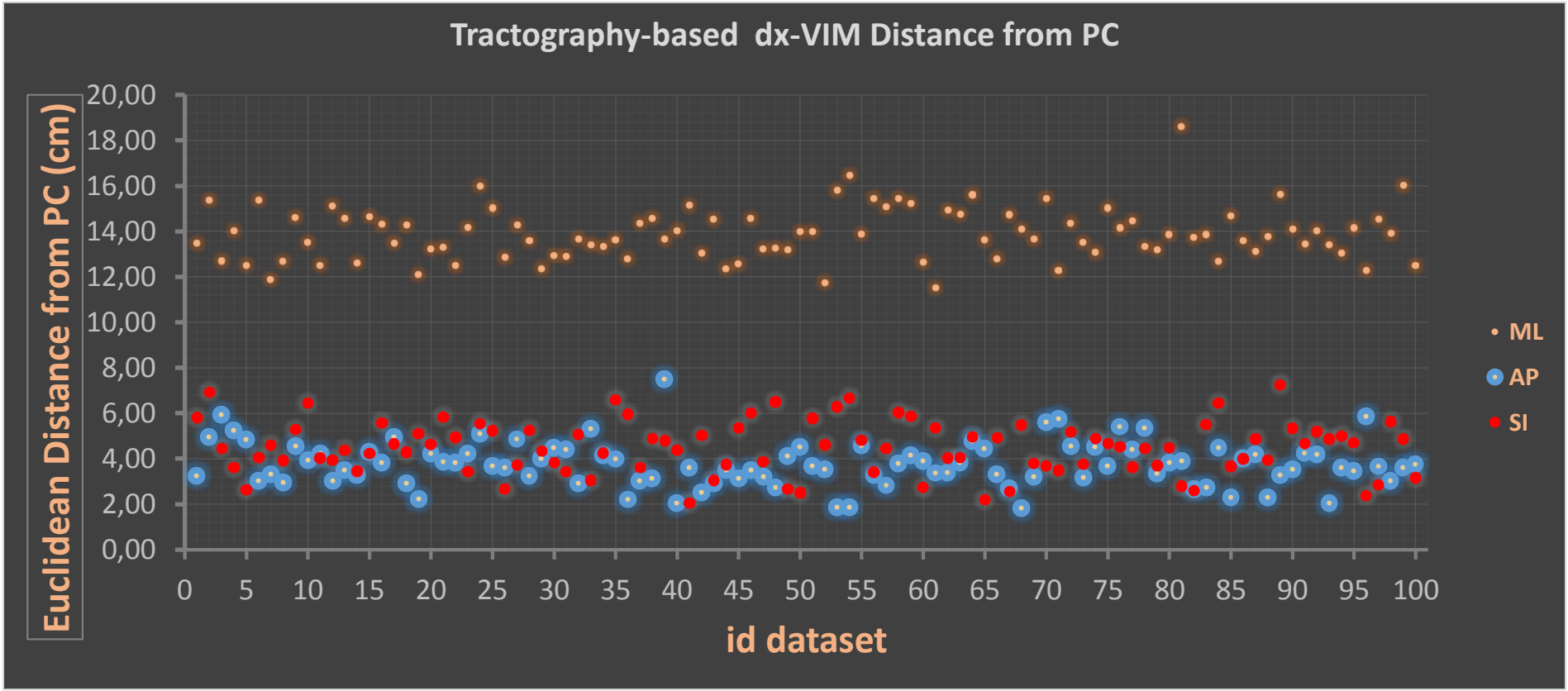
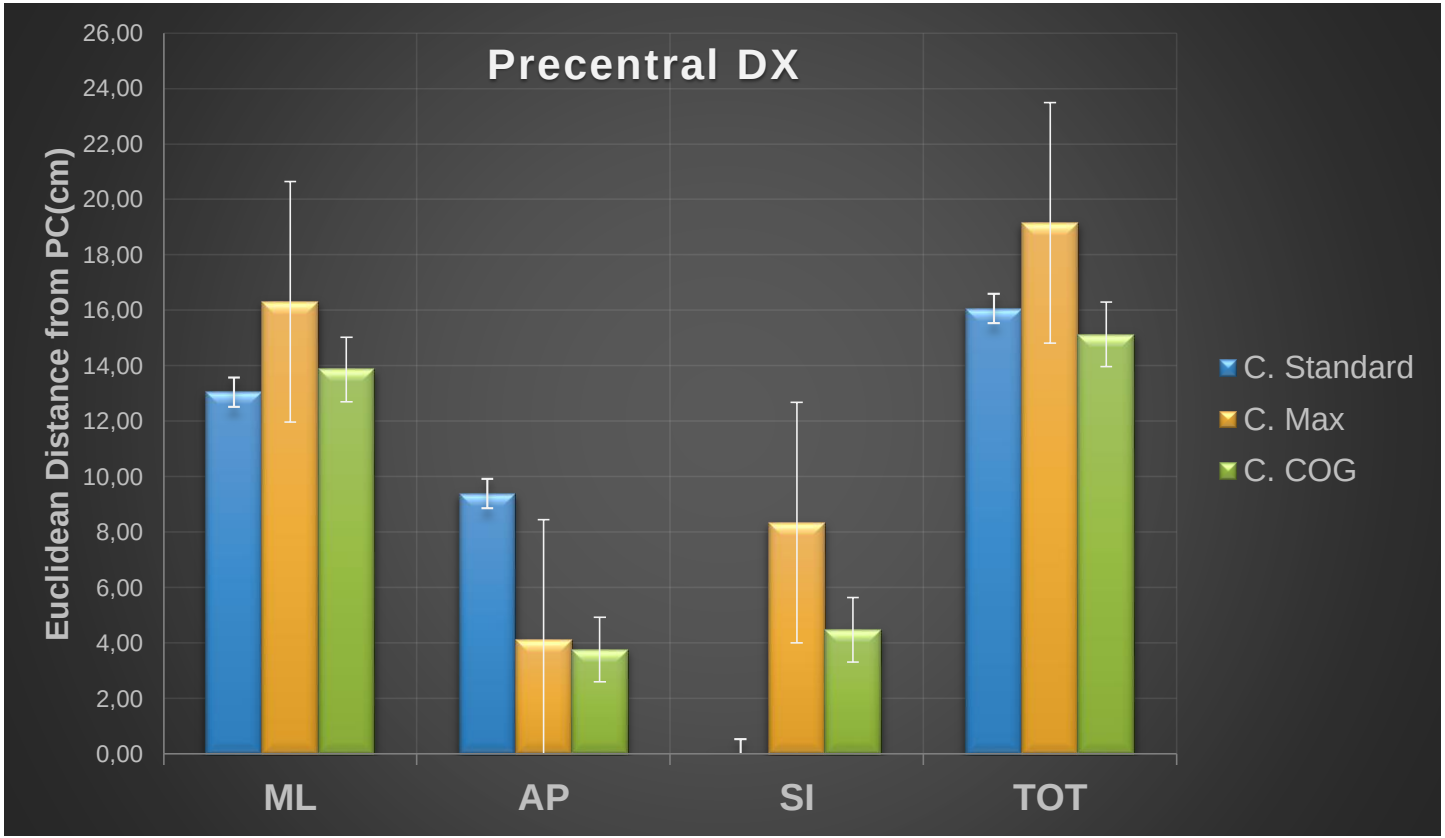
RESULTS


stereotaxic coordinates-based dx-VIM Distance from PC
Euclidean Distance from PC (cm)
0
2
4
6
8
10
12
14
16
18
20
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
id dataset
ML
AP
SI

RESULTS


Tractography-based dx-VIM Distance from PC
Euclidean Distance from PC (cm)
20,00
18,00
16,00
14,00
12,00
10,00
8,00
6,00
4,00
2,00
0,00
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
id dataset
ML
AP
SI

RESULTS


Precentral DX
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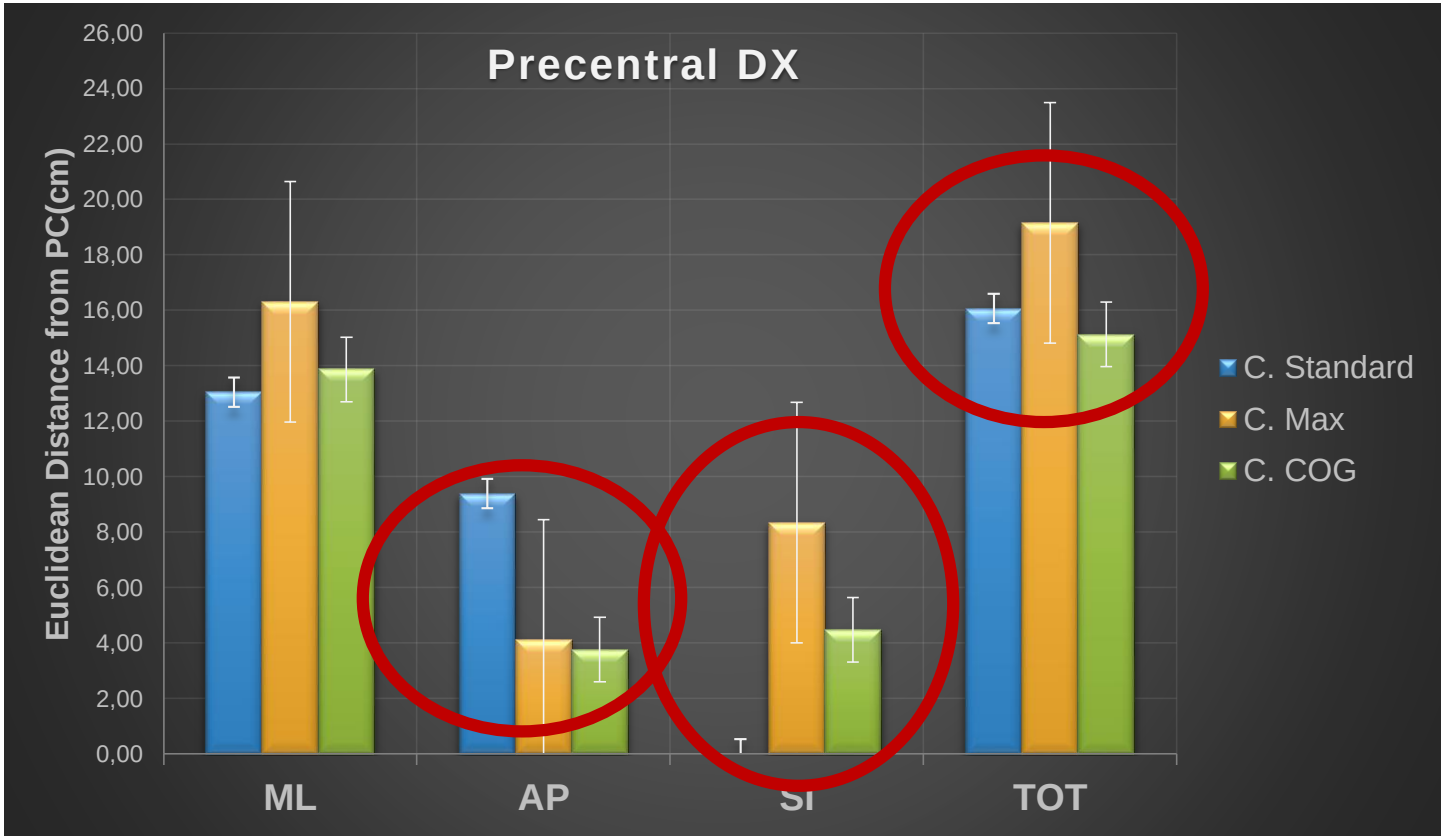
RESULTS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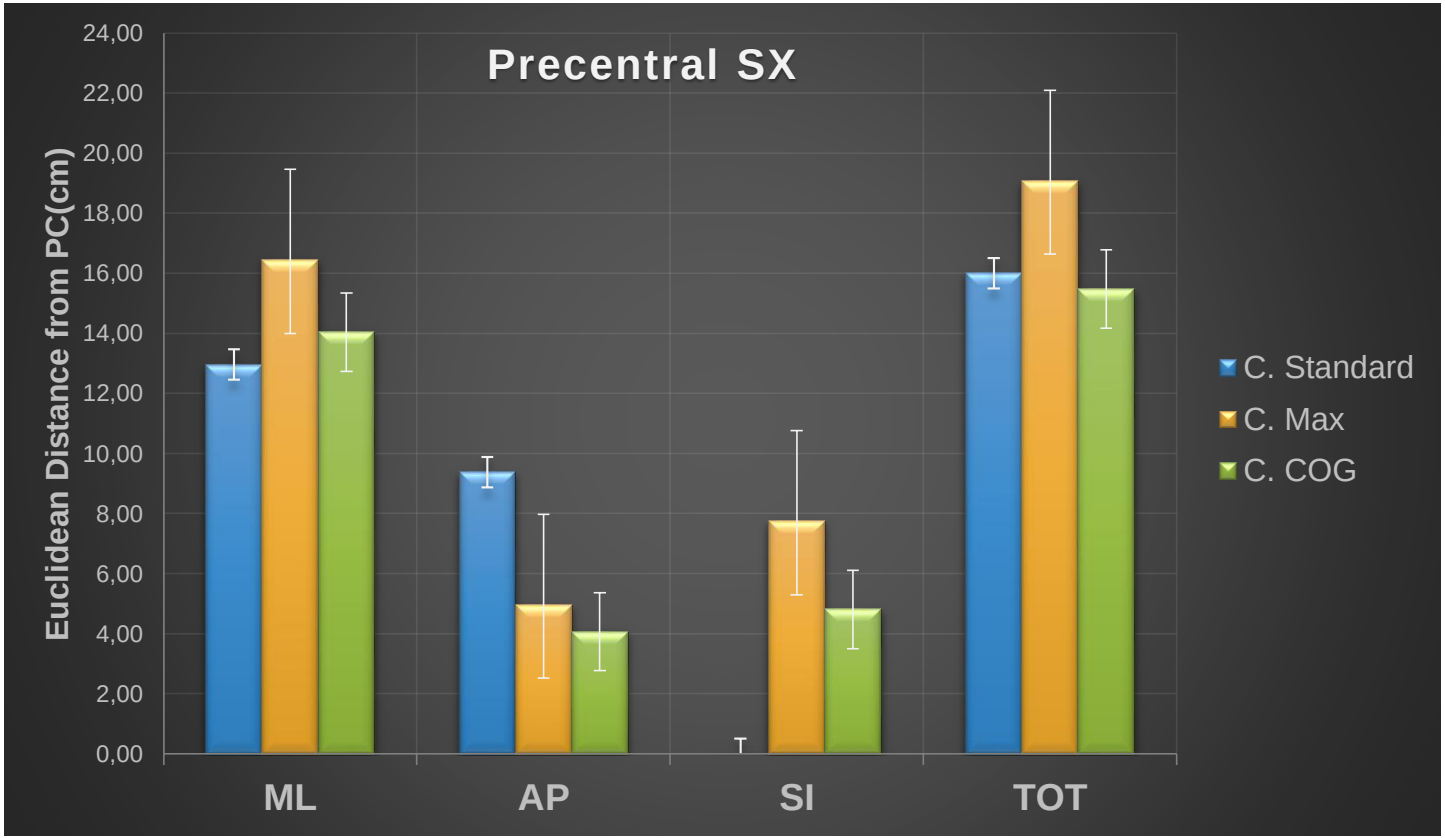
RESULTS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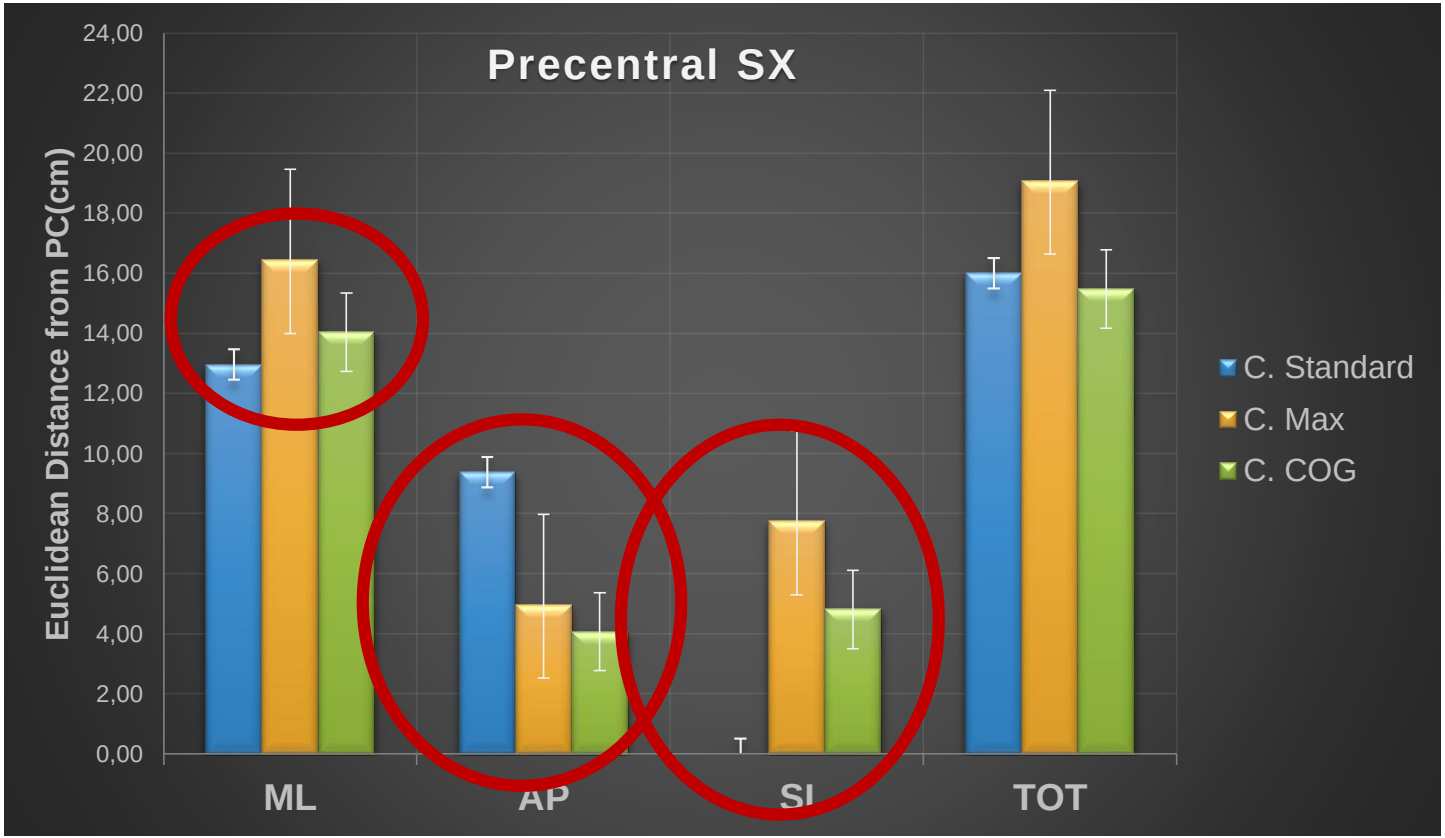
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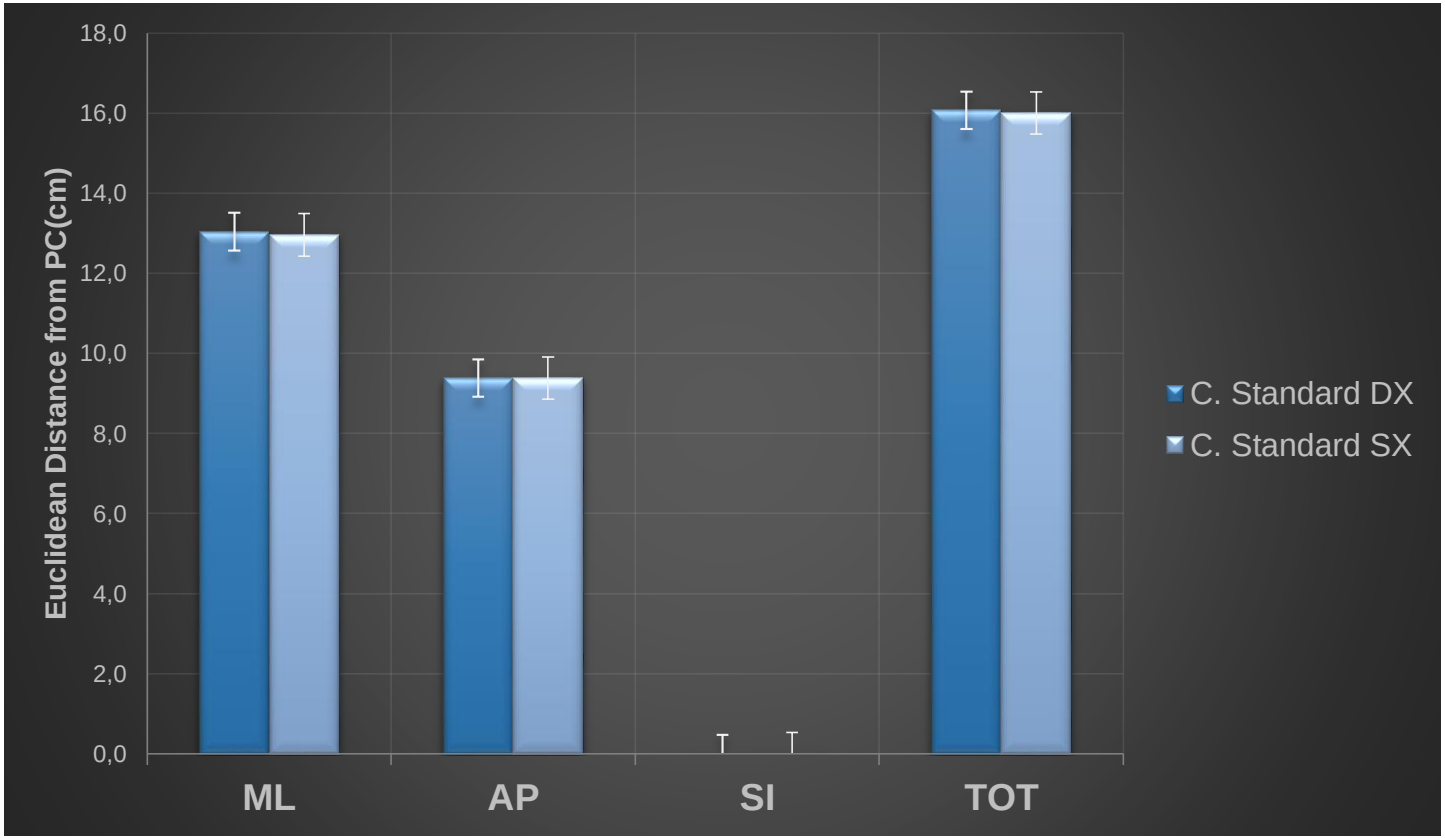
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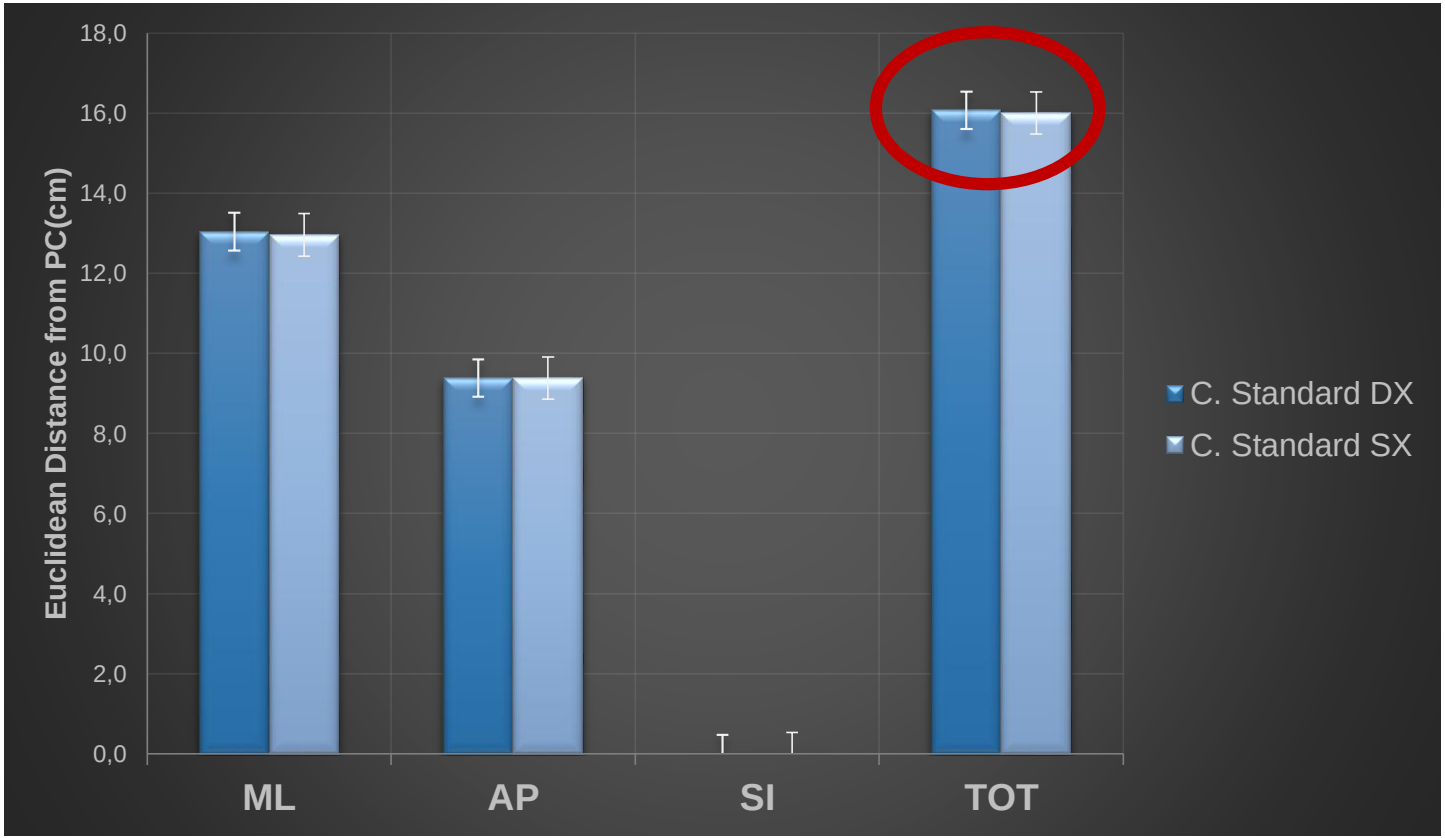
RESULTS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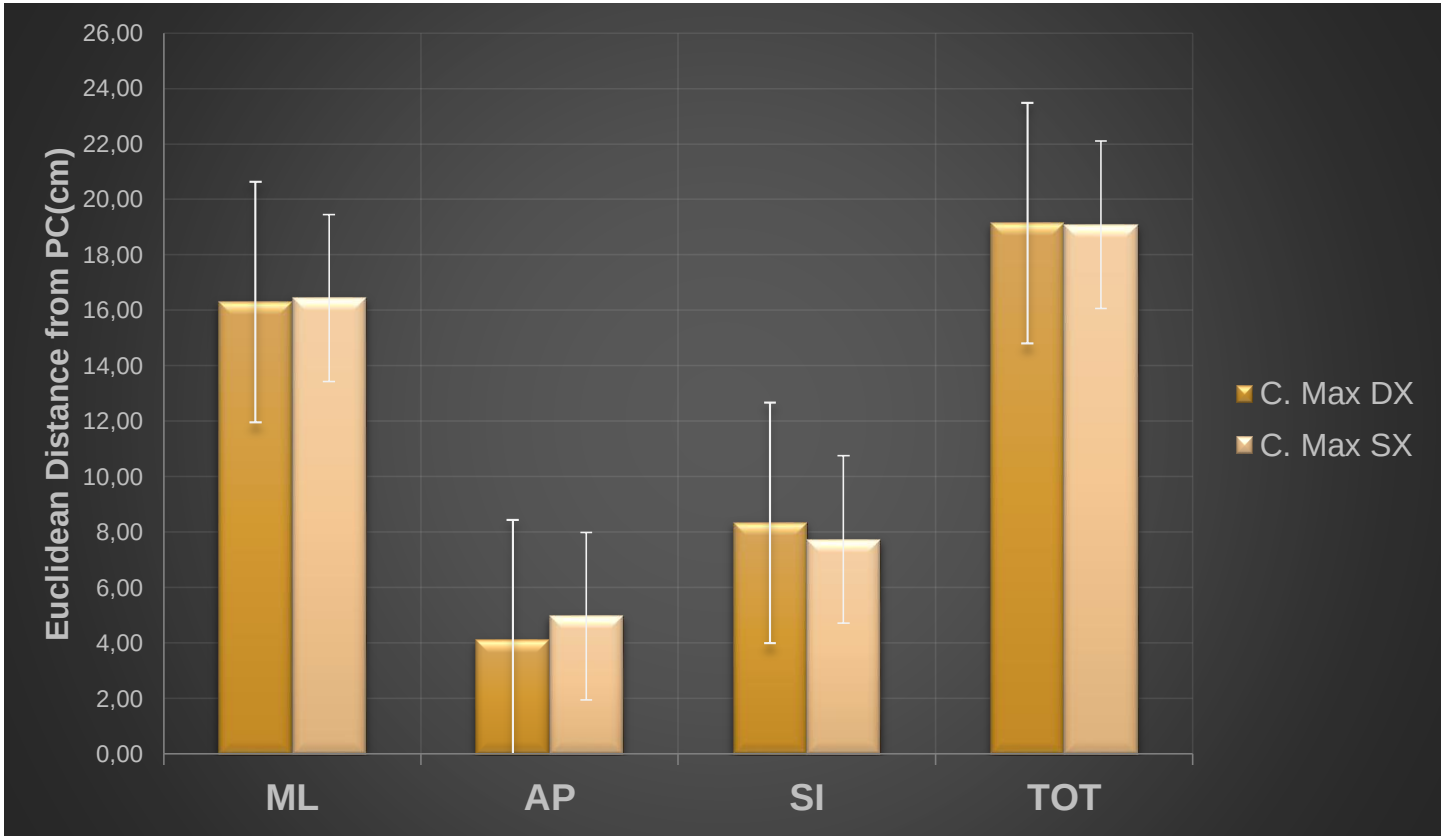
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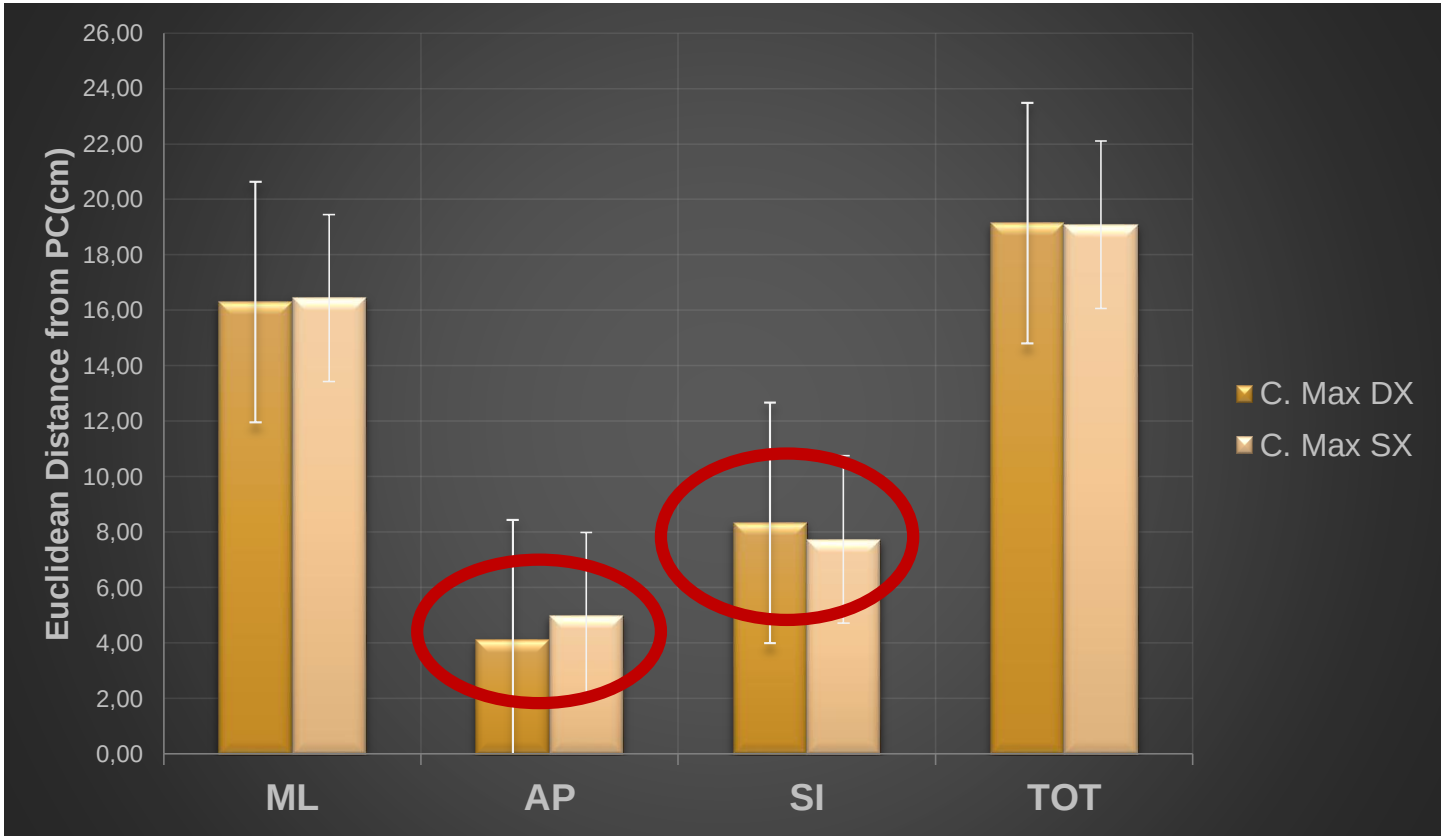
RESULTS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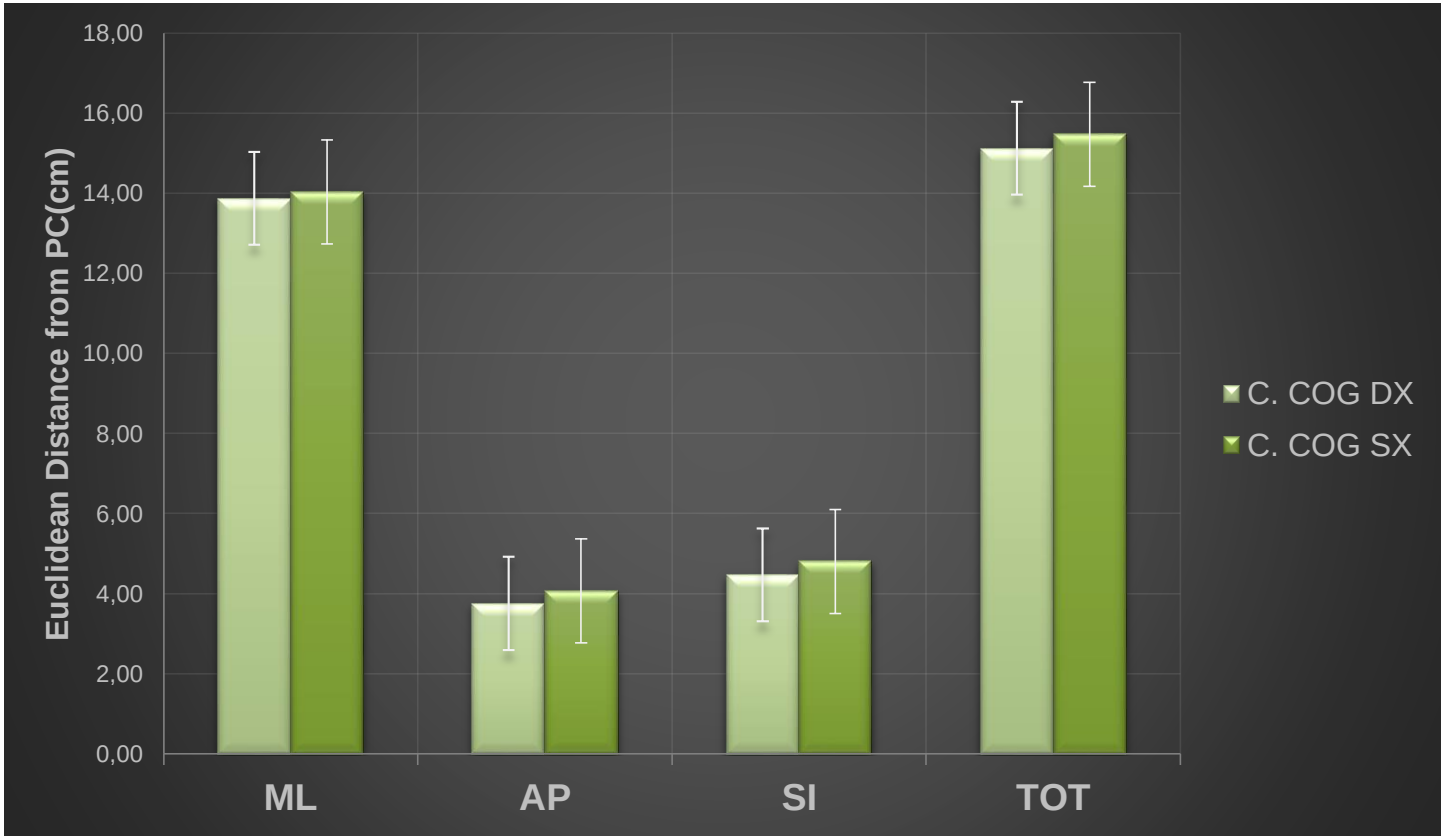
RESULTS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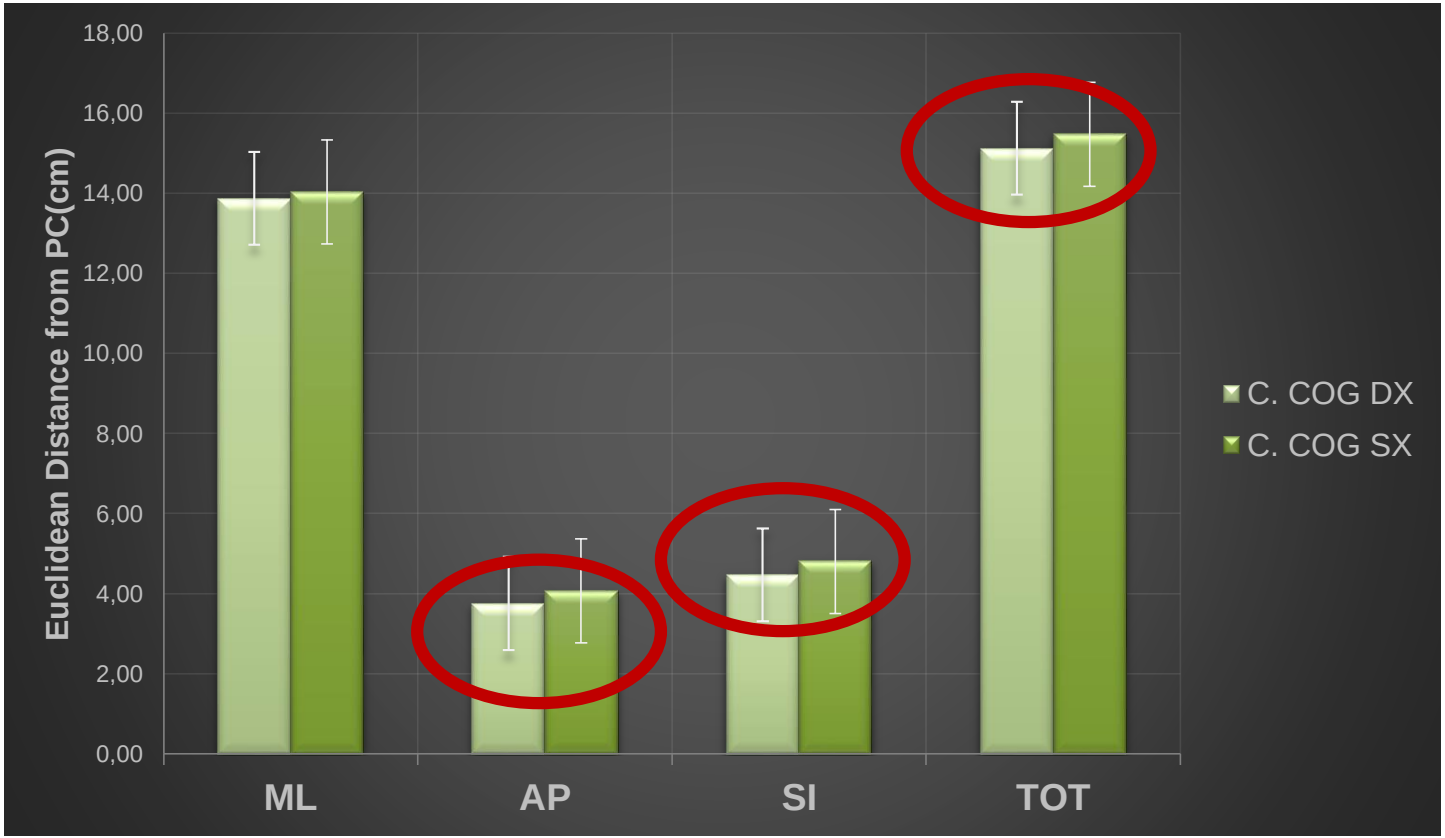
RESULTS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CONCLUSIONS AND PERSPECTIVES

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- We have shown that **tractography-defined Vim localization** can effectively **capture anatomical variability** *in vivo*
- These analyses will be applied **in a predictive way** during the planning of the **tcMRgFUS** treatments and could allow the **temporal optimization**

FUNDING

Project GR-2016-02364526 (Ricerca Finalizzata 2016 - Giovani Ricercatori): "*Trans-cranial MRgFUS for the treatment of medication refractory essential tremor: Italian and world-first trial using a 1.5T MR unit.*"

Ministero della Salute

UNIVERSITÀ DEGLI STUDI DI PALERMO

Ministero dell'Istruzione, dell'Università e della Ricerca

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107° CONGRESSO NAZIONALE
della SOCIETÀ ITALIANA DI FISICA

Thank you!