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Research 6.0
Epilepsy 1.0
MRI 2.0

Spike and seizure analysis using BESA pipeline

Recipe for LTM - EEG

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Assumptions

It is assumed that you have installed the **BESA Research version for LTM (Nov. 2014)** by expanding the self-extracting files into **C:\BESA LTM** (or on another drive). This folder contains all files relevant for the BESA-LTM tutorial and the BESA program (except for your own data).

Some of the initial work steps of data preparation are not described in this tutorial. The steps 1-6, for example, are outlined in more detail below in this document.

Important advices:

1. Before you start on your own data, make yourself familiar with the tutorial located in the documents folder (**BESA - Mapping and Localization - LTM Tutorial.pdf**) and run BESA with the provided teaching example. The better you do this job, the more easily you are going to work on your own data!
2. The new file export and concatenation batches (Sept. 2014) are designed to ease working on your own data by exporting LTM-EEG data in optimized, compressed form to the folder **C:\BESA Data**. This will help, in particular, when using BESA Epilepsy (BE) for spike detection as well as the pattern search utility in BESA Research (BR) to obtain high-quality averages prior to 3D-onset mapping and localization.

1. Prepare individual MRI segmentation and FEM using BESA MRI (BM)

- Start BESA MRI (BM) and create a new segmentation project using patient T1 / T2 data. When starting the project, consider anonymization and name convention (see below).
- Prepare MRI as outlined in the BM manual (~ 5 min.) and start automatic finalization.
- Anonymize and save the project. Use a systematic name convention by 'location & patient number': LOC, Pxxx (e.g. SZ, P001 for Salzburg). For saving your own data use a specific BESA MRI Shared folder in **C:\BESA Data** or on your LTM server.

  Note: At any time, the MRI projects (i.e. subfolders of your patients) can be copied to a different BM Shared folder (or zipped and transferred, e.g. by FTP).

2. Run BESA Epilepsy (BE) over an epoch having sufficient spikes

- When you start BE Detection on your LTM-EEG data, make sure that the same electrodes are assigned to each file correctly. For this, you should have created a standard electrode file in BE, i.e. Standard.elp. This file is located in the subfolder **Standard Electrodes** of the **BE Shared Data** folder (cf. Database Configuration).
- Run BE Evaluation (typically over a 24-h epoch) and decide on epileptiform hyperclusters.
- It is recommended to close BESA Research (BR) before sending triggers to BR.
- In BE, type **Ctrl+B** to send triggers and file names of the 24-h (or shorter) epoch to BR.
- Now, BR should open automatically with all files and show the last transmitted EEG file with the triggers 51…5x sent from BE in the event bar. If BR does not come up, click onto the BR icon in the task bar to bring BR to the foreground. If an error occurs, close BR and send triggers again from BE to restart BR.

Important note: Do not switch between files in BR, because this will change the file sequence sent from BE as required for concatenation. Proceed to concatenation immediately – next step!

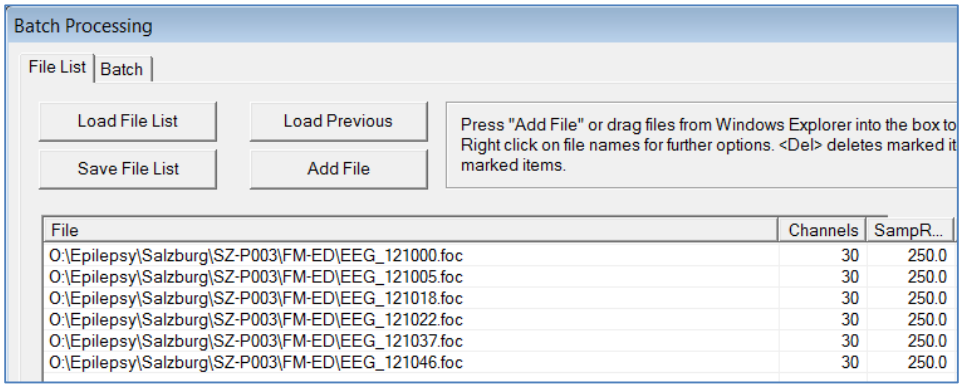
3. Export and concatenate to one 24h-EEG file for analysis in BR

LTM-EEG mostly consists of short files, i.e. 1 – 4 hour EEG files. If spikes are rare, it can be necessary to put all files together into one BESA file to obtain a sufficient number of spikes for averaging, e.g. by pattern search. Another advantage of having one continuous BESA EEG file is working speed by using only the channels required (EEG + EKG), i.e. leaving out superfluous channels, and down-sampling to a sufficient sampling rate while removing the 50/60 Hz mains interference at the same time. Together with storing in an effective compressed format, this data preparation in BR will speed up file handling and any further processing enormously, e.g. seizure detection, spike pattern search and averaging.

The most convenient way is to use the 24-h epoch defined in BESA Epilepsy to concatenate all files with all hypercluster triggers into one ~24-h compressed EEG file in only one step. This continuous 24-h file can then be used for automated seizure detection using a new algorithm published by Hopfengärtner et.al. 2014, or by performing a DSA scan.

Proceed in the following way:

- After you have sent triggers from BE to BR (see above), BR will open with all files loaded in the correct order for concatenation.
- In BR, select **Process→ Batch Scripts** or type **<Shift>+R** to open the tabs for processing a list of files. The list should be automatically in correct ascending order for concatenation, e.g.



  Otherwise, resort to obtain ascending order by right click onto file names at incorrect positions.
- Select the tab **Batch** at the top, and press **Load Batch** to open the following batch file in folder

  …\BESA\Scripts\Batch\Export & Concatenate:

  A_Concatenate_Open-Files-to_C-BESA-Data-Pxxx-at-250Hz_Notch50.bbat
- If you have created a standard montage for export to remove superfluous polygraphic channels and to keep only EEG and EKG, select the batch function

  B_Concat_Open-Files-to_C-BESA-Data-Pxxx_at-250Hz_Notch50_Standard-Mtg.bbat

  The standard montage **Standard.mtg** must be saved and located in the following folder:

  … BESA\Montages\Channels
- Press **OK** to start the concatenation batch.
- Finally, in the export data folder, **C:\BESA Data**, rename the exported and concatenated file **Pxxx.foc** to assign the correct location and patient ID, e.g. **SZ-P003_2014-07-15.foc**. Add the date (+time) information to protocol when this file was recorded.
- You may anonymize the concatenated BESA file at this stage using BESA Anonymizer.

Note 1: Files can also be exported individually using the batch functions provided in folder **Export & Concatenate** and then concatenated later. You may do this, for example to combine all files containing seizures to one BESA file containing all seizure over several days.

Note 2: If your mains frequency is 60 Hz, use a text editor to change the frequency in the required batches. Some important batches have also been provided for 60 Hz in this folder.

Note 3: If you want to keep the high sampling frequency or downsample only to 500 Hz, there are other concatenate or export batches where you can see the required settings. Use a text editor to modify a concatenate batch as needed.

Note 4: If you are using a different export folder, make sure to use a text editor to edit the batch files such that they show your path and location in front of the patient dummy name. For example, if your BESA folder is on the **D:** drive and you are working in Salzburg, rename the strings in the batches to: **D:\BESA Data** and **SZ-Pxxx**.

4. Register the concatenated BESA EEG file with the individual MRI

- In BR, open the concatenated EEG file **%basename%.foc**.
- Press **Ctrl-L** and **Browse** for Digitized head surface points (**.sfp**). If an individual digitization file exists, load this file (you may check for this by typing **V** to view the electrode cloud; if it does not look spherical and if the radius is not 85 mm, digitized surface points are already in the file).
- Otherwise, you need to pull standard electrode coordinates onto the individual MRI and adjust. Select Standard Electrode Folder to load **BESA-MRI-Standard-Electrodes.sfp**.
- Press **Edit/Coreg** to start registration. In BM follow the work steps as described in manual.
- **Important note:** With digitized electrodes un-tick **Scaling..** in **Advanced Settings** before Fit.

5. Inspect spikes detected by BESA Epilepsy to create selected averages

- In BR, accept the registration and press **F3** for standard filters and viewing in average reference montage. For spike review you may keep Av33 or select an appropriate source montage.
- Type **S** (= **View → Selected**) to view the trigger epochs detected in BE. Select trigger 51, type Pos1 to go to the first detected event and use the page buttons and/or keys N/B to inspect all epochs. Click into epochs with excess noise or very weak signals and type **D** to delete.
- Repeat this inspection and deletion of bad epochs for spikes type 2, 3 etc. (triggers 52, 53…).

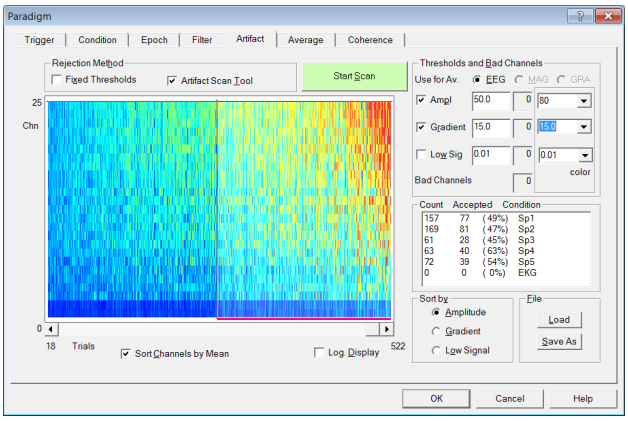
  Inspection is necessary to check, whether different types of events are mixed in a hypercluster, e.g. temporal lobe spikes and eye-movements.
- After completing the inspection type **R** to run the batch:

  Average-All-BESA-Epilepsy-Spikes.bbat.

  Note: If one consistent spike type predominates in the hypercluster, you can create an optimized selected average that only includes the spikes with low noise in the epoch before the spike rises. This is done by the following batch:
- Type **R** to run the batch:

  Baseline-Check-BESA-Epilepsy-Spikes-to-Create-Selected-Average.bbat.

This batch will stop after checking EEG amplitudes and gradients in the epoch of -280 to -80 ms before the spike event:



Use the vertical cursor to reject spikes with large preceding activities. Retain at least 40% or the spikes (not less than ~25).

Check Amplitude and Gradients.

You may adjust color scale at the right (here Ampl. was set to 80 µV).

The number of accepted spikes is indicated in the list for all spikes types Sp1-Sp5 at the lower right.

- Press **OK** to continue.
- BR stores the selected BEspike averages in %basename%_BE-sel.fsg, saving triggers in .evt.
- The batch opens the averaged file for inspection and sets the low forward filter of 5 Hz and the high filter of 40 Hz. Thus, you can map onset immediately.
- If the signals, spike types and number of averaged spikes appear sufficient, you may proceed from here to workstep 8.

  Note: Automated detection and averaging is not a substitute for careful visual scanning of the LTM-EEG, at least of selected 2- or 5 min. epochs every hour.

6. Scan EEG visually to find spikes and set tags to create selected averages

- Press **F3** to set AV33 montage and spike filters and epoch.
- For sharper spikes, press **F4** to obtain a higher low filter cutoff at 4 Hz.
- **Scan visually** for different spike types (5 different types can be stored in buffers 1-5).
- **Click on peak** to map, adjust cursor to maximum in 3D map, type **T** to tag and select pattern 1…5 or type number key (easiest way) to store different spikes types.
- After scanning, press **R** to run the batch: **C_Average-Visually-Detected-Spikes.bbat**.
- BR stores the averaged visual spikes in **%basename%_VS.fsg**, saving triggers in **_VS.evt**.

Normally, you will not mark very many spikes of the same type. Therefore, it is recommended that you use averages of the visually marked spikes as templates for pattern search over the whole file as explained in the next workstep.

7. Find spikes by pattern search using single or averaged spikes

See chapter 5 in the **BESA - Mapping and Localization - LTM Tutorial.pdf** for details on marking a single event in an EEG file as template for pattern search. Here, we want to give some additional hints after a brief summary:

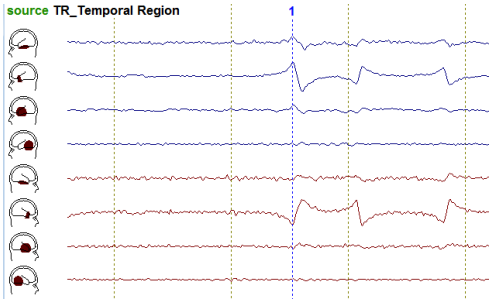
- Press **F3** for standard spike viewing, then **F4** for sharper spikes to increase the low filter.
- Press **SAV** to start pattern search. Check for the filters and interval you want to use.
- Press **OK** to run search. Do not click anywhere in BESA while search is going on.
- After completion, type **Pos1** to start reviewing from the first epoch. Click into epochs with noisy signals before the spike or with weak spike signals and type **D** to delete.
- Press **F6** to average, or better with many spikes, type **R** to run

  D_Baseline-Check-Pattern-Search-Spikes-to-Create-Selected-Average.bbat

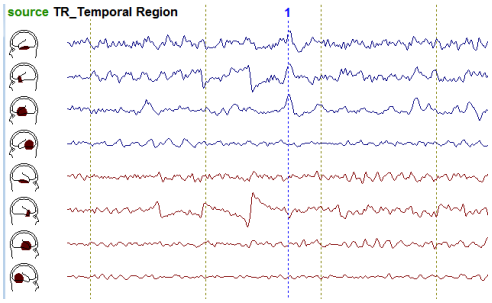
  in order to select only the epochs that have the lowest noise (cf. diagram above).

Hints:

- It is recommended to use the **Av33** montage with all channels or a specific source montage. e.g. TR_Temporal Region.

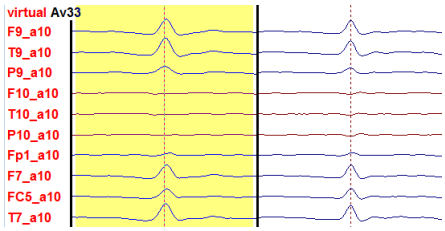


Lateral eye movements

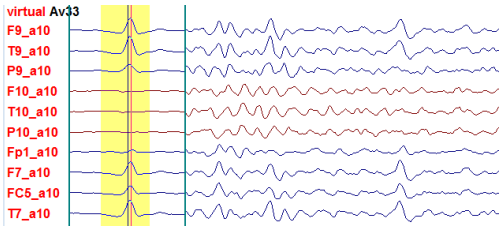


Spike - in same patient, preceded by eye mov.

- However, especially with temporal lobe spikes, eye movements can be included since they can have a similar topography in scalp montages, e.g. **Av33** (used for the search example above with relatively low correlation threshold). Therefore, it is advised to check detected events carefully.
- Typically, lateral eye-movements have opposite polarities on the right and left. Therefore, it is useful to check for the absence on one side (best seen in source montages, e.g. **TR**). Ideally, you should mark all channels of the selected source region on both sides for spatio-temporal pattern search (e.g. the first 8 channels in **TR_Temporal** Region).
- Averaged spikes can be used as templates in the following way:
  1. Open the original EEG files and then the averaged file.
  2. Press **F3** to set the filters in the averaged file. Press **F4** if you want to use a narrower filter band and epoch.
  3. Mark the whole segment (or most of it) as illustrated below.
  4. Type **Ctrl+C** to copy into buffer (select, e.g. Buffer 5).
  5. Press **–F** to return to the original EEG file. Press **F3** as well as **F4**, if you did this in the averaged file, to obtain exactly the same filters for template and original data.
  6. Select **View → Average Buffers**, to view the buffer overlaid over the EEG and click and adjust latency to map the peak. You are now ready to use the cleaner averaged signal – filtered in the same way as the EEG! – for pattern search.



Marked segment in average



Click to mark search pattern in copied buffer

7. Press **SAV** to start pattern search and make sure to select Current Filters, if you have used **F4** filter settings. Epoch settings can be as desired.

8. Localize spike onset region visually by 3D voltage mapping

- Open an averaged spike file.
- Press **F5** to set optimal filters for onset mapping (you can increase the low filter cutoff by pressing **EdF** and setting frequency to 10-15 Hz, if the spike is sharp and baseline noisy).
- **Click** onto onset and peak to map (use scroll wheel or arrow keys ← → to change latency).

See chapter 4 in the **BESA - Mapping and Localization - LTM Tutorial.pdf** for details on how to localize on the basis of spike voltage mapping.

9. Localize and image spike onset automatically using individual MRI

See chapters 6 & 7 in the **BESA - Mapping and Localization - LTM Tutorial.pdf** for details. Here, we want to give some additional hints:

- Press **F7** to if you want to fit the EEG spike in the 1st segment, Sp1. If you want to fit another averaged spike (Sp2…Sp5), type R to run the batch **2_EEG_Fit-Averaged-Spike_Sp2.bbat** or batch **3_EEG_Fit-Averaged-Spike_Sp3.bbat** etc.
- After you have defined the onset and localized the onset source, you may set a **cursor** at the maximum of the source waveform in the onset epoch and press **CLARA** to image. The, control if a focus consistent with the onset dipole is found.
- You may have to advance through the maxima by pressing the Max button ()., because the EEG background can generate an additional source in deep regions.
- **Note:** CLARA images are always deeper into the brain due to the smoothing constraint of LORETA. In combination with the onset dipole, the onset region can be defined considering that source extent cannot be imaged (!) and depth is only a crude estimate.

10. Seizure onset analysis by phase mapping

See chapter 8 in the BESA-Guideline-to-Mapping-and-Localization for details. Here, we want to give some additional hints:

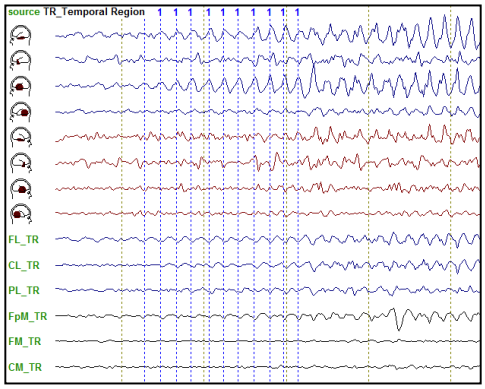
- After you have navigated to a seizure onset, first press **F8** to set a 1 s default block when you click onto the EEG.
- Next, press **F9**, **F10, F12** to observe in which montage you can observe an oscillatory onset pattern best. **F11** restores the TR_Regional Source montage.

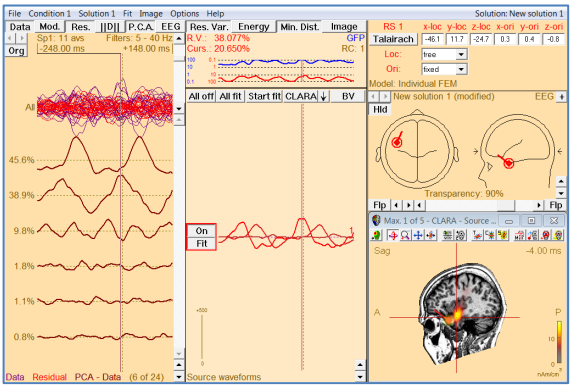
- **Click** onto the pattern and adjust the 1 s block to cover the earliest oscillatory onset pattern. You may also drag over several cycles before the pattern changes and propagations sets in. Note, however, that a minimum of approximately 600 ms is required for FFT.
- Type **F** to compute and display FFT. If the header is **Ampl. Spectrum**, click onto it to switch to **Power Spectrum**.
- Check if a focal spectral peak dominates. Then, **click** onto the peak value and **right click** into best viewpoint of the power map to view and interpret the phase maps.
- You may repeat this for different epochs during the onset, but remember to stay early enough and not extend the marked epoch over 2 s or over an obvious frequency change.

11. Seizure onset analysis by averaging over onset cycles

The basic idea is to mark the seizure onset cycles manually and use the average function. Make sure to mark only the earliest cycles before propagation sets in and frequency changes. As a rule of thumb, frequency gets lower as more cortical tissue gets involved.

- After you have navigated to a seizure onset, first press **F8** to set filters and default block.
- Next, press **F9**, **F10, F12** to observe in which montage you can observe an oscillatory onset pattern best. **F11** restores the TR_Regional Source montage.
- You may want to press **EdF** increase the low filter to 6 or 8 Hz (zero-phase) or 10 Hz (forward) for a better definition of the sharper rising ramp that can often be seen in seizure onset cycles.
- **Right click** onto the peak cycles that are not contaminated by background EEG to set tags (e.g. Pattern 1, if spike triggers are not present in the file, or Pattern 5 – make sure corresponding triggers 45 are not in the file – otherwise save events and delete).





- Press **F6** to average and, in the averaged file, **F7** to localize, if Pattern 1 was used. If Pattern 5 was used, type **R** to run **5_EEG_Fit-Averaged-Spike_Sp5.bbat**.

The fit batch for spikes will also work for the average seizure onset cycle. Mark the onset prior to the cycle peak as onset interval. Use the regional source model as reference and try out **CLARA** at the peak of the cycle (see above right). Note: The number of averages is small and the signals are noisy. Localization is less reliable as compared to spikes.

References: Beniczky et al. (2013). Epilepsia 54: 1743-1752. Kovac et al. J. Clin Neurophysiol. 31: 10-20. Rosenzweig et al. (2014) J. Clin Neurophysiol. 31: 1–9 (phase maps).

Summary of function keys and fast operations

Function keys in BESA Research 6.0 for LTM

F2-F5/8	***Set montage to***	***Set filter***	***Set block around cursor***
F2	**BiHL** - bipolar mixed	LF: 0.53 Hz fw / TC 0.3 s	+- 20 ms
F3	**AV33** – aver. ref. a10	LF: 2 Hz zp – 35 Hz zp	-250 ms : +150 ms
F4	no change in montage	LF: 4 Hz zp – 30 Hz zp	-150 ms : +90 ms
F5	no change in montage	LF: 5 Hz fw – 40 Hz zp	-250 ms : +150 ms
F8	**TR-source** for seizure	LF: 3 Hz fw – 20 Hz zp	-500 ms : +500 ms

F6-F7	***Run autom. process***	***Batch - modify association by pressing Shift+Fkey***
F6	Convert tags to triggers 41-45 and average	F6_Spike_Convert-Tags_and_Average.bbat
F7	Fit sources to 1st spike onset & peak (Sp1)	F7_EEG_Sp1_Fit.bbat (also prepares CLARA image)

F9-F12	***Set montage to***	***Optionally modify by***
F9	**AV33** - average ref. a10	pressing Shift+F9 to associate key with current montage
F10	**BiHL** - bipolar mixed	pressing Shift+F10 to associate key with current montage
F11	**TR** - temporal sources	pressing Shift+F11 to associate key with current montage
F12	**FR** - frontal sources	pressing Shift+F12 to associate key with current montage

Paging and navigation

<Space>	page forward	start & stop of automatic paging, if on.
B	back half page	
N	next half page	
A	automatic paging	toggle on/ off
Scroll wheel	page for- / backward	easy paging by using the mouse wheel
<Tab>	Go to next event	type as defined in Tab menu
Shift+<Tab>	Go to previous event	type as defined in Tab menu
S	Selected view	select trigger or tag to view epochs

Mapping

Click onto EEG	3D map	center view shown automatically
Scroll wheel	shift cursor	easy to find peak and remap at cursor
Arrows ← →	shift cursor	3D map rotates automatically
<Esc>	remove cursor and	close map & top view windows