(Electric) Source Analysis

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What is source analysis?

- Source analysis or electric and magnetic source imaging (ESI/MSI) aims at the reconstruction of the location of sources, as well as their activity over time.

- The results can be used in the process of epilepsy workup to support diagnosis with regard to electro-anatomical correlation, direct comparison with other modalities, as well as for planning of intracranial recordings and epilepsy surgery.

Clinical Value

- EEG source analysis localization had a sensitivity of 84% and a specificity of 88% when comparing localizations with resection volume and outcome.

- It has been demonstrated that resecting such localizations, possibly beyond an epileptogenic lesion in MRI, results in a higher chance for stable seizure freedom

(Brodbeck et al., 2011) (Vadera et al., 2013)

Clinical Value

- In patients with complicated epilepsies, source analysis may provide accurate localizations, e.g. in patients with large lesions, multiple lesions or with no (visible) lesion at all.
- Fast propagating interictal or ictal activity may be resolved by both ESI and MSI.
- If patients require invasive evaluation, e.g. due to the vicinity of epileptic and functional areas, source analysis optimizes electrode placement and can potentially replace invasive recordings in some cases.

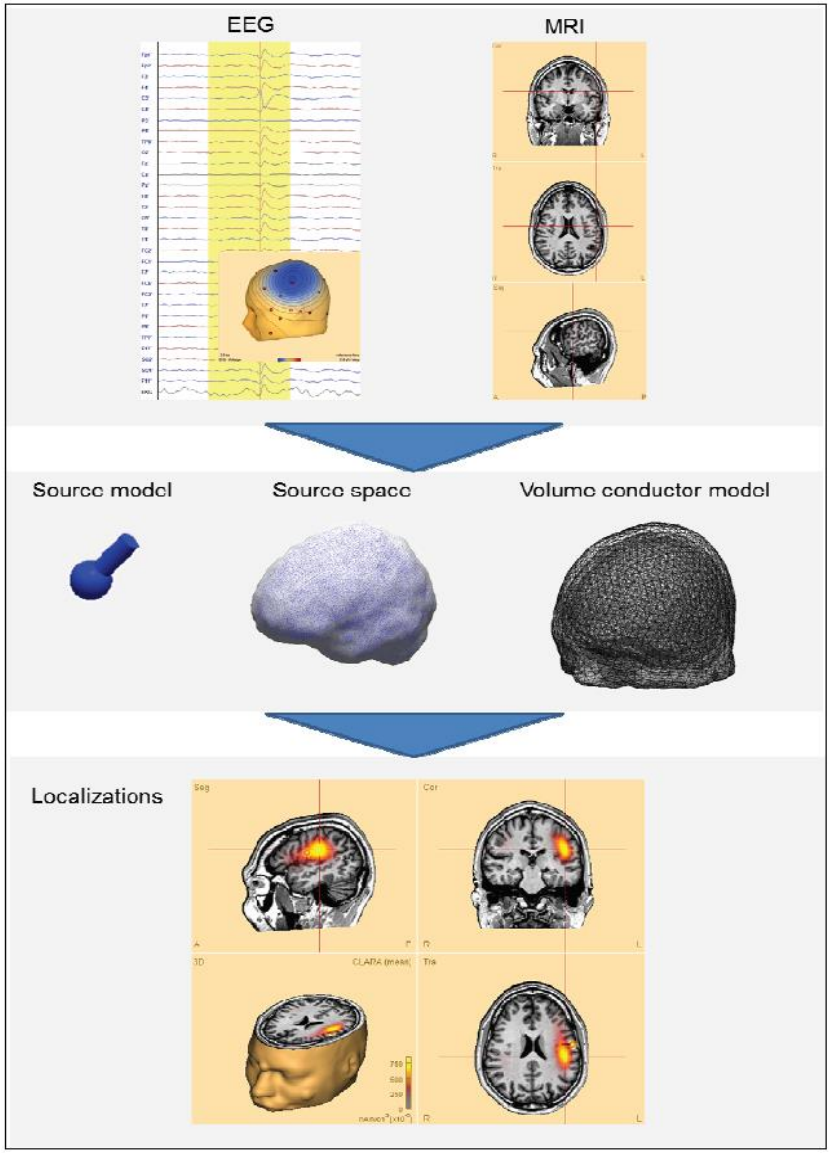
(Brodbeck, Lascano, Spinelli, Seeck, & Michel, 2009), (Stefan et al., 2004), (Rheims, Jung, & Ryvlin, 2013)
(Beniczky et al., 2013; Chang, Nagarajan, Mantle, Barbaro, & Kirsch, 2009; Kovac et al., 2014; Rosenzweig et al., 2014)
(Knowlton et al., 2006; Sutherling et al., 2008; Yamazaki et al., 2012)

Basic Concepts

- The **forward problem** is then to calculate the a certain potential within the brain, on the surface of the head, which would be measured by EEG.

- A certain potential is recorded using a specific EEG electrode montage and the underlying source is the item in question. This situation is referred to as the "**inverse problem**".

Source analysis overview



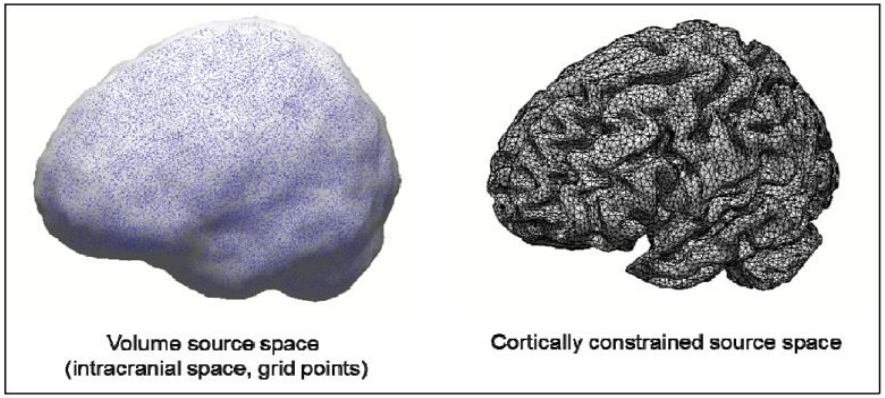
Source Model

- A theoretic model approximating the source and its characteristics.
- In case of focal epilepsies, a point-like source as introduced above, termed "**dipole**", may be sufficient.
- In contrast, ictal propagation may be better described as **extended patches of activity**, which may change the degree and extent of activation over time.

Source Space

- is the compartment, which confines all putative source locations. Commonly, the whole intracerebral volume is selected as source space.

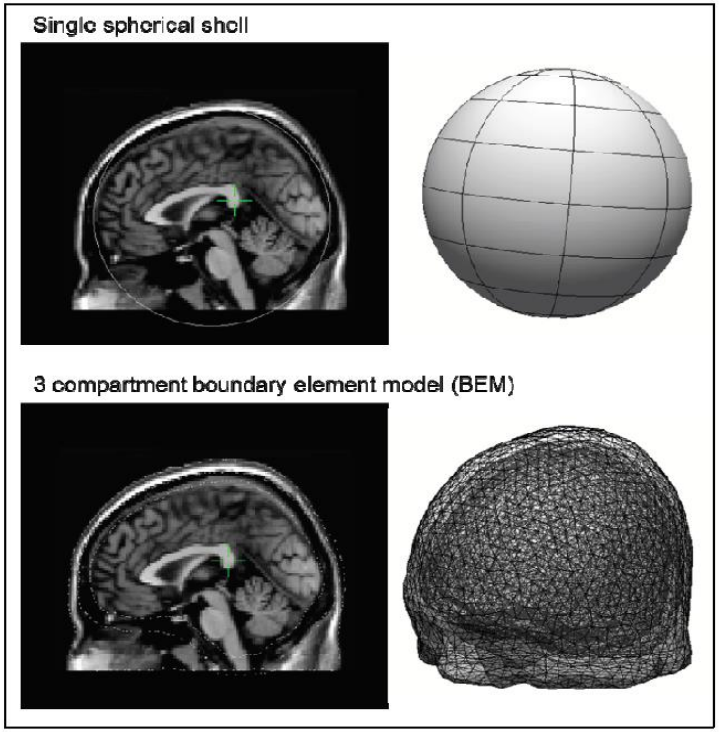
- More restrictive assumptions limit the locations of possible generators to the gray matter, resulting in “cortically constrained” solutions.



Volume Conduction Model

- A model typically constructed from segmented MRI data to approximate the different tissue and compartments that influence the appearance of potentials on the surface as measured e.g. by EEG electrodes.

- This "volume conductor model" then describes how currents are altered by conductivity differences.

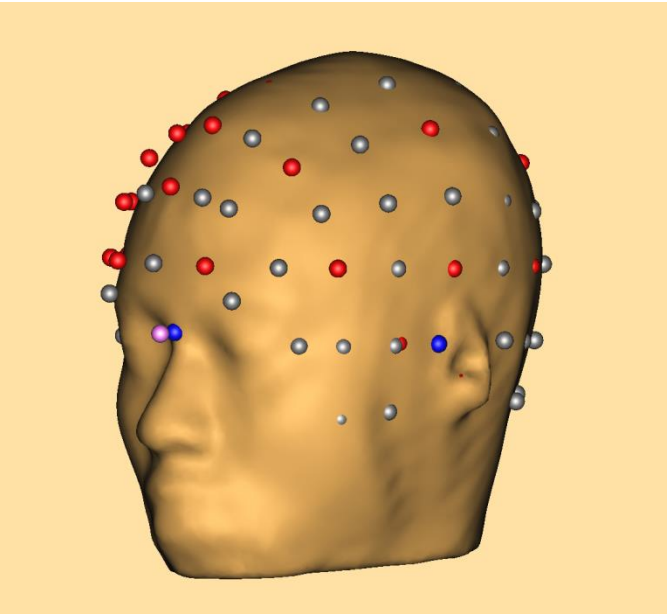


Aydin et al., 2014)

Volume Conduction Model & Leadfield

- The most detailed volume conductor for actual use in source analysis is the **"finite element model"** or **FEM**, which approximates and fills the different compartments with voxel elements.

- The **leadfield** is a mathematical concept, which connects the various locations in source space to the different EEG electrodes and their positions on the head.



Source Localization

- A focal source activity, a single dipole (**dipole model**) will be selected as the source model. Then construct a volume conductor model from an individual MRI and derive a leadfield.

- Dipole location highlights an equivalent center below the active cortex while orientation points to the location of the more superficial activated patch.

- A first dipole is then calculated to explain the first dominating activity, e.g. as indicated by a **principal component analysis** (**PCA**), whereas a second or third is constructed for the residual, still unexplained components of the data.

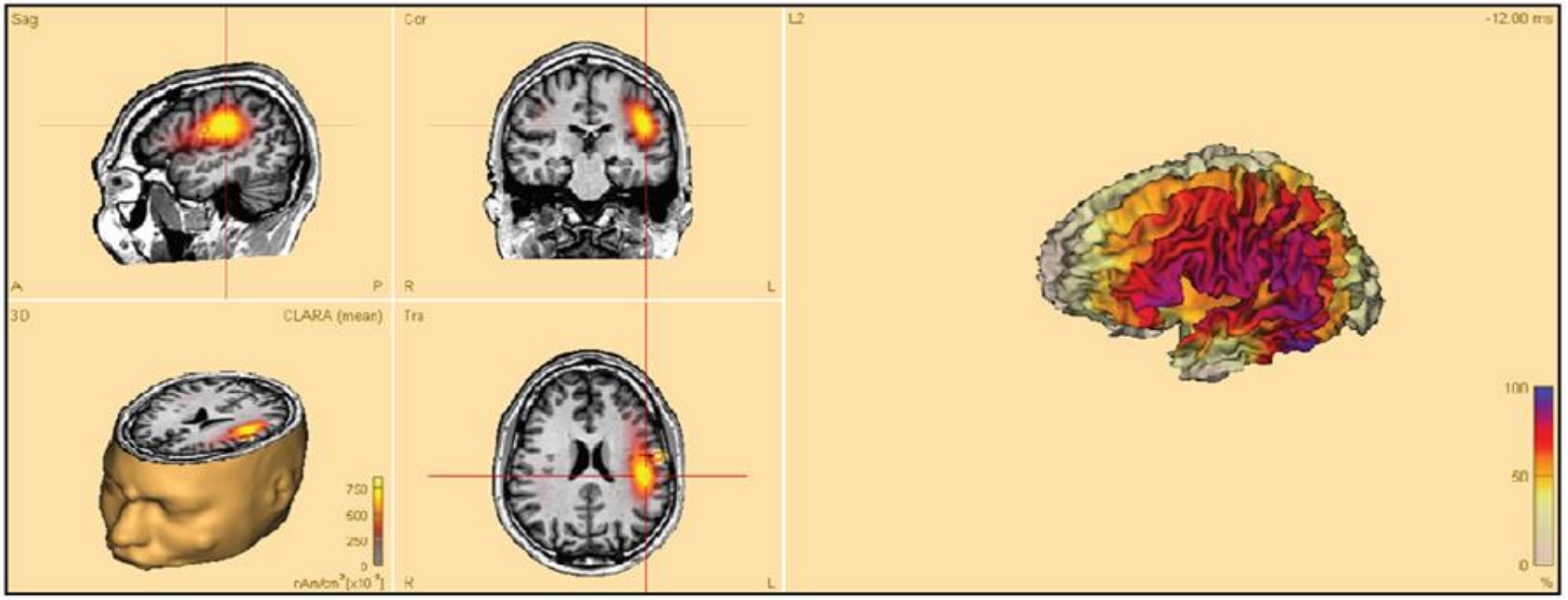
(Scherg & Berg, 1996; Scherg, 1992)

Source Localization

- The distributed source approach models the underlying sources as **distributed patches of activity**. The source space is subdivided into discrete source positions structured as **a grid**.

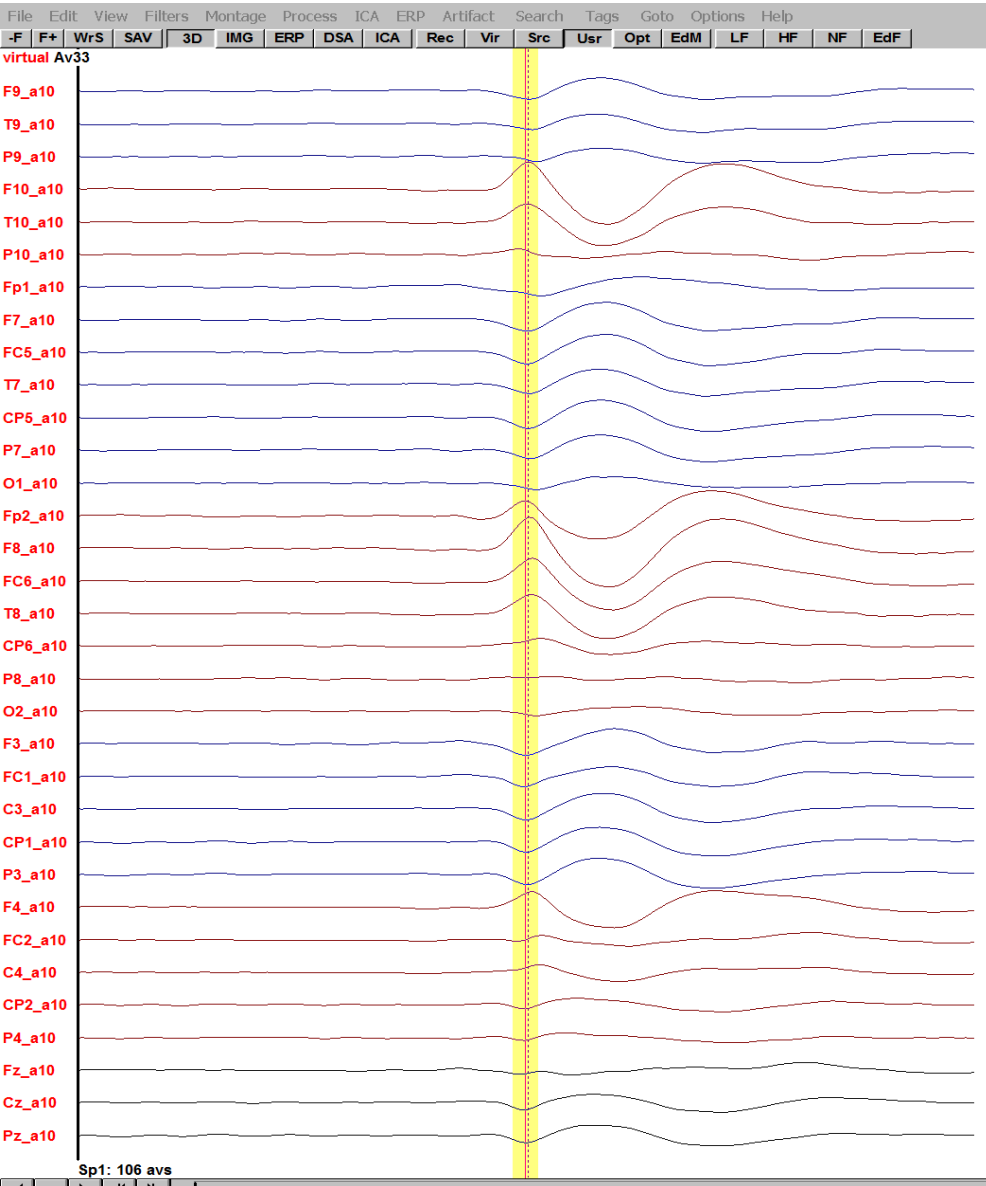
- Mathematical implementation (smoothness), differentiates the various forms of distributed source models: Minimum Norm, L1-, L2-Norm, and LORETA (Low-Resolution Electric Tomography).

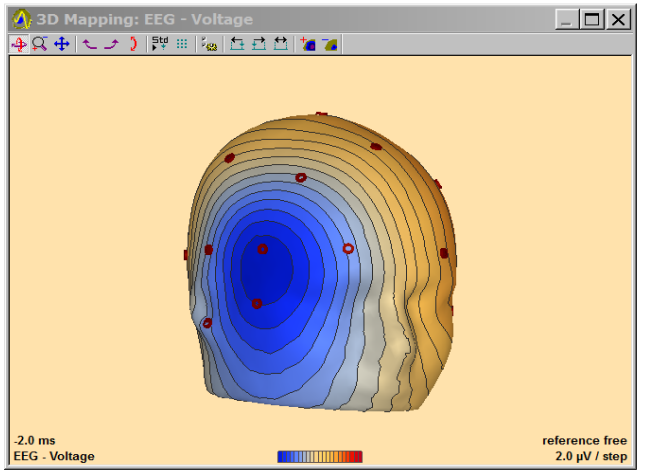
Source Localization



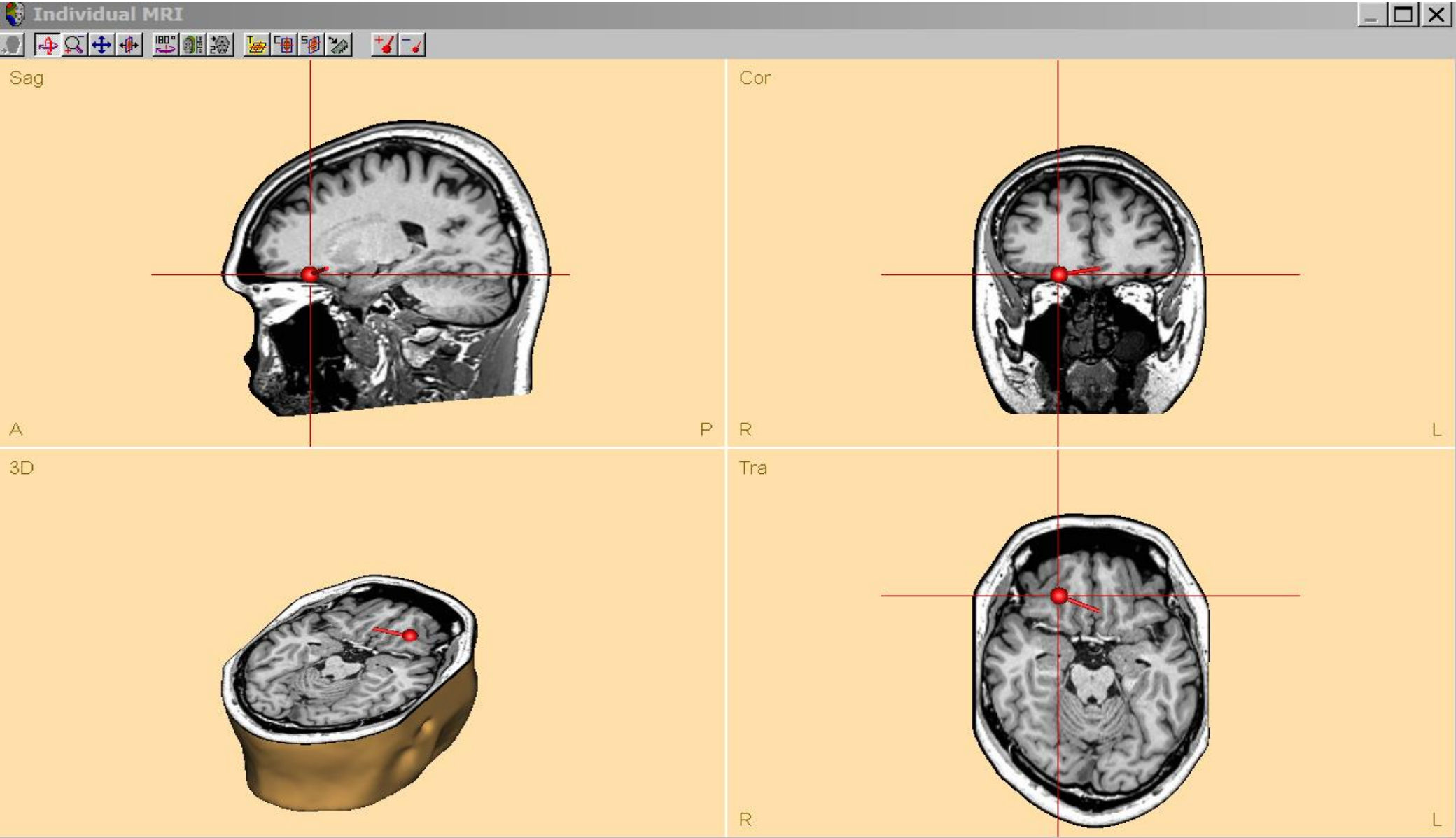
Left: Single dipole and CLARA, Right: Minimum norm

Case 1_spike averaging

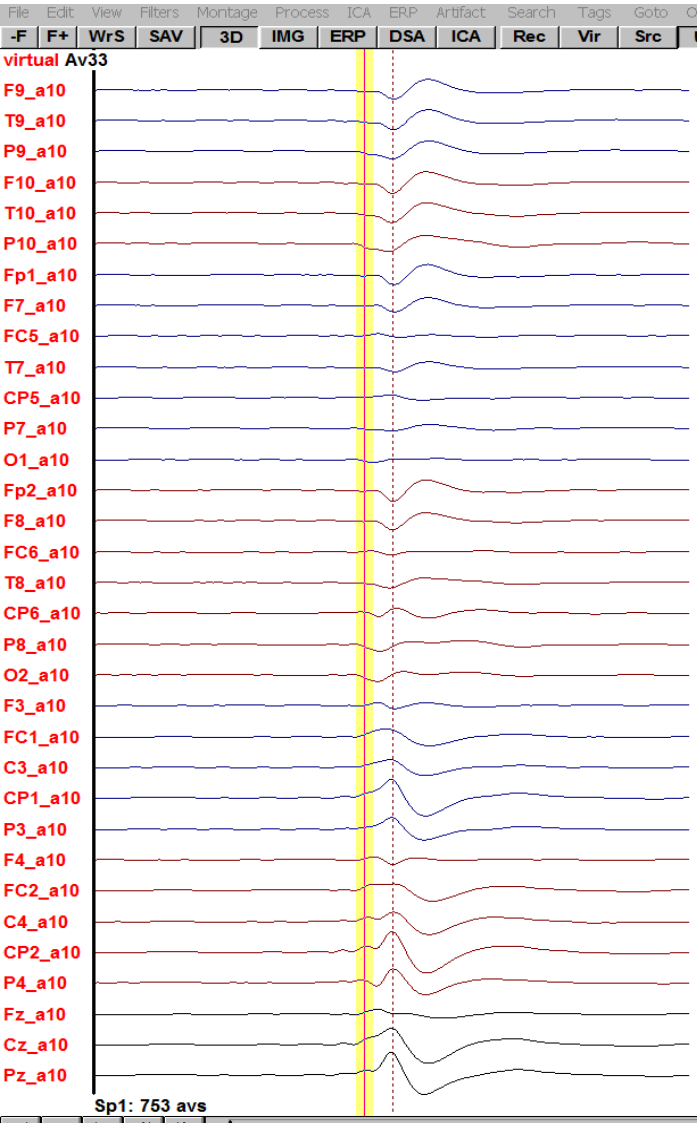


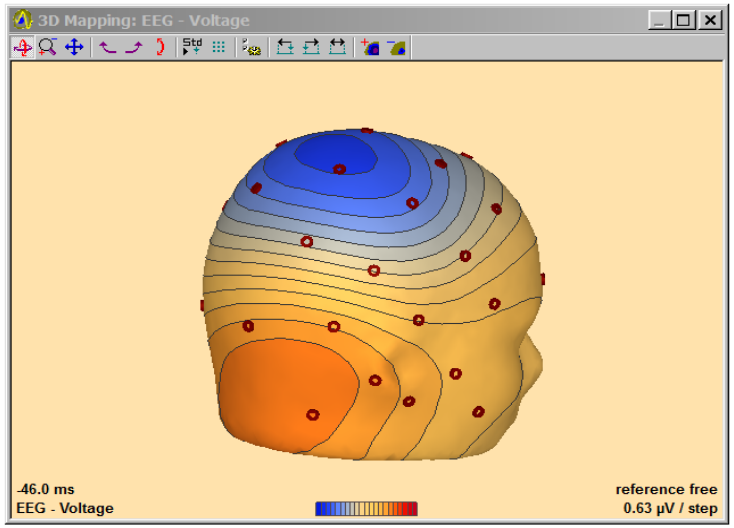


Case 1_spike_dipole Localization

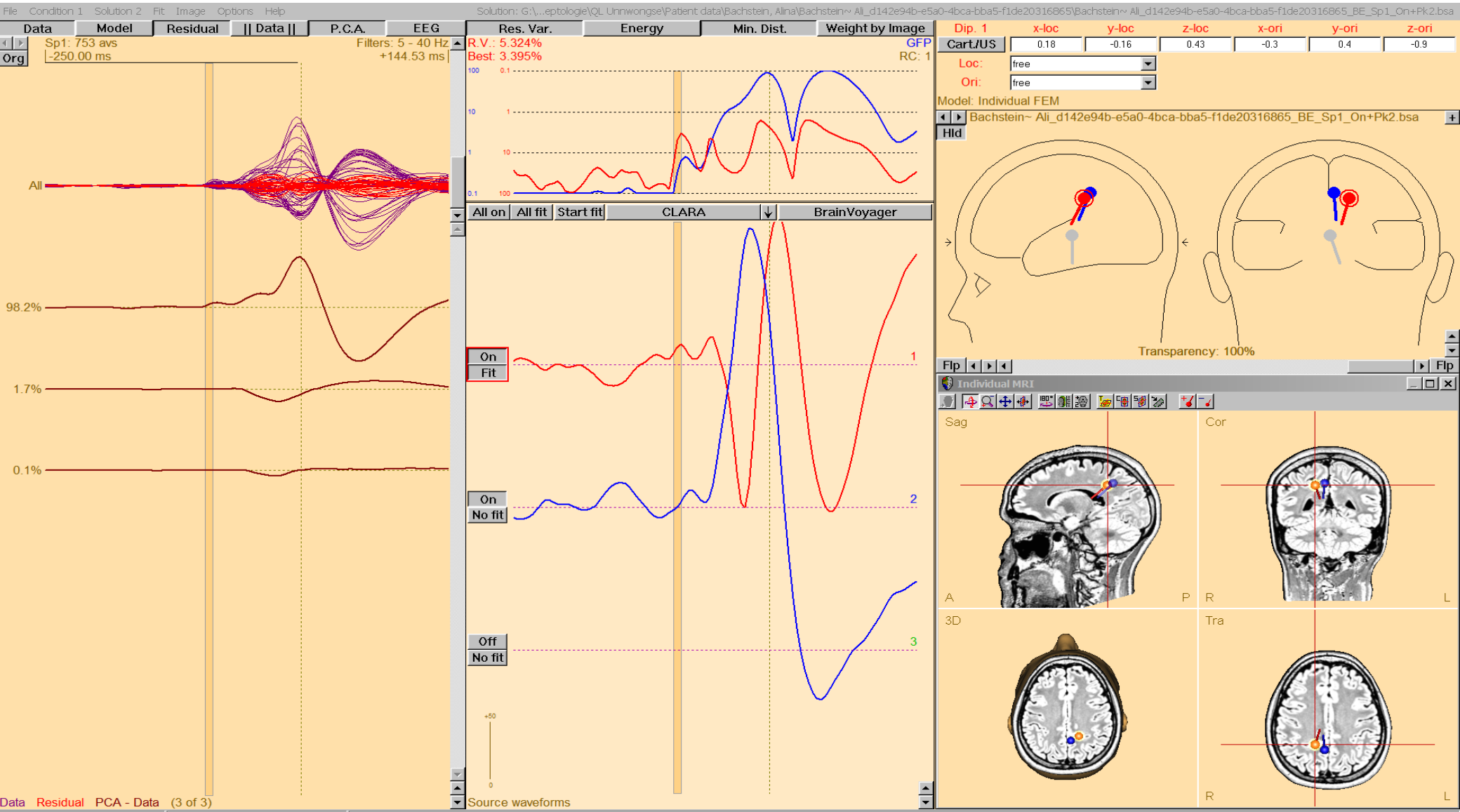


Case2_spike averaging



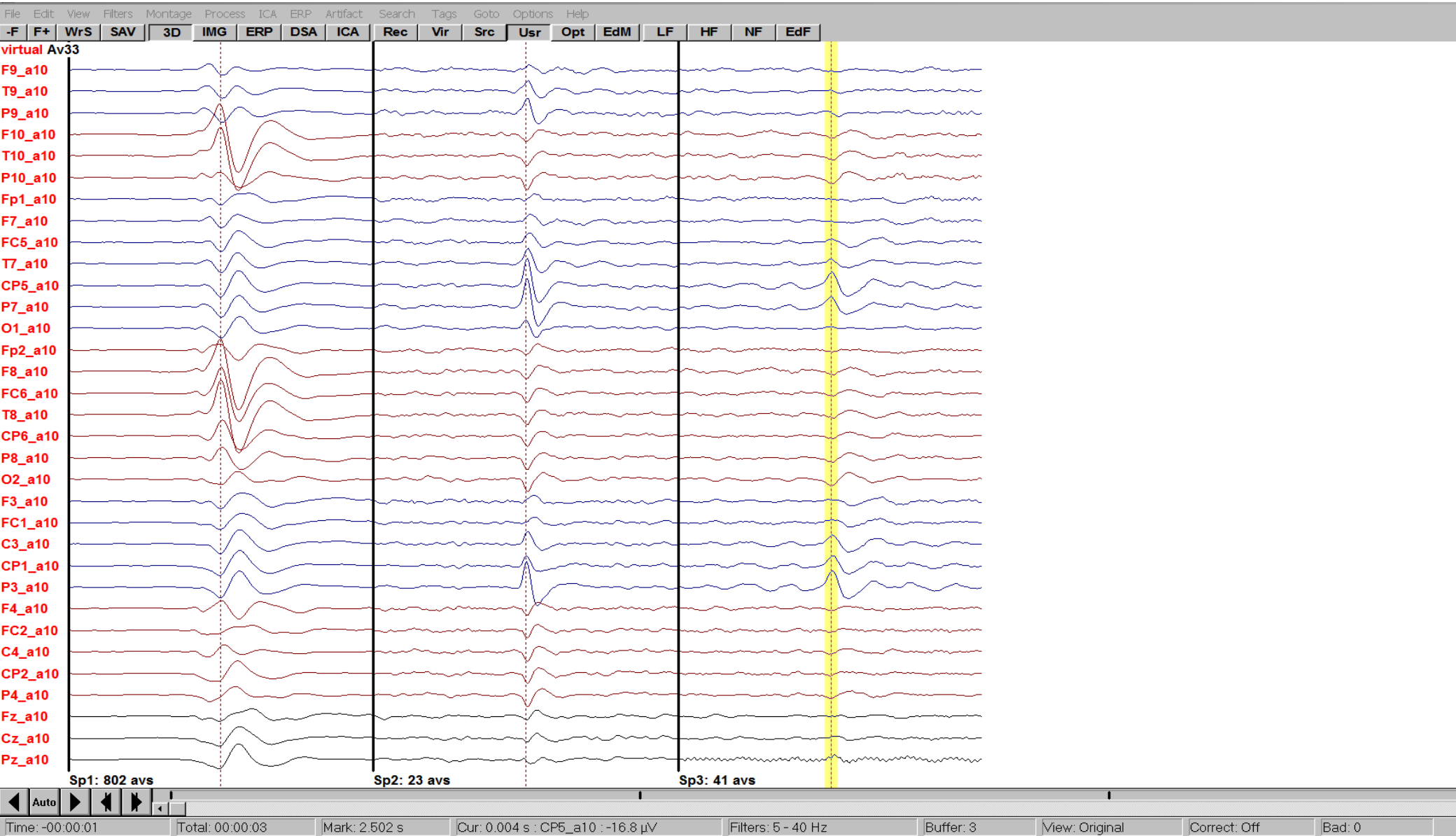


Case2_pre-spike_dipole localization_on Flair

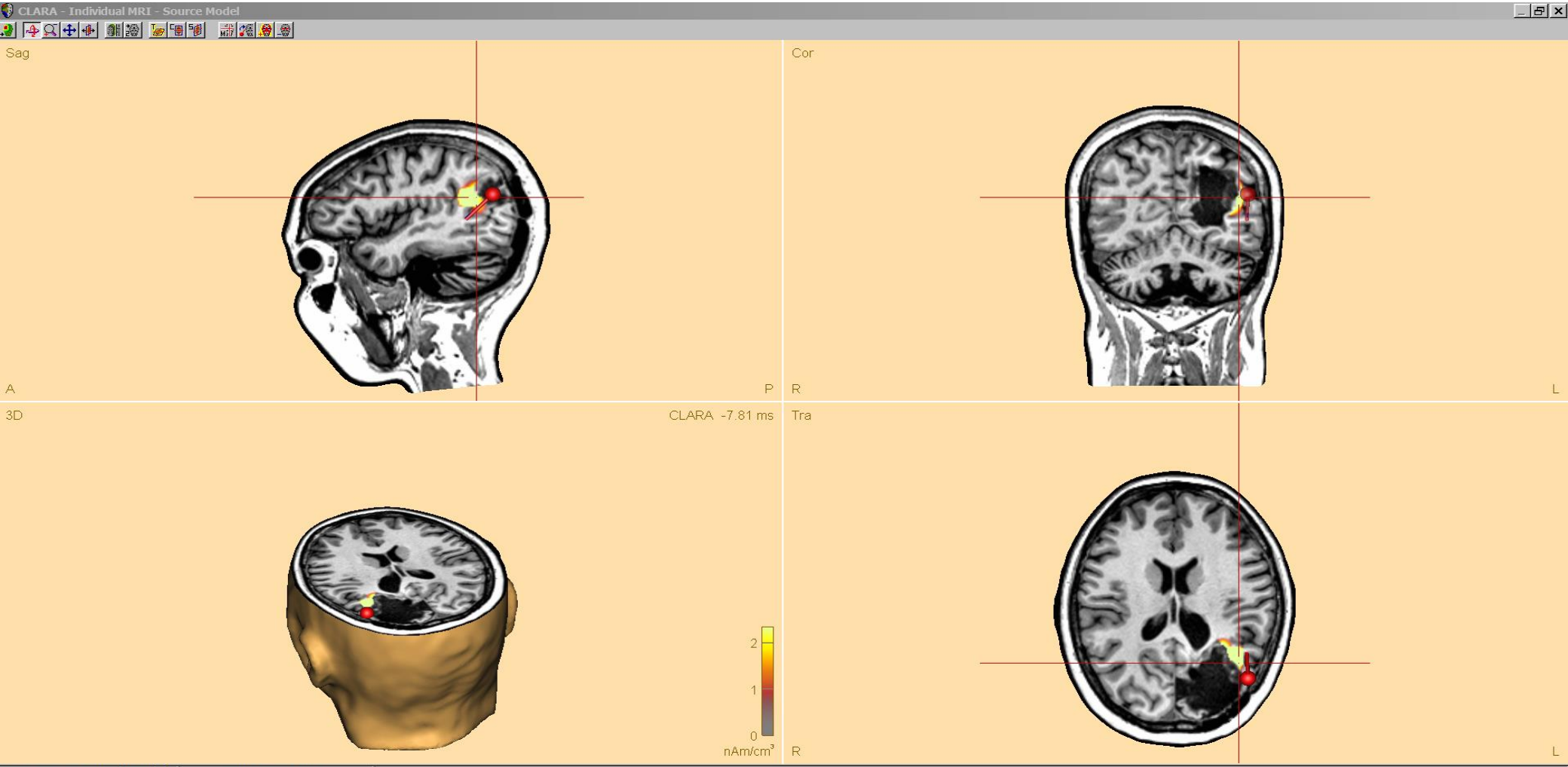


Case2_pre-spike_dipole localization_on Flair

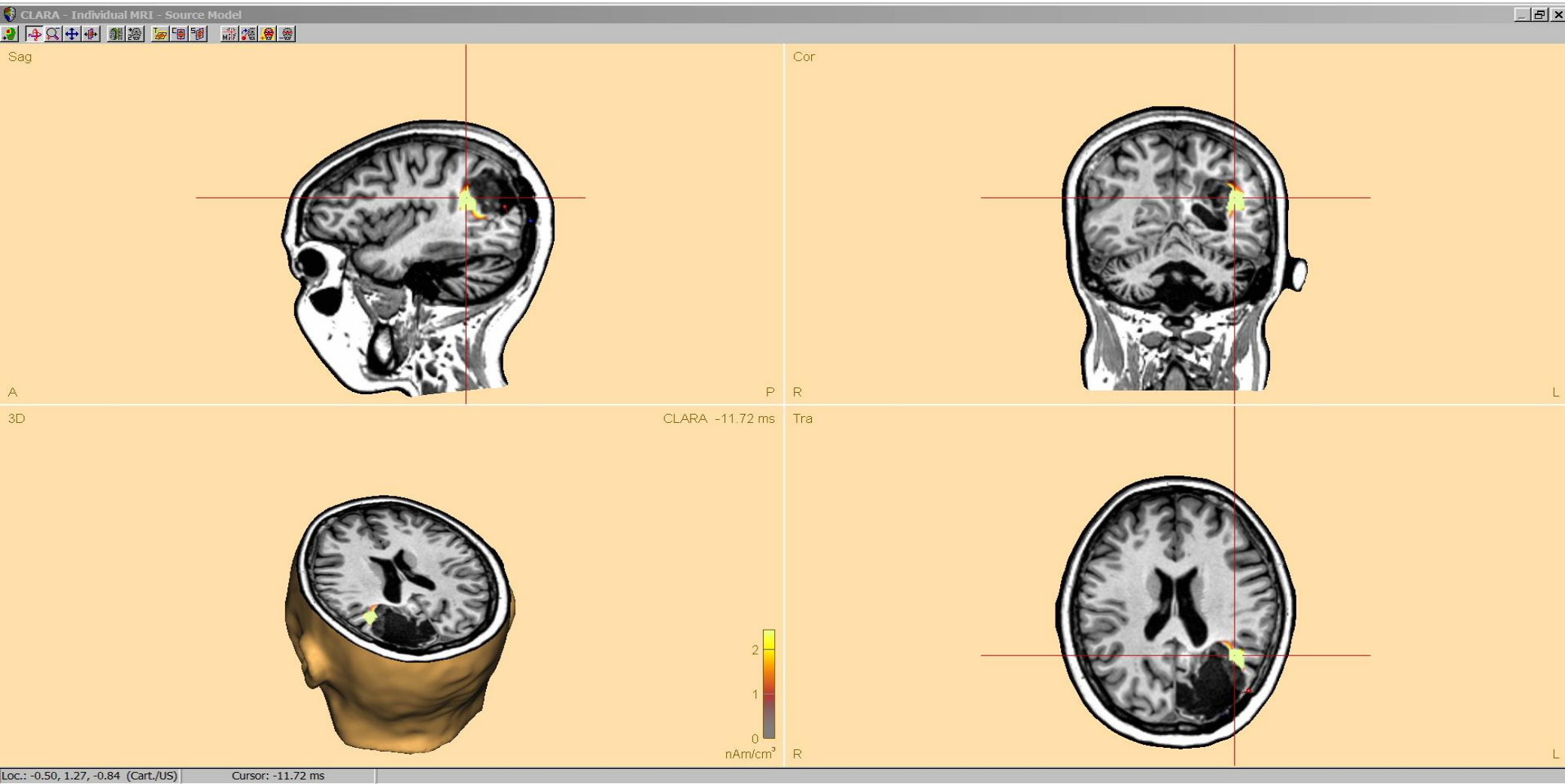
Case3_spike averaging



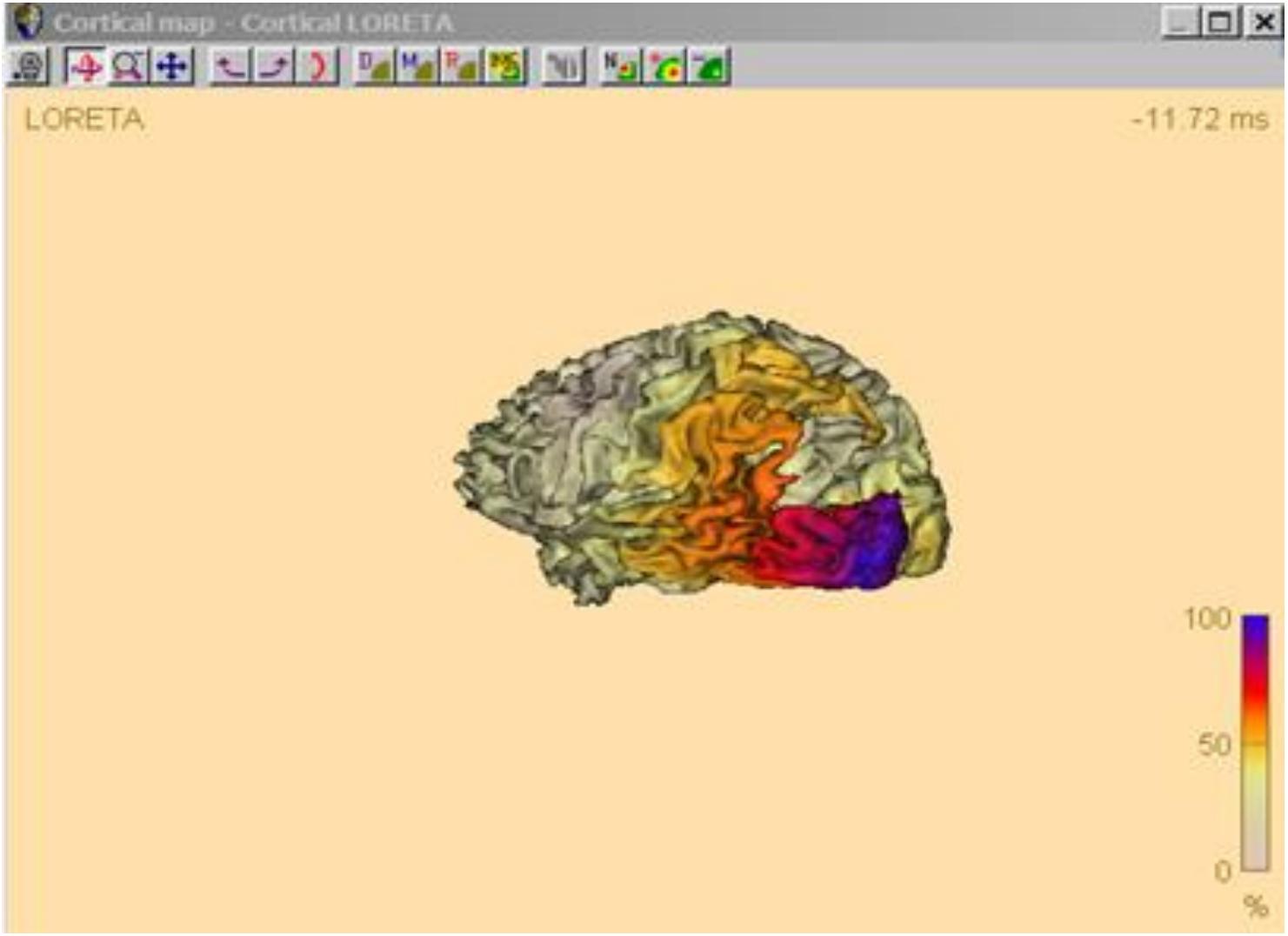
Case3_spike_dipole & CLARA localization



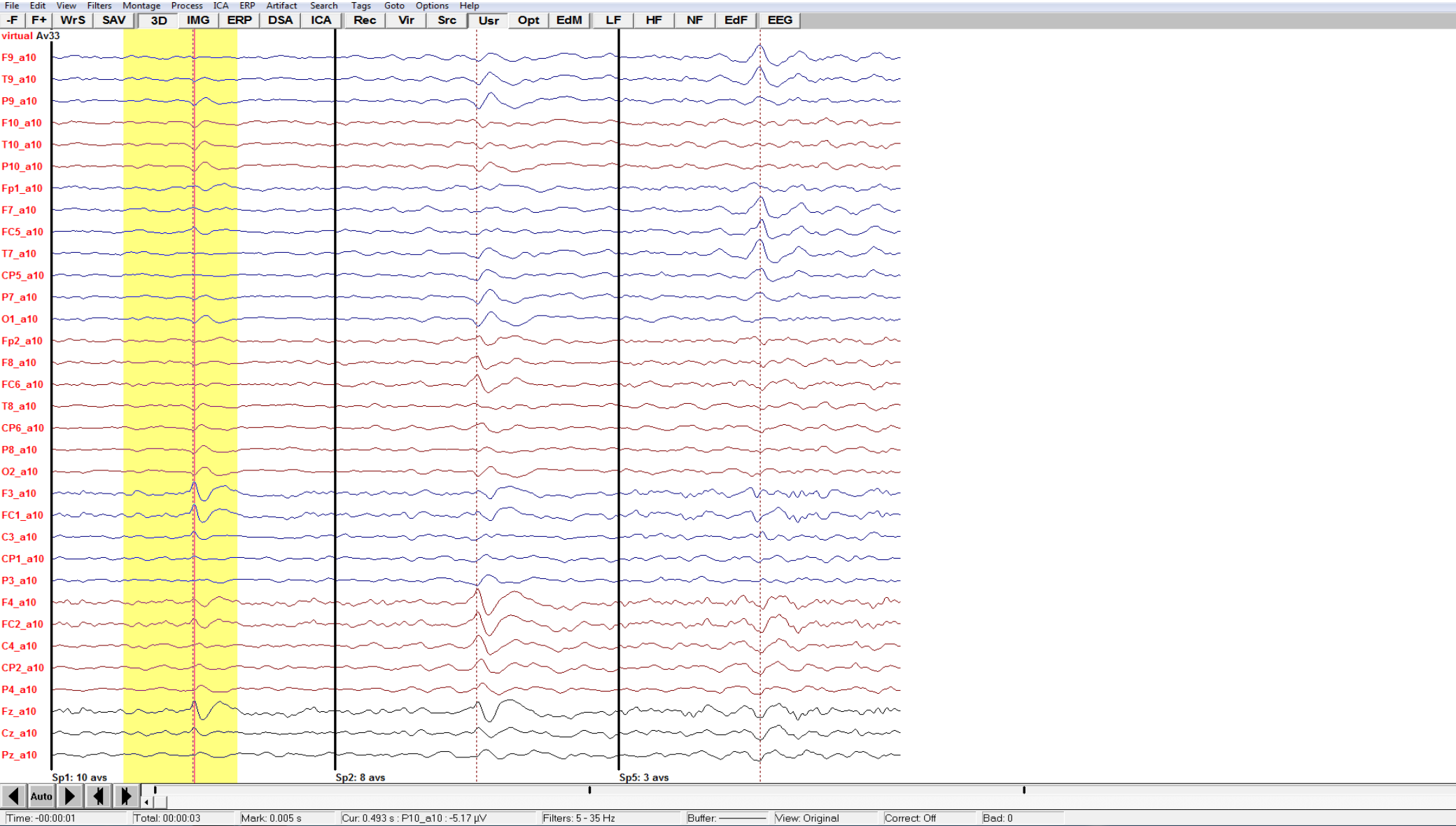
Case3_seizure_dipole & CLARA localization



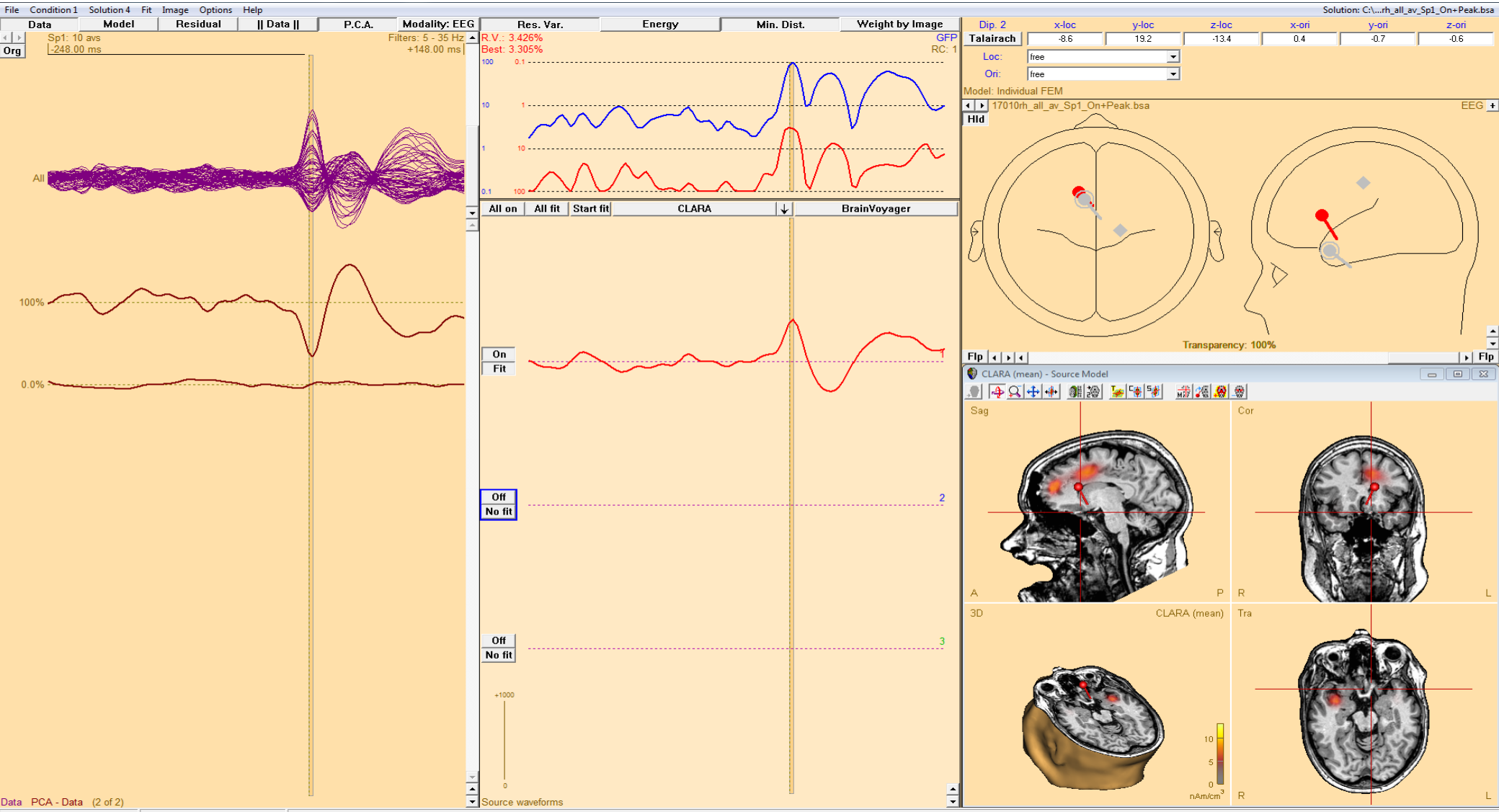
Case3_seizure_cortical LORETA



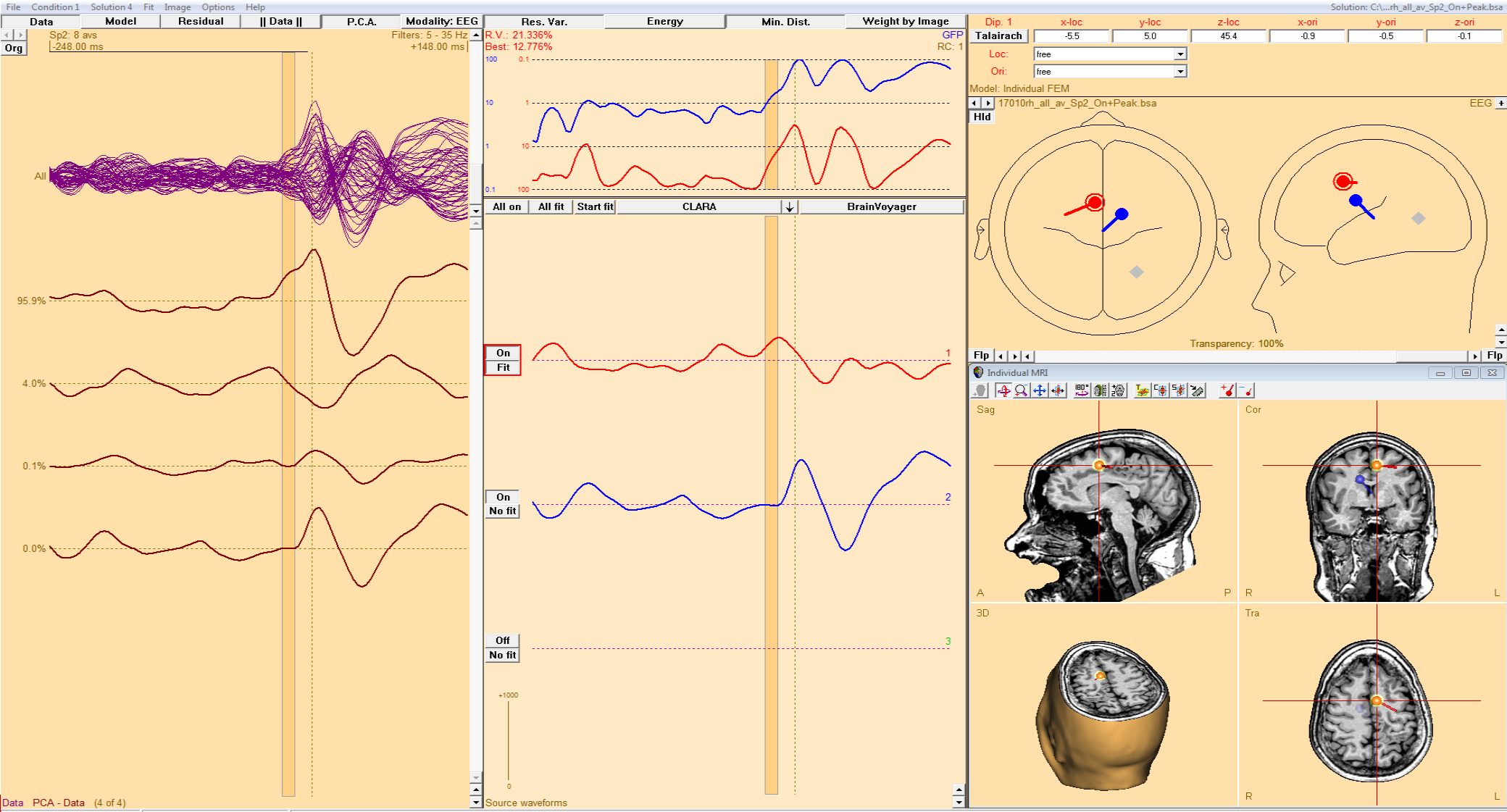
Case4_spike averaging



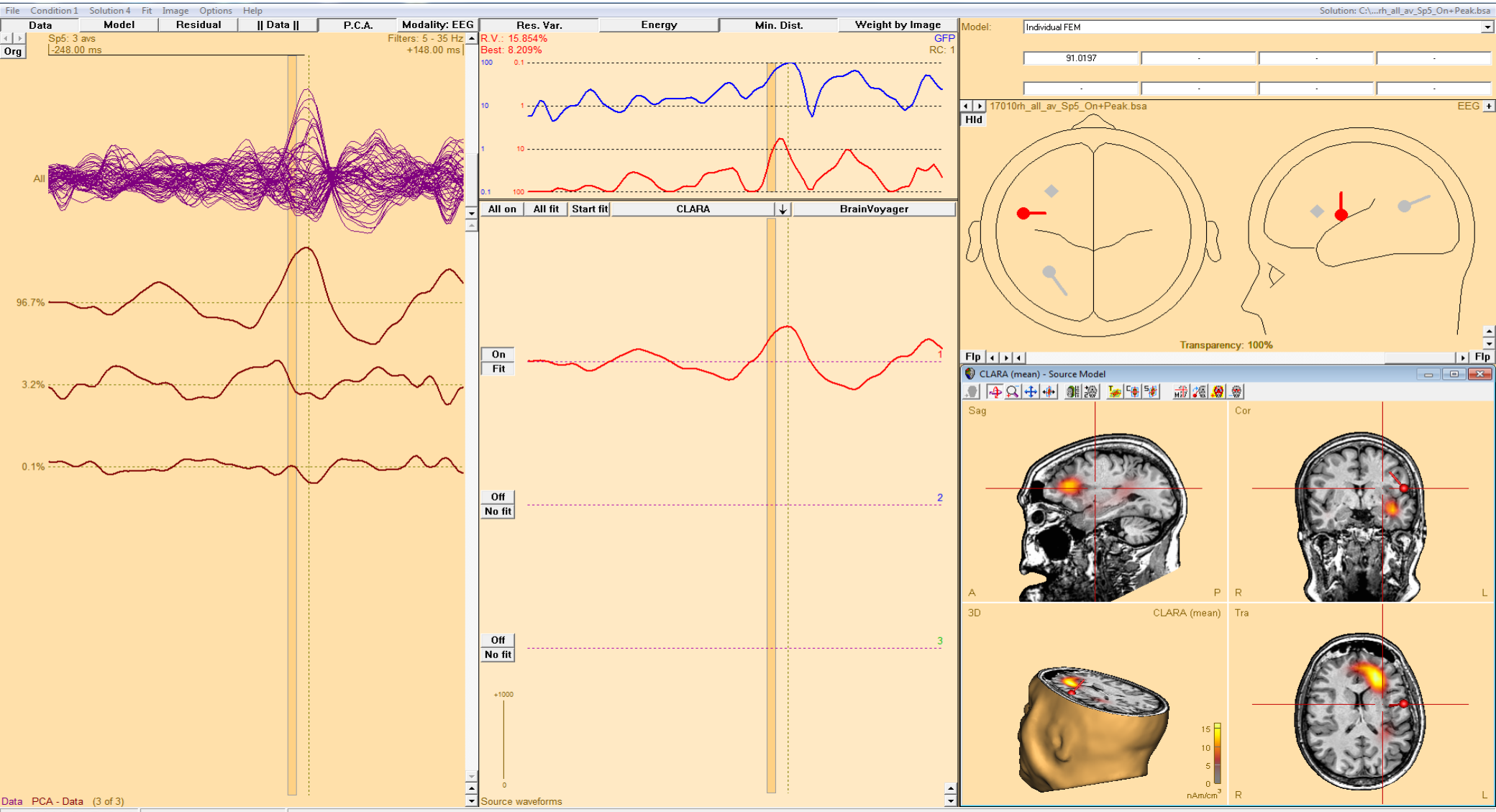
Case4_spike1_dipole & CLARA localization



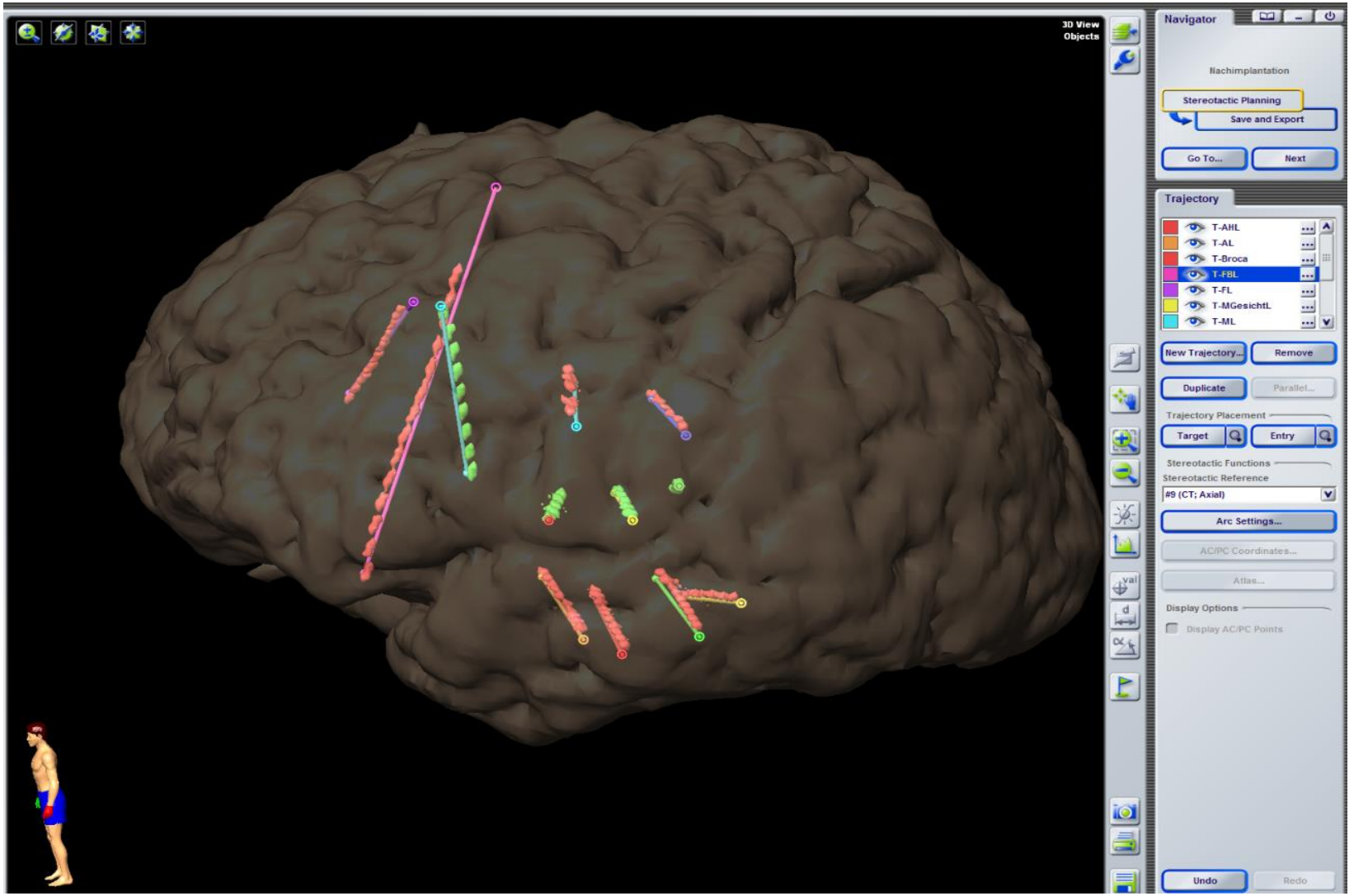
Case4_spike2_dipole localization



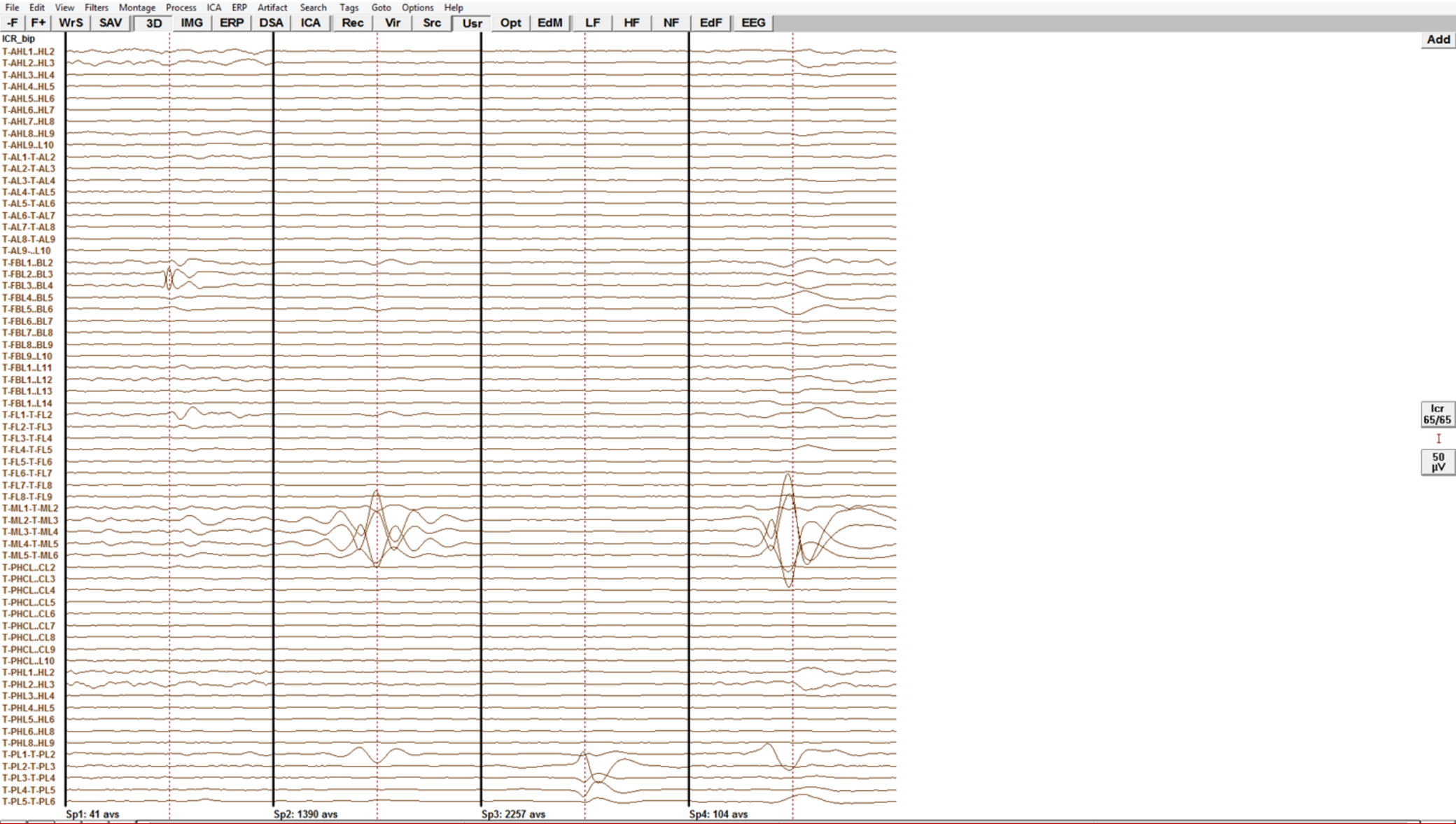
Case4_spike3_dipole & CLARA localization



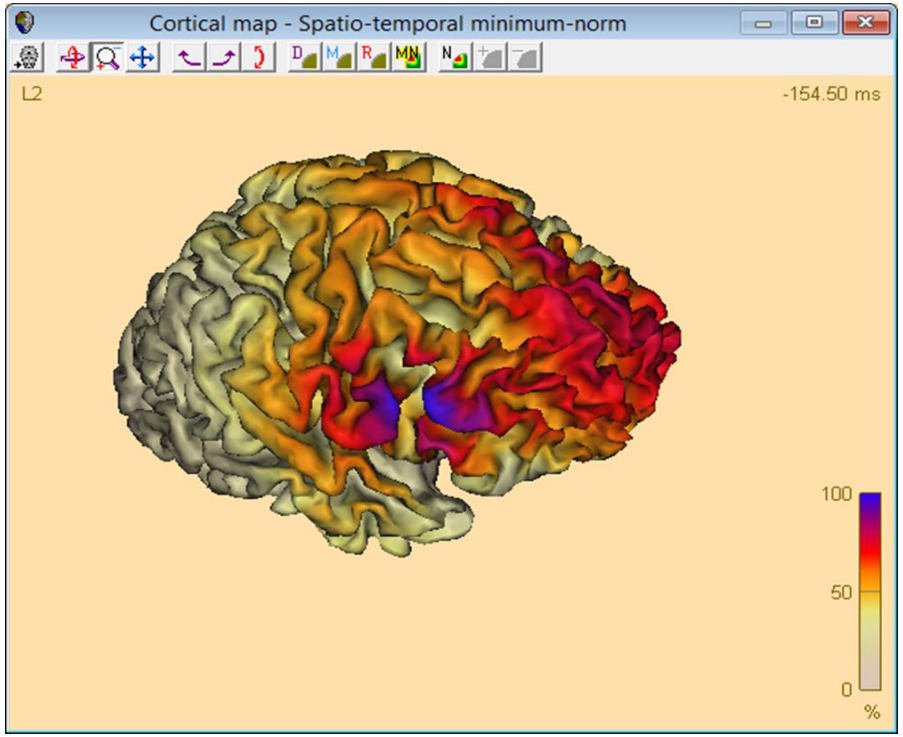
Case5_Invasive triggered scalp EEG_source analysis



Invasive Triggered Scalp EEG_averaging

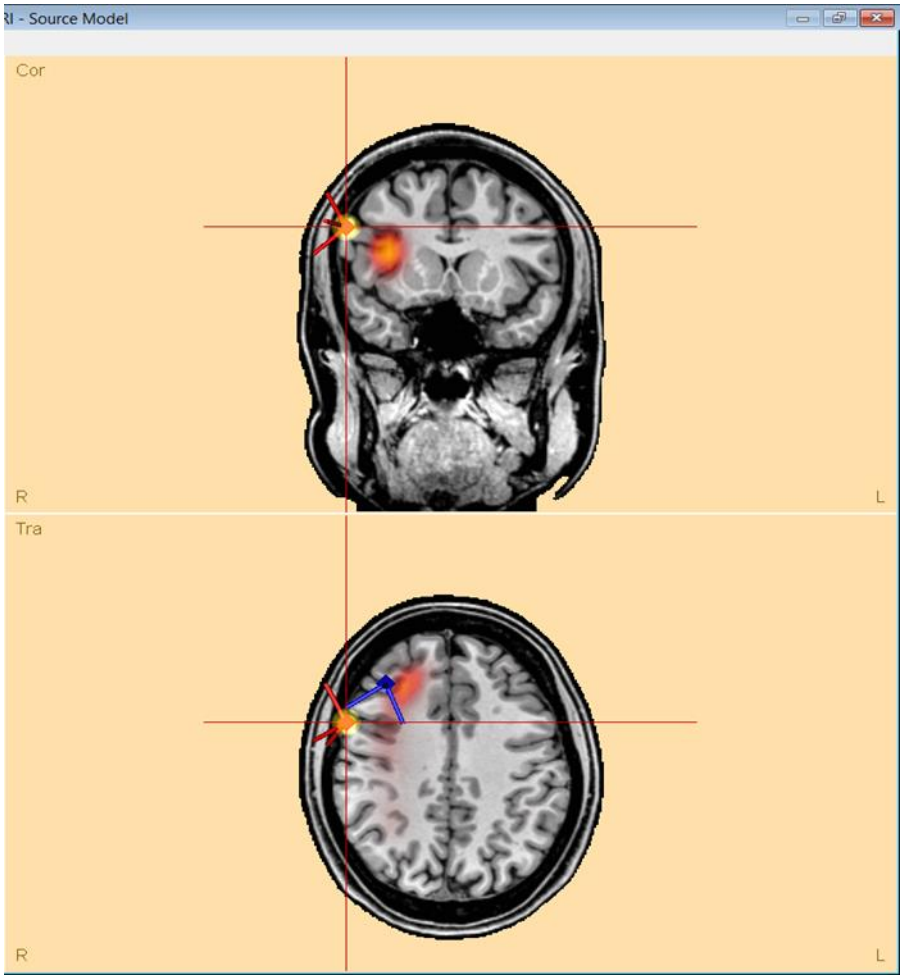


Case5_Invasive triggered scalp spikes_localization



TPL2-5, pre-spike localization (76)

TML2-5, Spike localization (1390) > & TBL2-4 (blue)



Voxel-based Morphometry (VBM)

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VBM (Morphometric Analysis Program, MAP)

- Following the principles of **VBM** this technique primarily includes a normalization and gray matter segmentation using **SPM99** (Department of Imaging Neuroscience Group, London, UK). and the detection of aberrant neuronal tissue extending beyond the normal cortical ribbon by comparison with a normal database.

- A novel voxel-based image post-processing method for enhanced visualization of blurred gray–white matter junctions.

(Ashburner et al., 2003; Ashburner and Friston, 2000)

Data Acquisition and Processing

- Magnetization-prepared rapid-acquisition gradient echo (**MPRAGE**) sequence was employed (TR = 9.7 ms, TE = 4 ms, flip angle = 12◦, matrix = 256×256, voxel size=1mm×1mm×1 mm) to obtain a high-resolution T1-weighted 3D dataset, consisting of 160–180 sagittal slices.

- Data sets were transferred in digital imaging and communication (**DICOM**) format and converted to **ANALYZE** format. Off-line processing using a batch script for SPM99 to employed standard procedures (e.g., normalization, segmentation, calculation of a difference image, conversion to a binary image, masking, etc.).

(Hüppertz HJ at al., 2005)

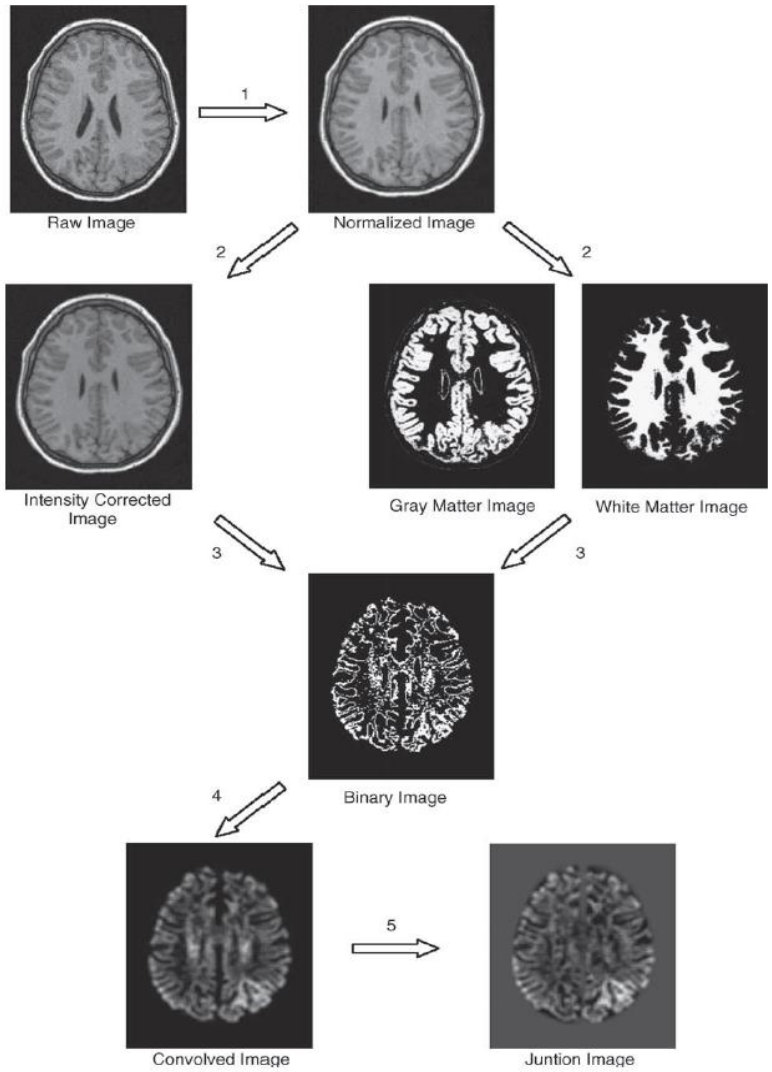


Fig. 1. Overview of the image processing steps required for calculating the junction image: (1) normalization, (2) segmentation and intensity correction, (3) conversion to a binary image, (4) convolution, and (5) comparison with the normal database (see text for details).

Normalization

Intensity Correction & Segmentation

Conversion to binary

Convolution

Comparison to normal database

(Ashburner and Friston, 2000)

Interpretation

- The calculation of the **extension image** comprises the following steps: normalization, segmentation of a gray matter image, smoothing by a Gaussian filter, and comparison with a normal database by subtracting the **mean gray matter image** of the normal database from the smoothed gray matter map of the analyzed patient.

- Then the **junction image** was compared to both the **extension** and the original **T1-weighted** MR image.

(Kassubek et al., 2002)

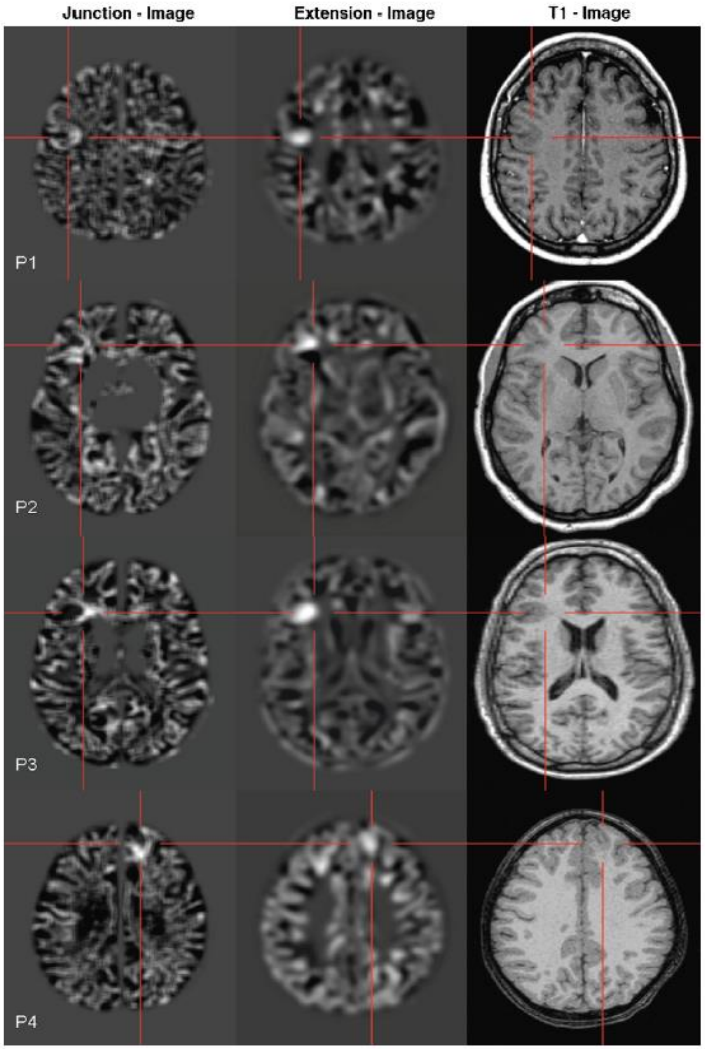
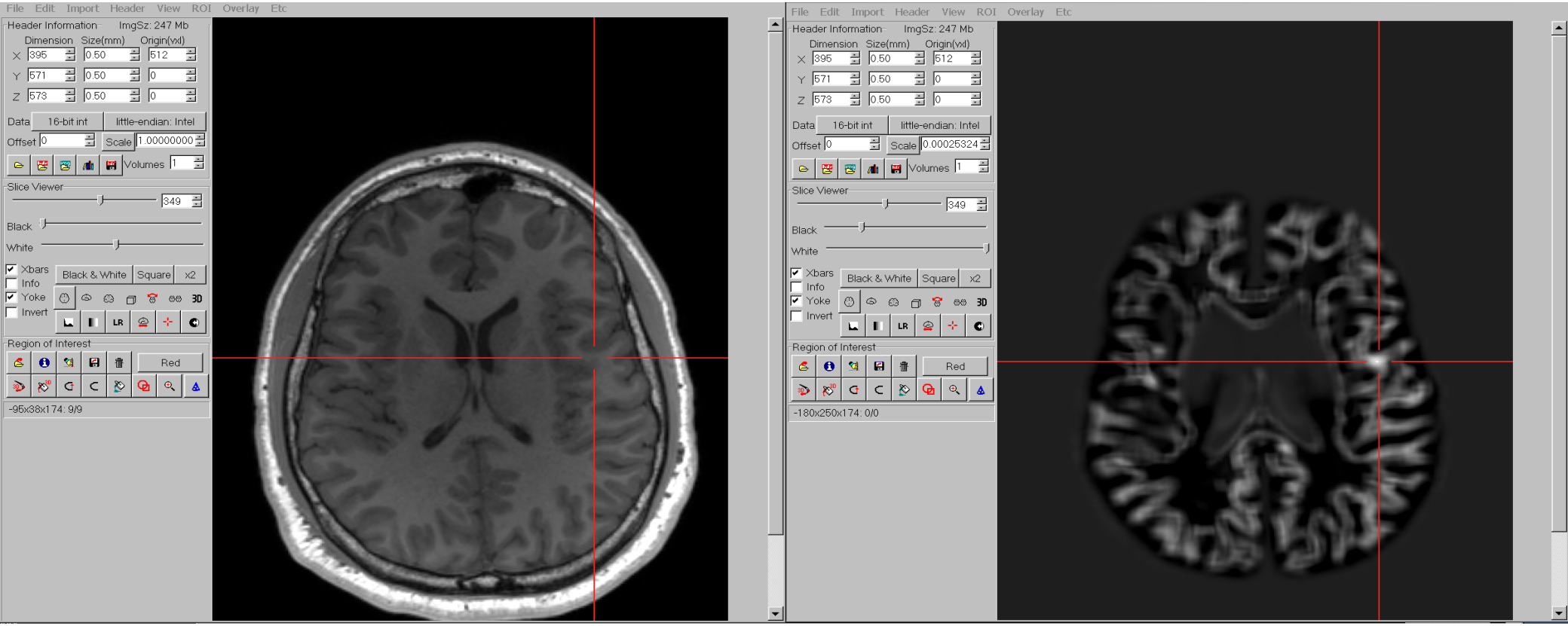
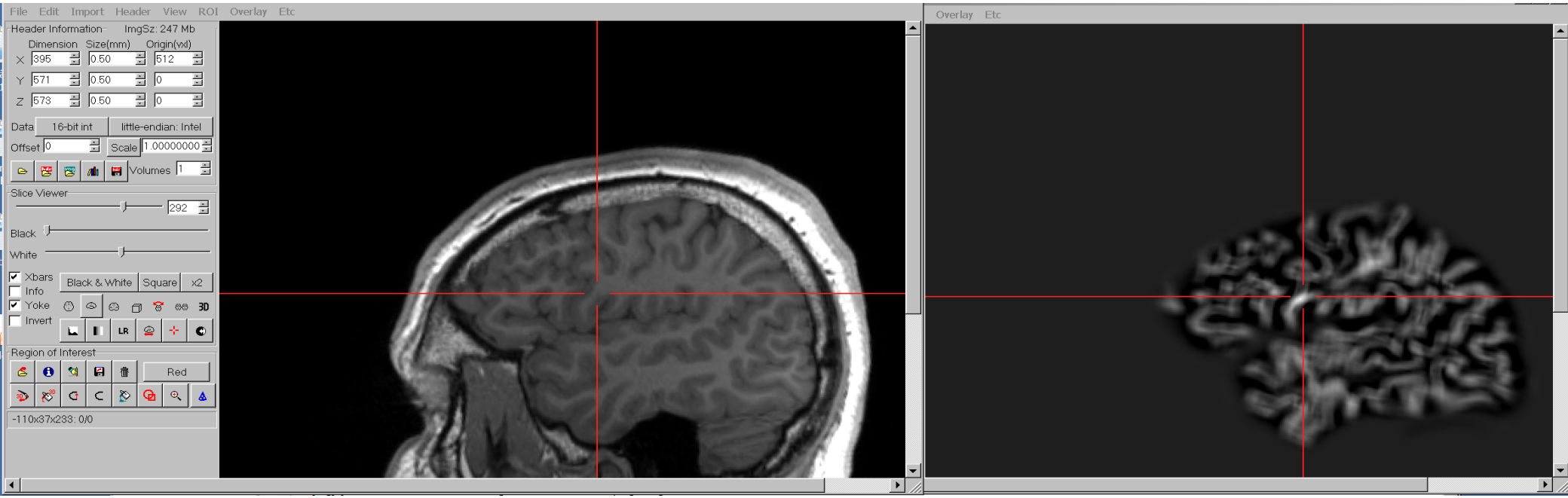


Fig. 3. Results of four patients with histologically proven FCD Palmini 2: the 'junction' images in the left column highlight brain areas with blurred gray–white matter junction, the 'extension' images in the middle column emphasize gray matter extending abnormally into the white matter as compared to the normal database, the right column shows the corresponding slices in the original T1 weighted image.

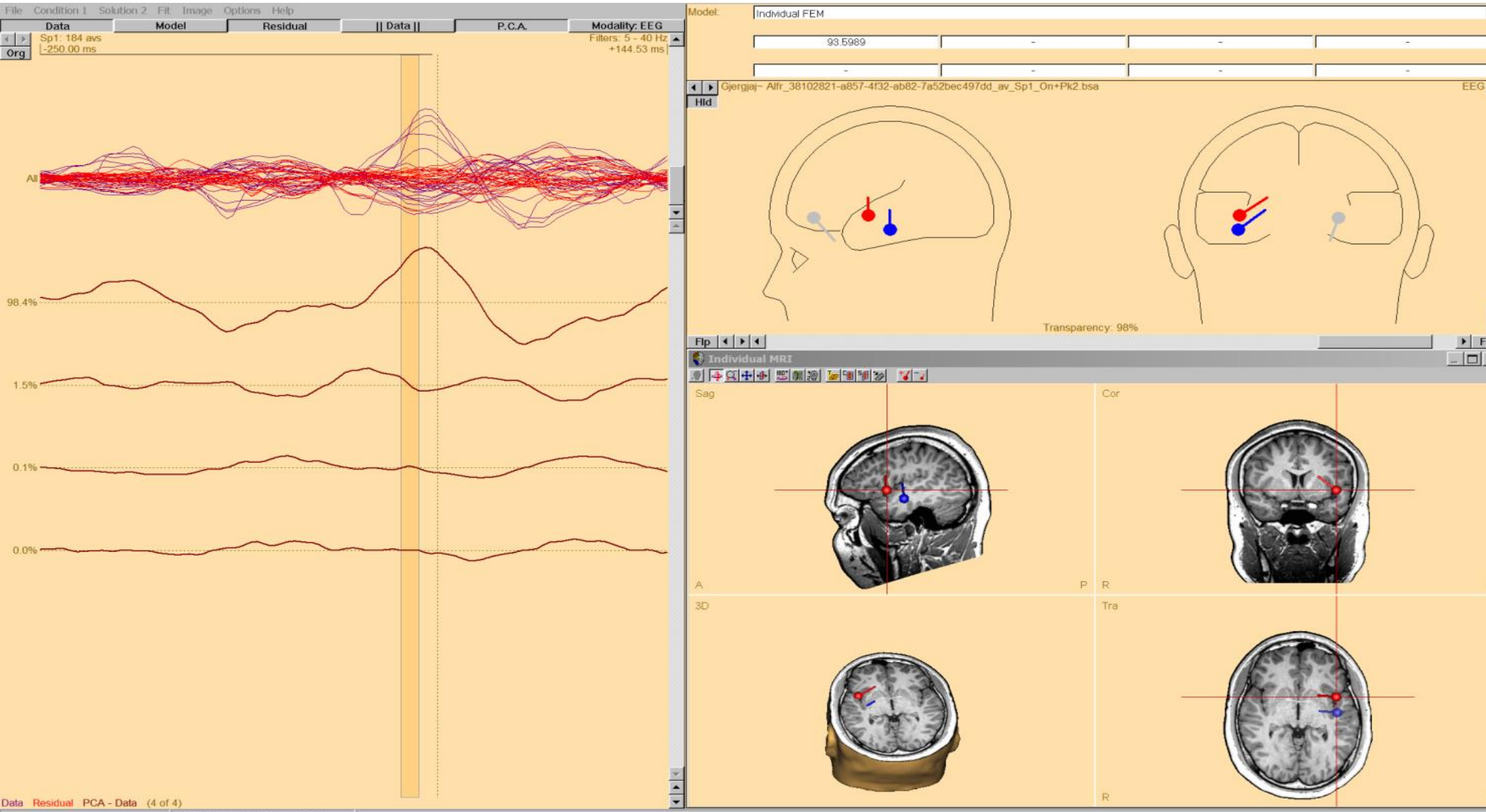
Case1_ non-lesional MRI_junction image



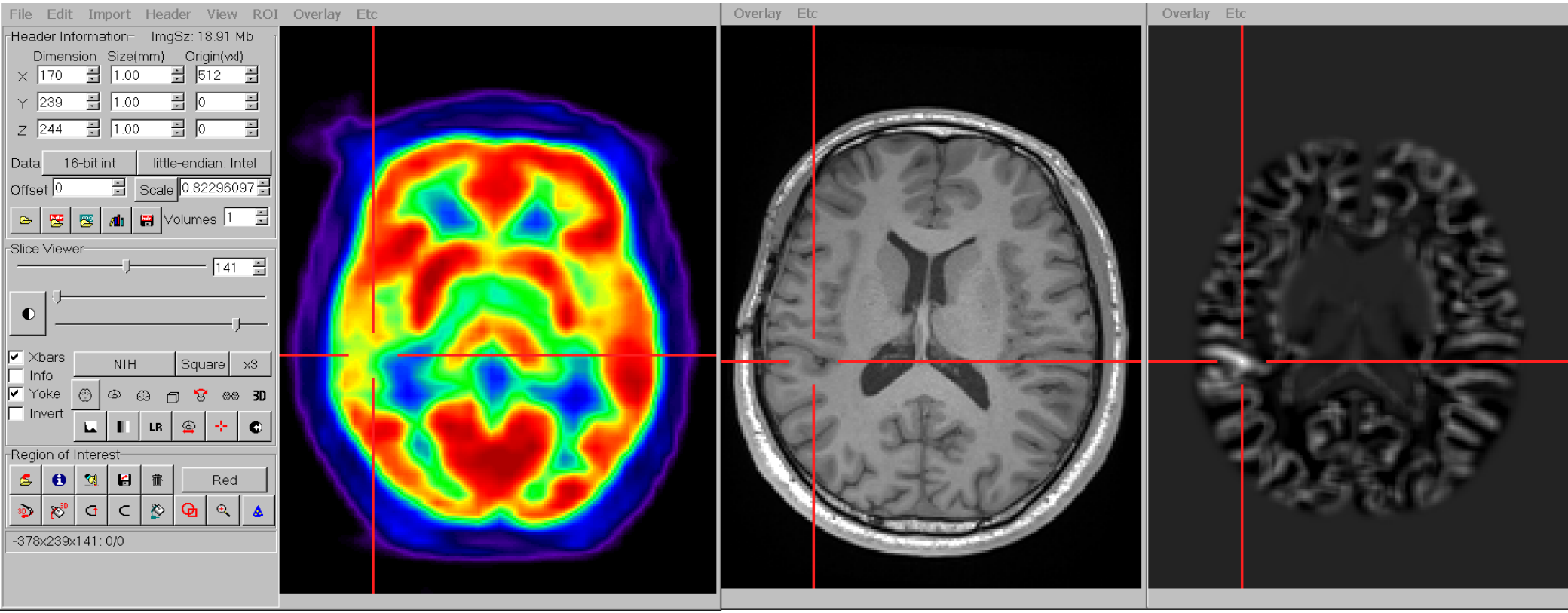
Case1_ non-lesional MRI_junction image



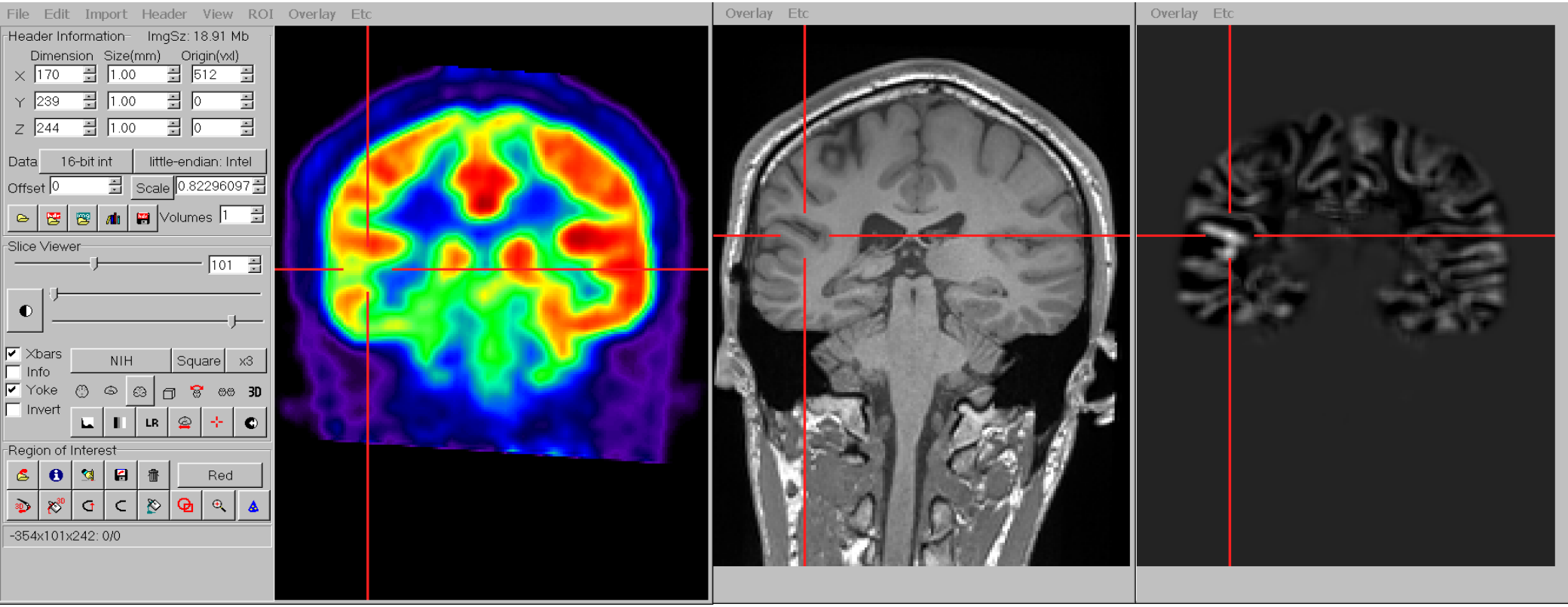
Case1_Seizure_Dipole localization



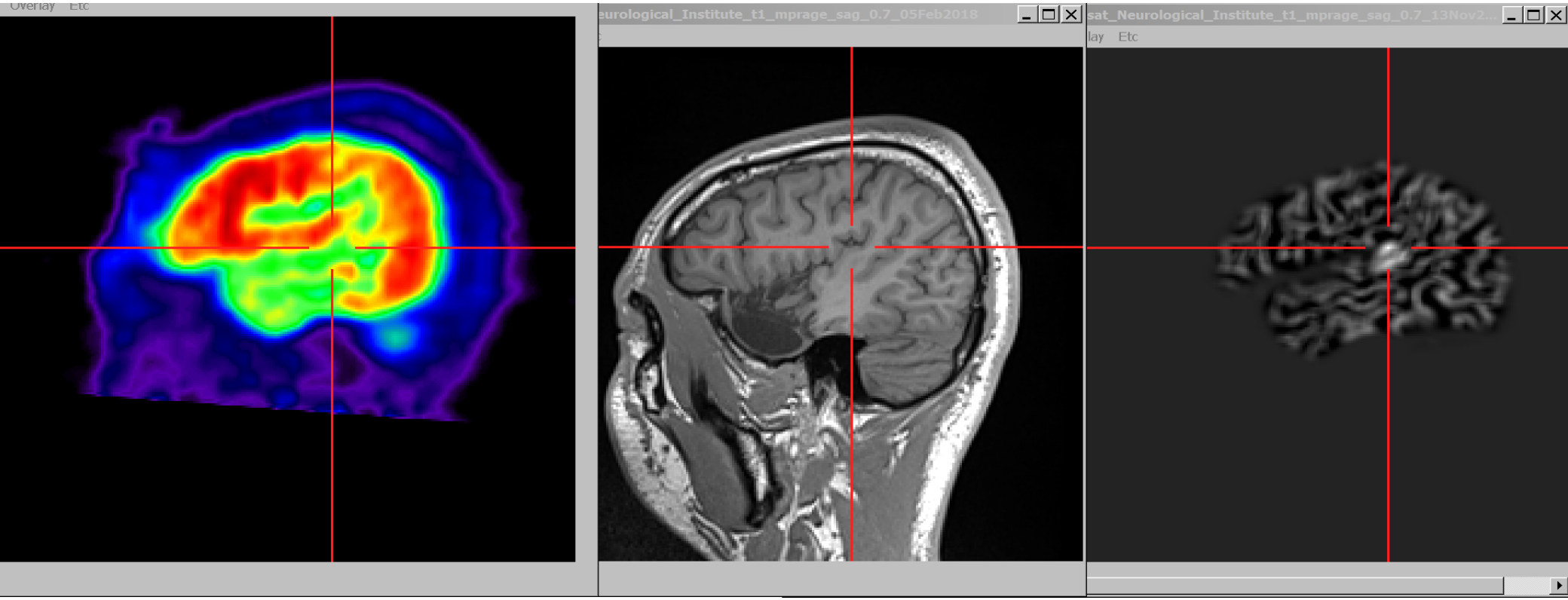
Case2_ PET_MRI_junction image



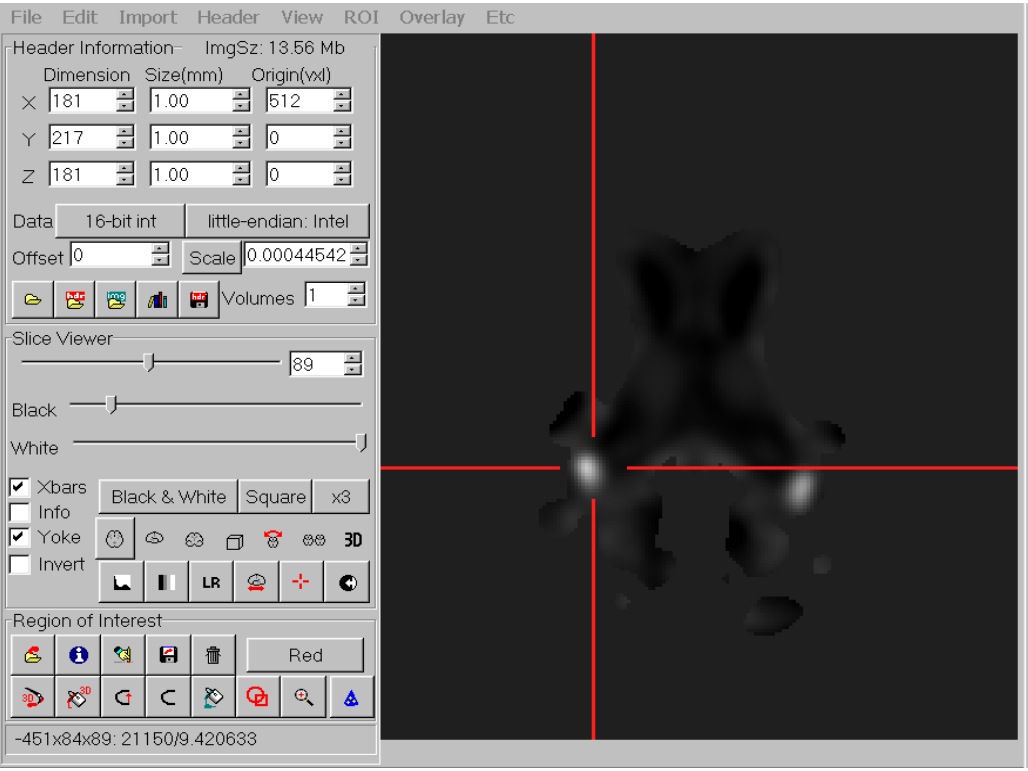
Case2_ PET_MRI_junction image

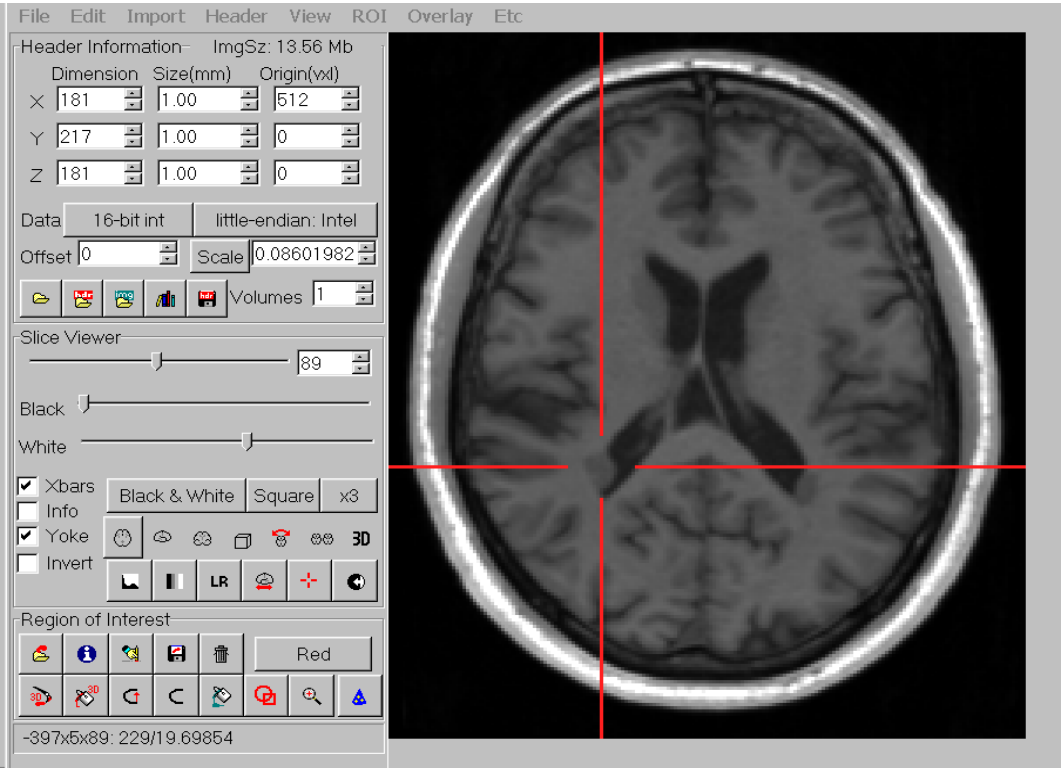


Case2_ PET_MRI_junction image



Case3_Perinodular Heterotropia





Case4_False Positive