ELAS TOOLBOX

Assignment of iEEG electrodes

Manual

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Content

The ELAS (electrode assignment) toolbox is a MATLAB tool, which combines several methods and software to assign iEEG electrodes to anatomical areas.

After explaining how to set-up the toolbox, a short overview is given to reveal the procedure of the electrode assignment approach. Subsequently the different methods and software are explained and how to use them.

Chapter 3 describes the handling of the pre- and post-implantation images before the electrodes are localized. For interhemispheric and stereotactic electrodes, the pre-implantation MR image has to be segmented into the different matter types.

Chapter 4 explains the tool for labeling the electrodes and gives an insight of the needed MATLAB format of electrodes and landmarks.

Chapter 5 describes the assignment of the electrodes to the anatomical regions. The first section explains the hierarchical probabilistic assignment of electrodes based on MNI coordinates (see Ruescher et al.). This assignment technique requires MNI coordinates of electrode positions (for PA) and, if available, information on the cortical lobe where the electrode is implanted (HPA). The second section presents an approach for the assignment of depth electrodes, based on the probabilistic assignment and the segmentation into matter type, reverting to the SPM Anatomy toolbox.

Chapter 6 presents the visualization tool for assignment results.

Chapter 7 gives a short overview of some extra tools provided by the ELAS toolbox.

The following code is required:

- ELAS toolbox
- SPM, e.g. SPM12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/)
- SPM Anatomy toolbox, e.g. v2.2c (http://www.fz-juelich.de/inm/inm-1/DE/Forschung/_docs/SPMAnatomyToolbox/SPMAnatomyToolbox_node.html)

1. Download and start the ELAS toolbox

Using git:

```
$ git clone https://github.com/joosbehncke/elas
```

For updates browse to ELAS working directory (…/elas) and type:

```
$ git pull
```

To start ELAS, browse in MATLAB to the toolbox directory and type 'startup_elas'. The first time you start ELAS, you will be asked to select the SPM installation folder, *this is mandatory for the functionality*. At first the fMRI mode of SPM will be opened and subsequently the ELAS toolbox (see fig. 1). Consider that SPM should be not closed until the processing is done, otherwise it will kill running processes and delete all variables.

Each step is isolated and can be run individually. Therefor certain individual variables which will be loaded have to exist or should be created in previous steps (see chapter 2).

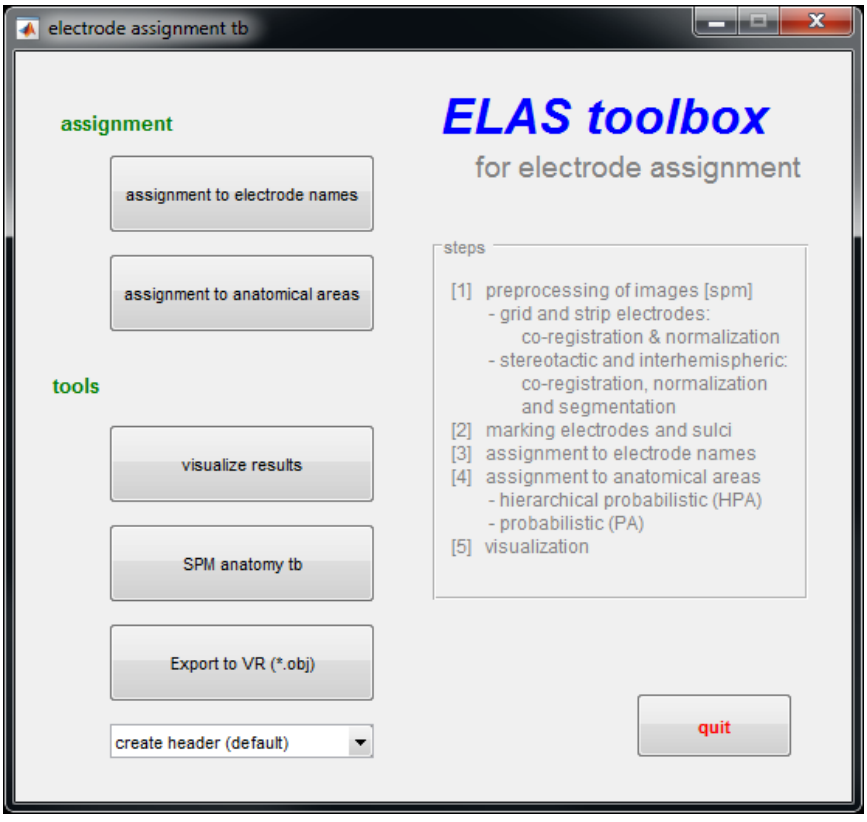

Figure 1: Welcome screen for the electrode assignment toolbox

2. The ELAS approach

The following table gives a short outline of the idea of electrode assignment. It is divided into the two different assignment approaches, namely the hierarchical probabilistic assignment (for grid and strip electrodes) and the probabilistic assignment (for depth electrodes).

	Steps (HPA, grid & strip)	**requirements**	**Steps (PA, depth)**	**requirements**
[1]	Preprocessing MR images (SPM): • co-registration • normalization → see chapter 3	MR images	Preprocessing MR images (SPM): • co-registration • normalization • segmentation → see chapter 3	MR images
[2]	Marking electrodes (and sulci) → see chapter 4	processed MR images	Marking electrodes (and sulci) → see chapter 4	processed MR images
[3]	Assignment to electrode names (ELAS) → see chapter 5	electrode coordinates	Assignment to electrode names (ELAS) → see chapter 5	electrode coordinates
[4]	Assignment to anatomical areas (ELAS) → see chapter 6	struct E	Assignment to anatomical areas Assignment to matter type → see chapter 6	- struct E - matter imgs (*.img,*.nii)

Table 1: ELAS approach

3. Processing of the MR images (SPM)

In this step, SPM is used to prepare the MR images for further processing. This comprises the co-registration of pre- and post-implantation images (first §), normalization of both images (second §) to a standard brain and subsequently the segmentation of the pre-implantation images into matter type (third §). The segmentation is particularly needed for the assignment of depth electrodes to matter type.

Co-registration of pre- and post-implantation MR images

- Choose *Display* for rough reorientation of anterior commissure, load image; select anterior commissure in image and shift position in each of the three orientations in opposite direction of mm value of crosshair. Select *Reorient images…* and the loaded file to save changes. This procedure has to be done for both image types.

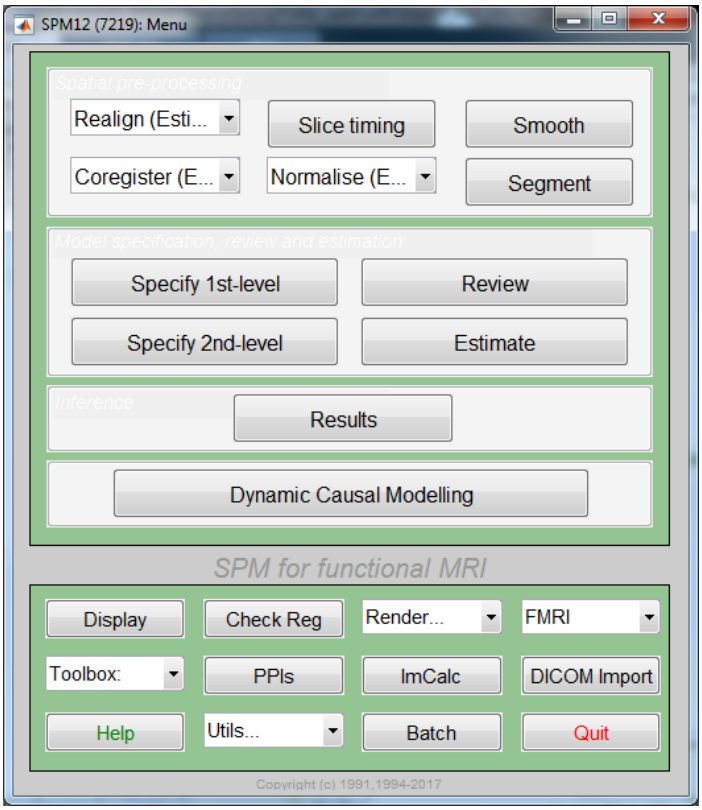

Figure 2: fMRI welcome screen of SPM12

- Choose *Coregister (Est & Res)* for co-registration.
- The *reference image* has to be the unchanged image type (post-implantation), the *source image* the one that will be changed. If there is only a post-implantation CT (the normalization doesn't work for this image type), the post-implantation image has to be chosen as source image and the pre-implantation MRI as reference. In this case, the normalization of the pre-implantation MRI has to be done before performing the co-registration.
- *Run* for starting co-registration. For the source image a file beginning with 'r' will be created.
- Choose *Check Reg* and load the old reference and the newly created source image to check.

Normalization of pre- and post-implantation MR images

- Choose *Normalize (Est&Wri)* (fig. 2)
- Batch Editor opens (fig. 3)

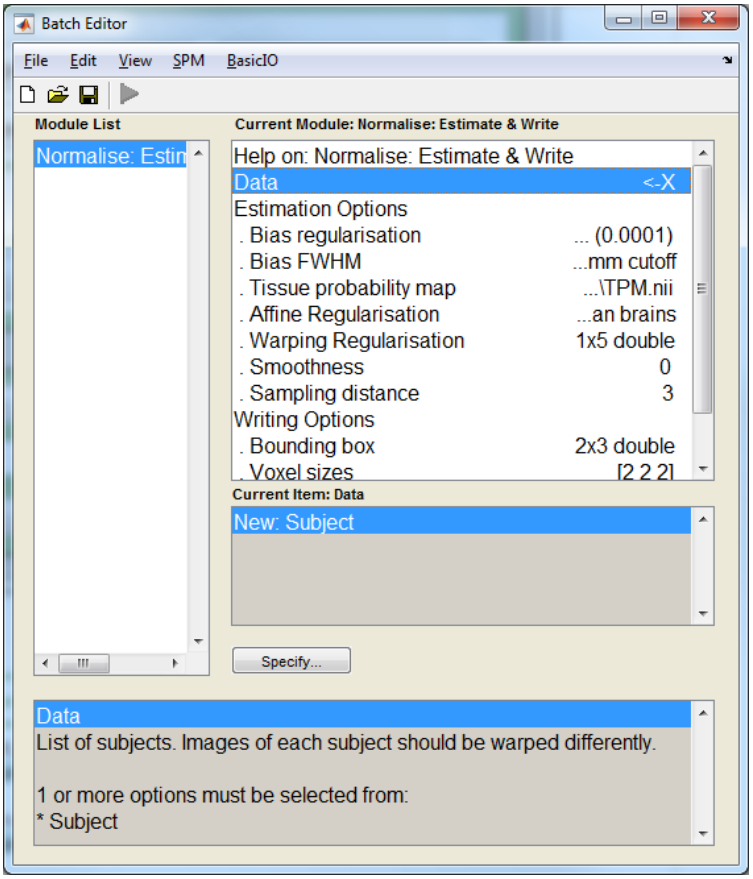

Figure 3: SPM Batch Editor for normalization

- Following modules have to be defined:

Data:	*Image to Align*	Select co-registered pre-implantation MRI
	Images to write	Select co-registered pre-implantation MRI ***and*** post-implantation MRI

(It is important to do the normalization of the two images with the same set of parameters, therefor for "Images to write" the both have to be selected)

Estimation Options:	*Template Image*	Select spm8\templates\T1.nii
Writing Options:	*Voxel sizes*	*E*nter 1 1 1
	Bounding box	*Enter* NaN(2,3)

The bounding box (mm) of the volume is relative to the anterior commissure. Typing NaN(2,3), SPM will get the bounding box from the data itself.

- Click *Run*

Segmentation into grey matter, white matter and CSF

- Choose *Segment* (fig. 2); again a batch editor opens. For *Data* choose the co-registered, normalized pre-implantation image (e.g. "wrPatientName.img").
- Clicking *Run* creates a segmentation image file and a segmentation header file for each matter type ("c1…" for grey matter, "c2…" for white matter and "c3…" for the CSF).

4. Assignment to electrode names and anatomical landmarks

Before labeling the electrodes, the marking of electrodes and individual sulci has to be done. This is not covered by this tool; other software implementations have to be used to do accomplish this work, e.g. brainstorm or MTV (toolbox for MR images, see chapter 7). MTV does the localization of electrode artifacts in post-implantation MR images (*.img/*.hdr or *.nii for normalization in SPM12) and the preservation of information on individual cortical anatomy. This step is done for each electrode type, including depth electrodes. In principle one can use any other method or software, ensuring the final input format of electrode and landmark coordinates (see below).

Next, electrode names (such as A1, A2…) from implantation schemes have to be assigned to the extracted coordinates. Per electrode group (grid, strip, chunk) the extracted coordinates (MNI space) have to be stored as a MATLAB file, containing the variable:

```
mni_dat = struct(...
                X, ...          (nx1 double) x-coords, electrodes
                Y, ...          (nx1 double) y-coords, electrodes
                Z, ...          (nx1 double) z-coords, electrodes
                sX, ...         (nx1 double) x-coords, sulci (optional)
                sX, ...         (nx1 double) y-coords, sulci (optional)
                sX, ...         (nx1 double) z-coords, sulci (optional)
                patID, ...      'str', patient ID (optional)
                group)          'str', name of electrode group (optional)
```

For starting the assignment click on the button *assignment to electrode names* in ELAS toolbox. You will be asked to type patients name and name of electrode group (e.g. G or FAL, TB,…) before the assignment interface opens (see fig. 4). Before you start, *get the y-coordinate of the end point of the horizontal ramus* (lateral sulcus), you will need it!

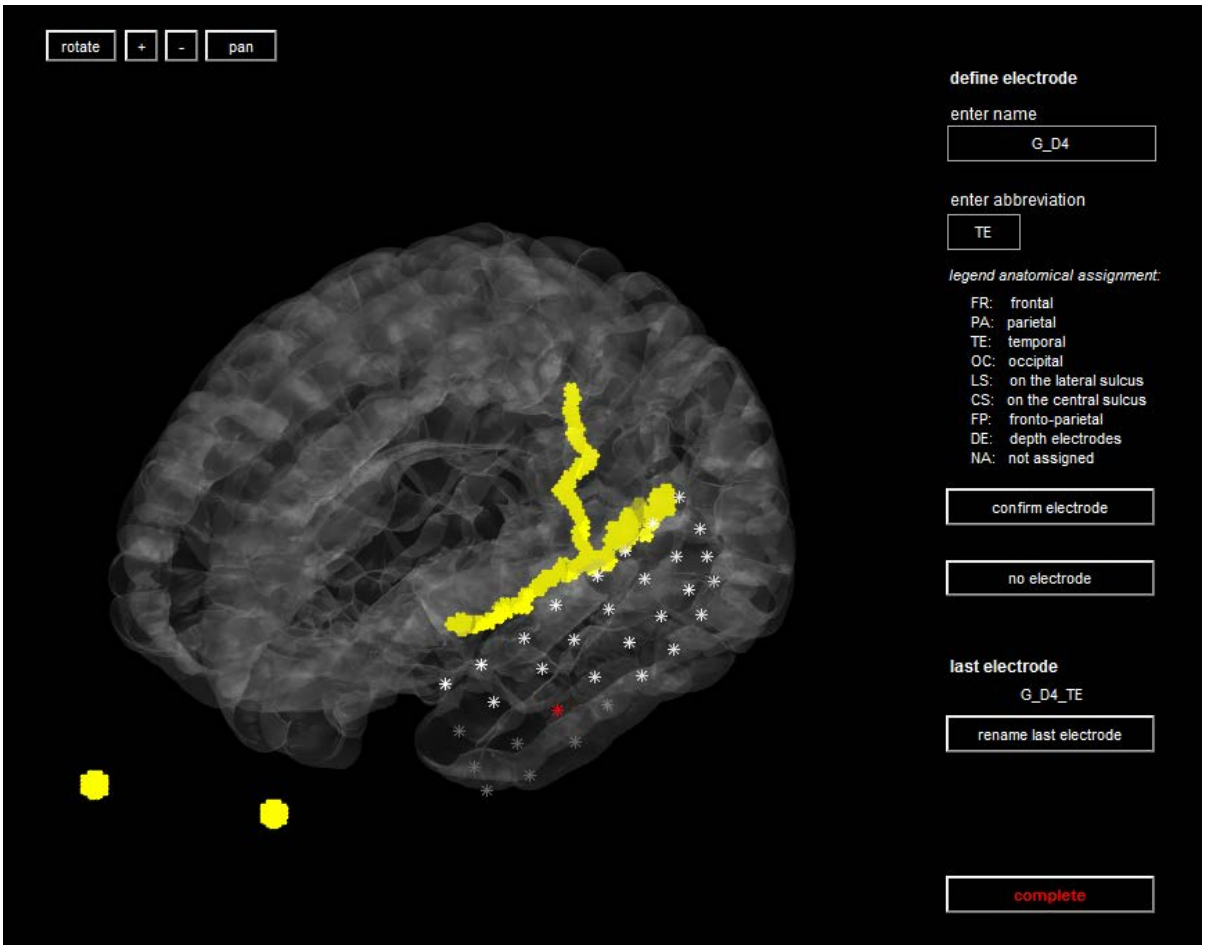

Figure 4: Figure used for pre-allocation of electrodes to lobes. Stars represent electrode markers; sulci (and eyes) are marked in yellow

- Use implantation scheme (clinics) in order to obtain the name of electrode currently marked with a red star (fig. 4). Grey stars represent electrodes already marked, white ones the electrodes that still have to be assigned to.
- At first, enter the electrodes name. Secondly, decide about an anatomical assignment. For depth electrodes use 'DE', if no anatomical assignment can be made or is not desired, just type 'NA'. The cursor is set to rotation mode, so you can have different views of the brain, but also can be changes to pan mode.
- When pressing *next electrode*, the red star moves to the next electrode, which again has to be assigned to name and anatomical area.
- If an error has been made, return to the previous electrode by pressing *rename last electrode*. You also have the possibility to skip electrode by pressing *no electrode*, or to end assignment by pressing *complete* (beware; assignment variable will be saved incomplete).
- Following the electrode naming, a dialog box asks you to enter the y-coordinate of the end point of the horizontal ramus (lateral sulcus). Look up the end point of the marked horizontal ramus of the LS and enter the y-coordinate as a number. If you don't want to include this information into your assignment, enter 'na'. Attention, you will have to define the right coordinate to use the HPA technique!
- The structure *E* will be created and saved.

5. Assignment to anatomical regions

Now, MNI-coordinates of electrodes can be assigned to anatomic regions, using Maximum Probability Maps (MPMs) obtained from the SPM Anatomy Toolbox of SPM. This step has to be done once for each electrode group. Start the assignment by clicking on the button *assignment to anatomical areas* in ELAS toolbox. Subsequently a second window will pop up, asking for file containing structure *E*. Select the file for the wanted electrode group and you will be guided to the selection of signal type of this certain group (see fig. 5).

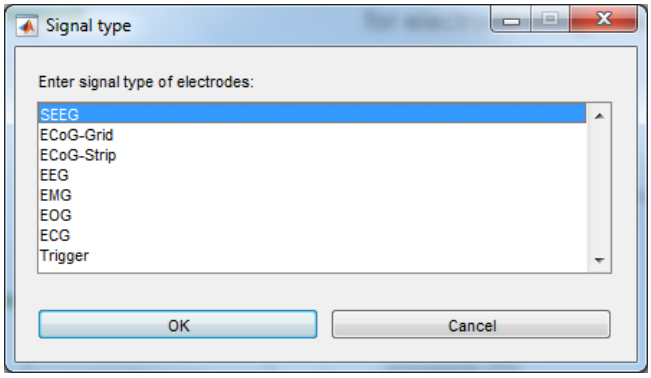

Figure 5: ELAS screenshot: Pop-up window after choosing assignment to anatomical areas

Choosing *ECoG-Grid* or *ECoG-Strip* will give you the possibility to choose between *hierarchical probabilistic assignment* and *probabilistic assignment*; meanwhile *SEEG* will run the *probabilistic assignment* for stereotactic and interhemispheric electrodes.

Hierarchical probabilistic assignment of electrodes

Note that this step only works for grid and strip electrodes! Each electrode is assigned using a patch of 5mm radius, containing on average 195 vectors which are projected onto a standard brain. The output-assignment is the most frequently assigned area underneath each patch. The mean of coordinates assigned to this area are also provided. Note that these are not necessarily the centers of the electrodes.

Probabilistic assignment of depth electrodes

For the assignment of the depth electrodes, the described hierarchical probabilistic assignment for electrodes doesn't work. Therefor another algorithm is needed, not using any hierarchical information. For this method, you will need the segmented matter files, which can be created by using SPM. The segmentation allows a distinction between matter types.

6. Visualization

Direct toolbox visualization

For the visualization, the individual information all electrode groups will be grouped to one header file. Either this has already been created or you will be asked to select the files for all groups. Together with all electrodes, the individual brain areas will be displayed color coded. You can select between all assigned areas, all cortical areas or all areas. The visualization tool provides different possibilities:

- Rotate, pan, zoom in and out
- Select and unselect electrode groups
- Select and unselect anatomical areas
- Save figure as *.fig or *.png file

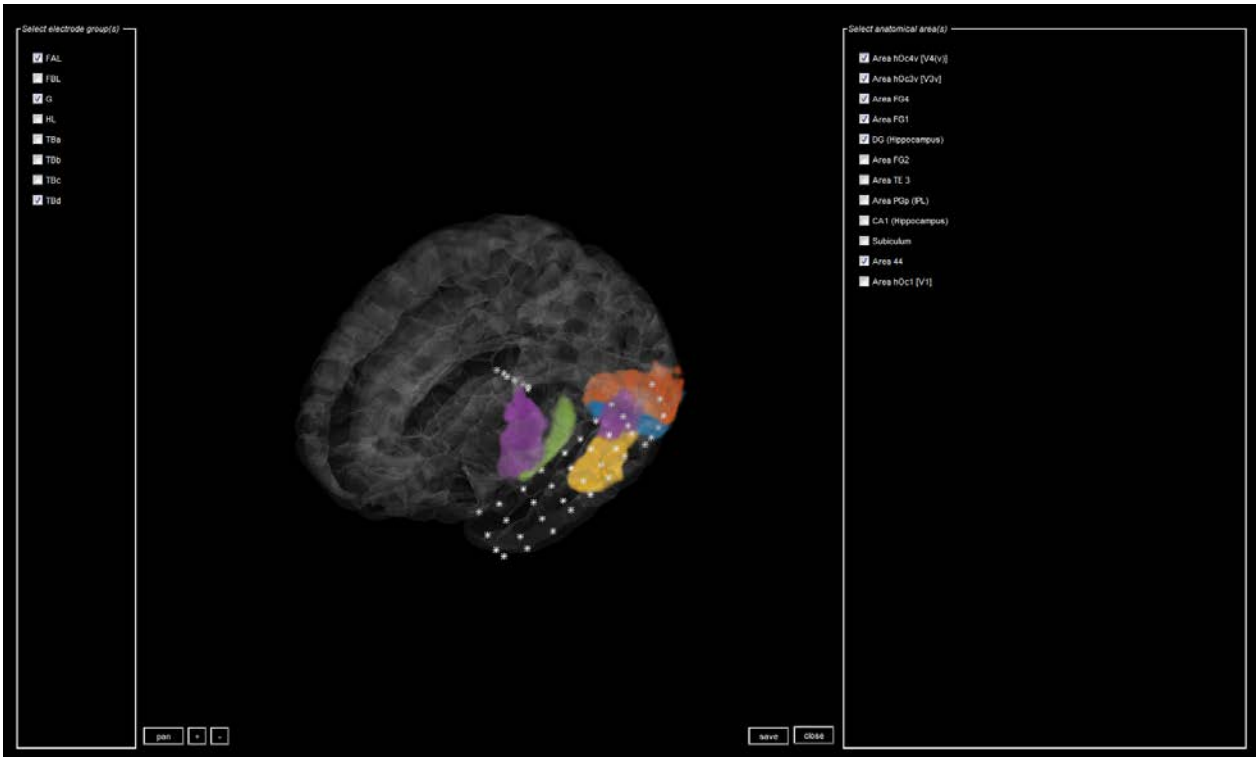

Figure 6: ELAS screenshot: visualization tool

Export to virtual reality (wavefront *.obj)

For an export to *.obj files you will be prompted to load (or create) the header file, containing information about electrodes and associated brain areas. The extraction tool provides the possibility to select an export of electrodes, brain areas and/or the standard ICBM brain 152, see fig. 7. For the electrode export two different modes can be selected. Selecting “real” extracts the coordinates inserted into the toolbox before assignment, just as they are marked inside the MRI. The option “projected” creates spheres according to the coordinates gained by the transformation process during the assignment. The projected coordinates can differ from the real coordinates and do not reflect the arrangement of e.g. grids or strips. They rather indicate the most probable location

according to the underlying brain areas. Furthermore the size of the extracted electrode sphere can be determined in mm.

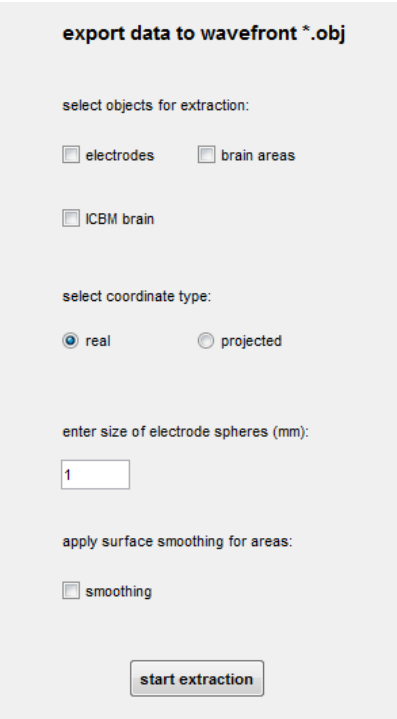

Figure 7: VR export tool

When choosing extraction of brain areas surfaces, only the areas that are matched in the assignment procedure are selected for the export. The surface extraction can be done for the raw isosurface created from the area point cloud or it can be exported in a smoothed version.

7. Tools

Furthermore the toolbox provides some simple tools.

Start SPM Anatomy toolbox

If desired, the SPM Anatomy toolbox can be started directly from the ELAS toolbox. If selected, the Anatomy toolbox start screen will be displayed in the big SPM window.

Create header (default)

This tool provides an algorithm to create a header file. Therefore, the files created during the step *assignment to anatomical* areas for all electrode groups are needed. This step only makes sense if the information set of electrodes is complete.

Convert img <--> nii

This tool allows an easy conversion of *.img file into *.nii and vice versa.

Start MTV

MTV can be started directly from the ELAS toolbox. Therefore, MTV has to be installed into: .../elas_open/MTV.

Marking electrode artifacts and individual sulci in MTV

Once the MR images are normalized, the electrodes can be marked. Therefor the software MTV can be used. In any case, it is useful to think about whether the sulci have to be marked or not. Therefore one could use the implantation schemes. If so, the sulci should be marked first. Subsequently the sulci session is to be saved. This session containing only the sulci markers will be the basis for the following marking of the electrodes. For each electrode group (meaning all electrodes belonging to one set, e.g. a grid or a strip) a session, containing the sulci and the electrodes of this certain type, has to be created. Don't forget to check the number of electrodes before marking!

- Load normalized image: - *file* → *NEW open background* → *MNI* ** select normalized image
- Create overlay: - *Overlays* → *New Overlay* ** define name for the new overlay, e.g. patients' pseudonym, and enter overlay type, which is rgb.
- Choose view, where you have all slices (coronal, sagittal, horizontal) in the same size:
  → Click 1**DataAspectRatio 1 1 1*; click 1**Axis Tight*; click *2*MODE* (white arrows in fig. 8)

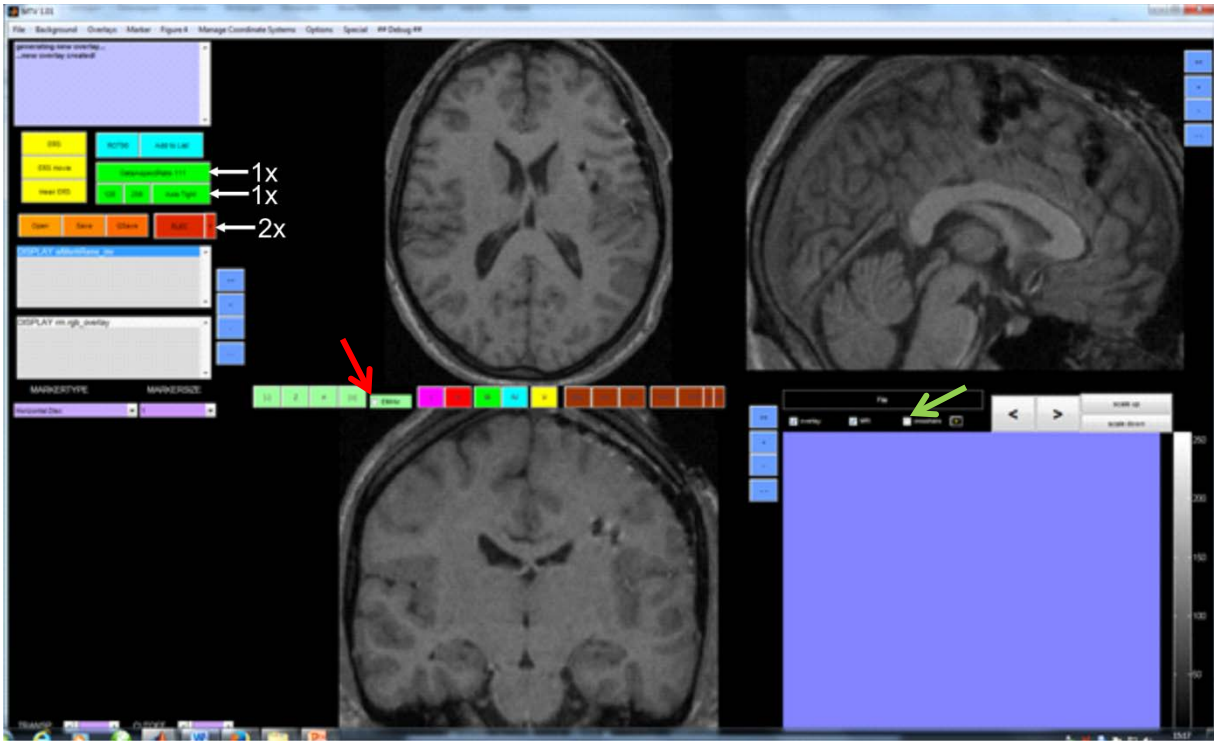

Figure 8: MTV screenshot: selection of suitable view

- Set markers for sulci
  - For hierarchical probabilistic assignments (HPA), central and lateral sulcus (CS and LS) are marked
  - Both sulci are only marked in cases, where electrode grids/strips overlap with the respective sulcus and are thus located on more than one lobe (such as fronto-parietal grids; in this case, CS must be marked)
  - Select MARKERSIZE (e.g. 2 for sulci), TYPE (Sphere) and color (use only **GREEN** for sulci)
  - Check for the **yellow dot** in the marker center: if existent, **remove** it by clicking on box *ElMrkr* (red arrow in fig. 8) in order to set markers without yellow center. Else, each marker of a sulcus is later identified falsely as electrode position.
  - Markers for CS and LS have to be set as close as possible to the cortical surface without overlapping with electrode markers. Set only one or two marker per plane (see fig. 9; left panel CS, right panel LS)

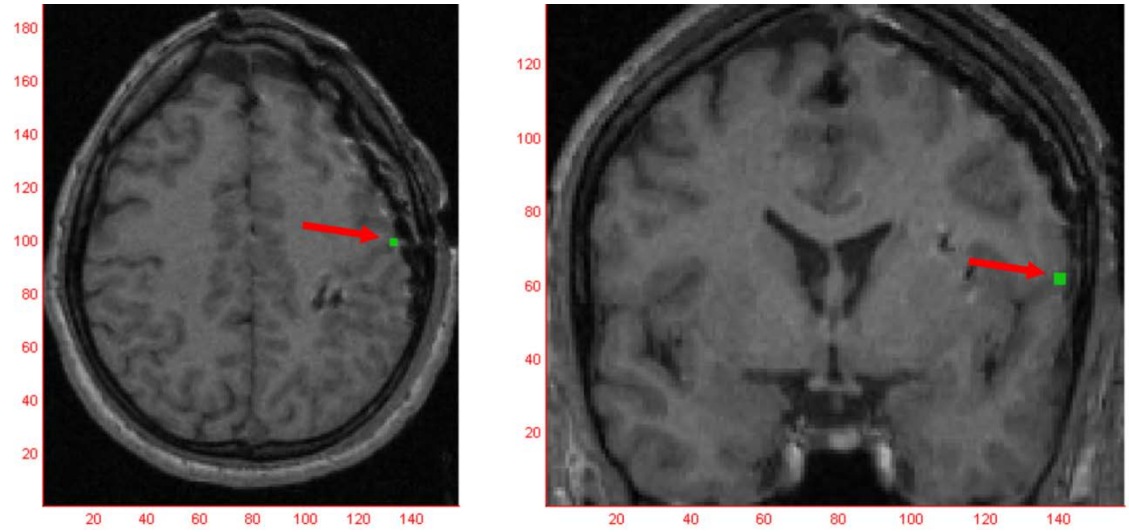

Figure 9: MTV screenshots demonstrating marker set on central (left panel, horizontal slice) and lateral (right panel, coronal slice) sulci

- CS has to be marked in its complete course, while it overlaps with electrodes. After identifying CS, start for example in a dorsal plane of the horizontal slice, set a marker and use – and + buttons to get to the next plane in the ventral or dorsal direction.
- For LS, only the horizontal ramus has to be marked. Although markers are set in vicinity to the cortical surface, the end of horizontal ramus can be distinguished easier in planes lying deeper in the sulcus. Do not mark further into ascending or descending posterior rami.
- Save your sessions regularly and rename it in doing so, since a file might be corrupted while saving!: *File → Save (General)*
- Sessions can be loaded and further processed using *File → open MRItv*

- Set electrode markers
  - Use crosshair (click box marked with green arrow in fig. 8) to find artifact center of an electrode in each of the three slices
  - Select marker: click either button I, II, III, IV,V
  - Select MARKERSIZE (e.g. 3 for electrodes) and MARKERTYPE (Sphere) in the left panel
  - Select marker color: *Marker → Define New Marker Color* →Use only **RED** for electrodes!
  - Select electrode marker: klick on box *ElMrkr* (red arrow in fig. 8) or use *Marker → Toggle "Use electrode marker"*; Set marker in order to check for **a yellow dot in the center** (see fig. 10). Only markers with this dot are later assigned as electrodes. If the yellow dot is missing, repeat clicking *Toggle "Use electrode marker"*
  - Set electrode markers at each artifact.
  - Save sessions as described before

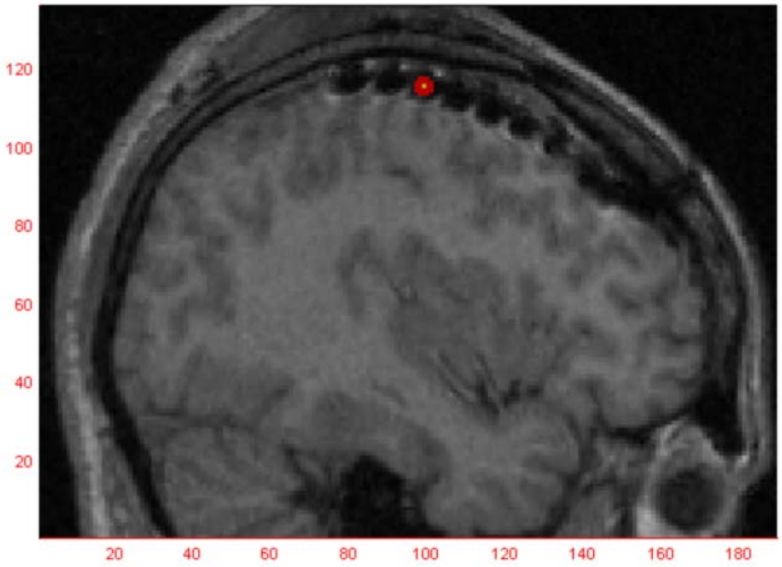

Figure 10: MTV screenshot of sagittal slice showing an electrode marker on a grid electrode artefact

- For an overview over markers present markers, use *Marker → Show Red and Green Markers in 3D.* An overview then appears in the lower right panel (see fig. 11). It can be rotated using *Marker → Rotate 3D ON* (Attention! Do not click in other panels while being in "rotate on"-mode! Before continue marking, use *Marker → Rotate 3D OFF)*
- Markers in the lower right panel can be clicked on in order to get directed to the respective voxel in MRI slices of the other panels

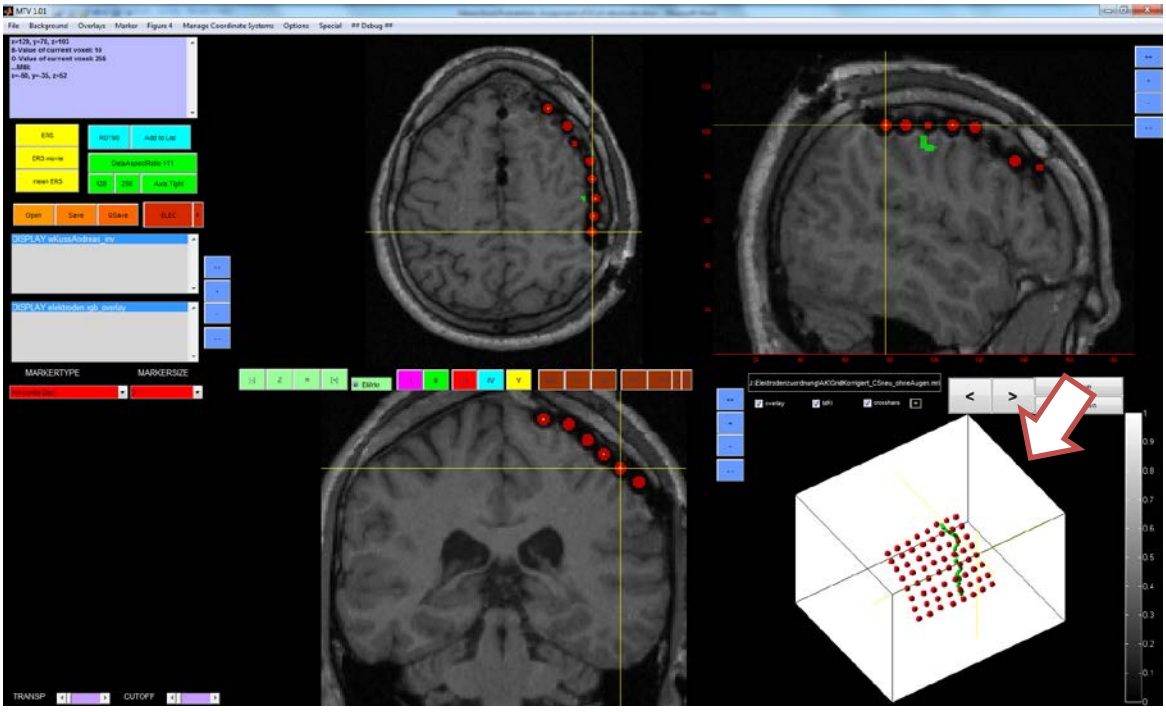

Figure 11: MTV screenshot of electrode markers and 3d view of red and green marker (arrow)