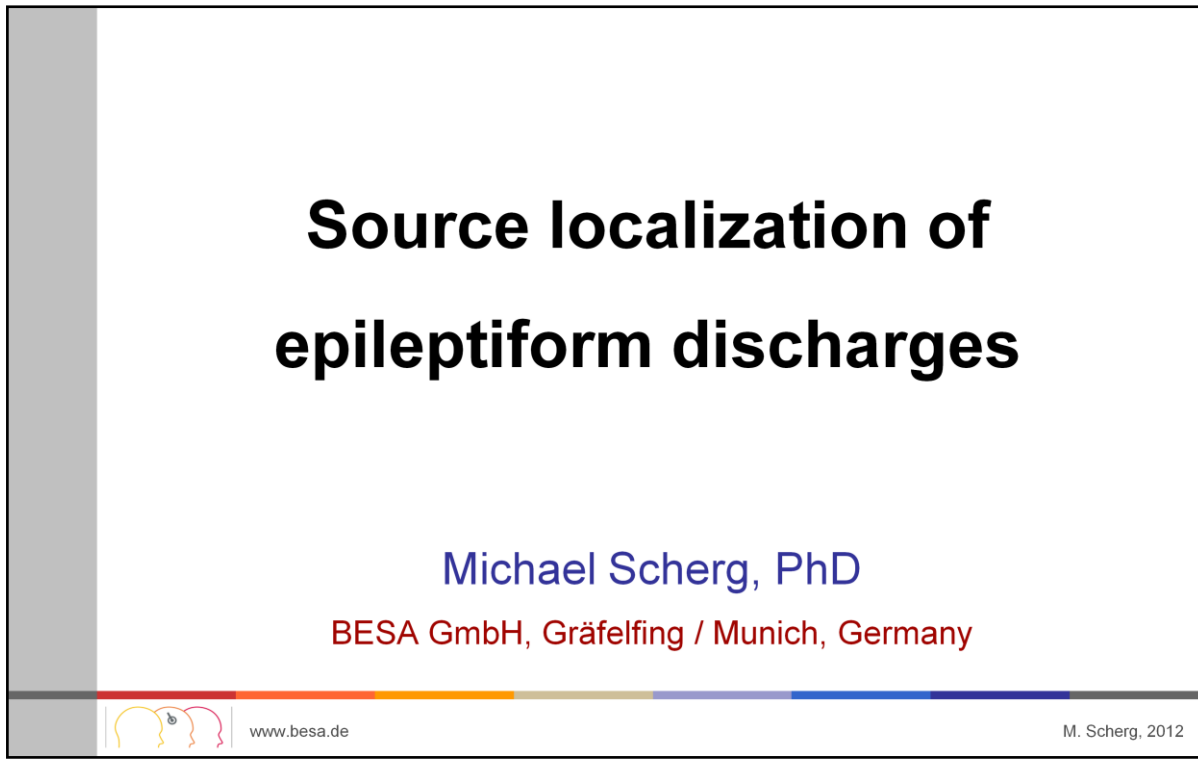


This presentation was given during the Dianalund Summer School on EEG and Epilepsy, July 24, 2012.

The main purpose of this tutorial talk is to give an introduction into the principles of source localization applied to interictal spikes and to demonstrate its feasibility and limitations in clinical practice. You should also learn the needs and practical steps for localizing averaged interictal spikes from scalp EEG.

Disclosure:

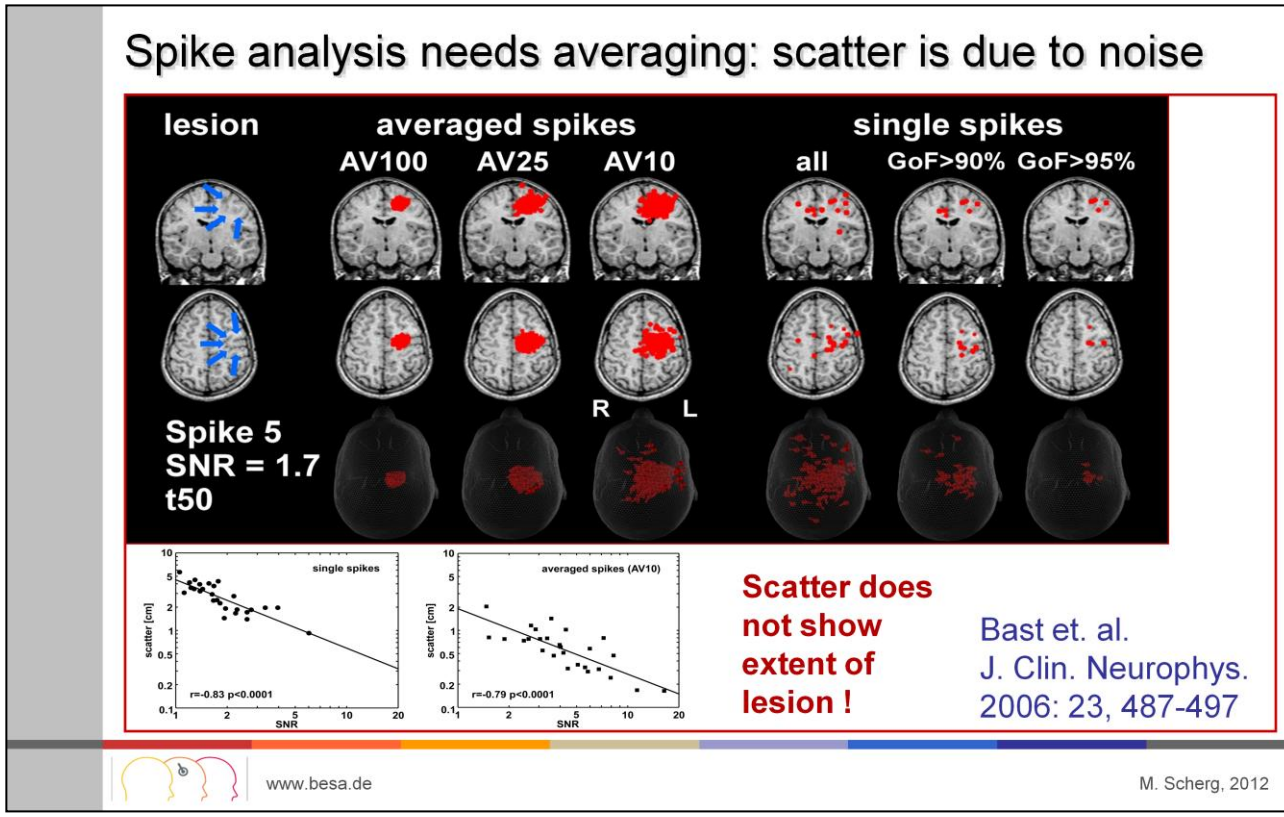
Michael Scherg is a shareholder and employee of BESA GmbH.

He has been heading the development of the software packages BESA Research and BESA Epilepsy.

Localization and imaging of spikes

1. Why do we need to average?
2. How do we average best?
3. How do we find out whether the peak is propagated?
4. How do we localize onset versus peak?
5. Which other imaging methods should we use?
6. How sure can we be about localization?

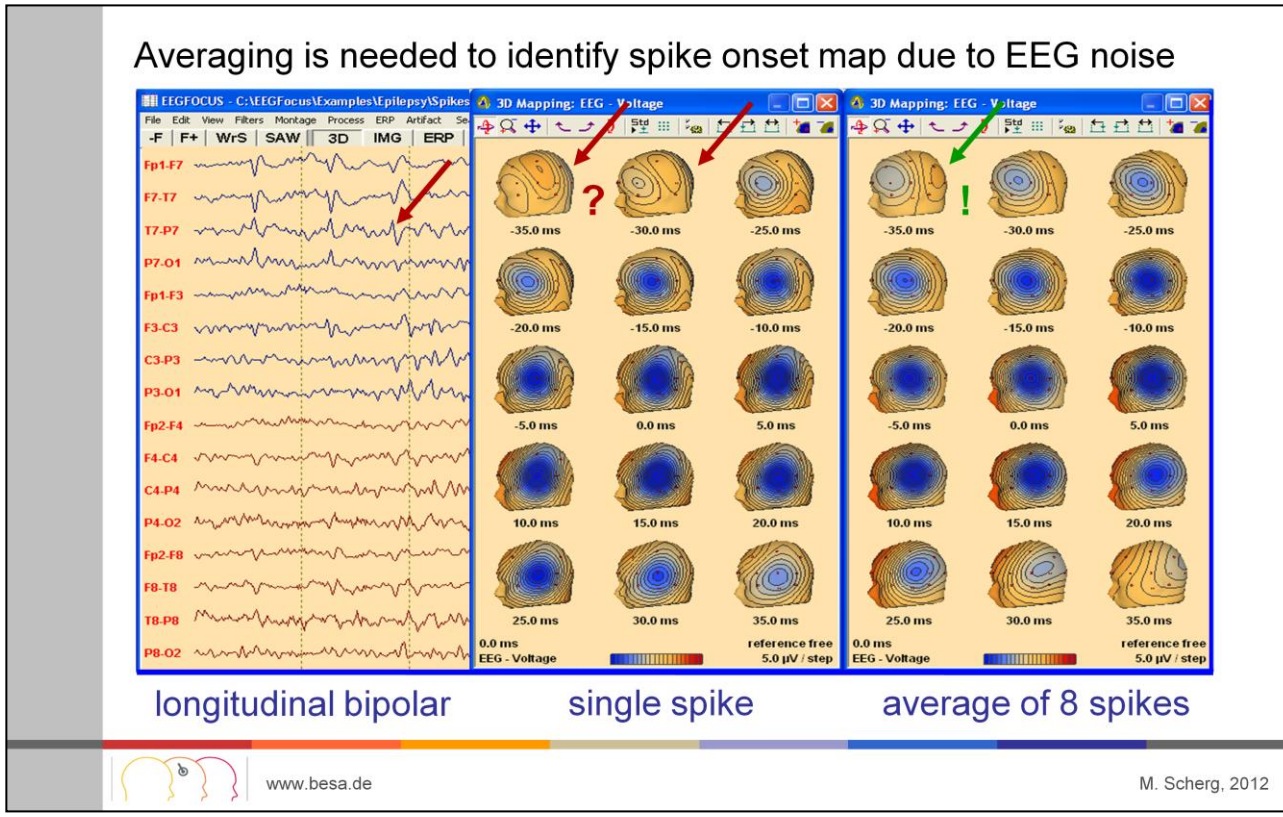
The listed questions will guide us through the necessary steps for adequate spike localization.



In a recent paper, Bast et al. (2006) showed that it is rarely possible to identify and localize spike onset using single spikes. Even at a latency half-way between onset and peak, only a very small number of spikes exhibit sufficient signal quality over the EEG background (right) such that they can be localized using a single equivalent dipole with a goodness of fit of more than 90%.

Thus, averaging of spikes with similar spatio-temporal distributions is mandatory to reveal the topography and localization of spike onset. This can be done best by doing a pattern search on the peak channel in a source montage using a good spike template or using all channels in a virtual average reference montage with wide coverage (AV33),see further on).

If one localizes single spikes or even groups of 10 or 25 spikes by equivalent dipoles, the center locations of these dipoles scatter (left). This scatter is highly correlated (>85%) with EEG background noise. Thus, scatter plots of dipoles or averaged dipoles do not reveal the extent of an irritative spiking zone. Rather, they reflect the uncertainty in estimating the center location. To estimate the center of the onset region reliably, at least 10-25 spikes need to be averaged.

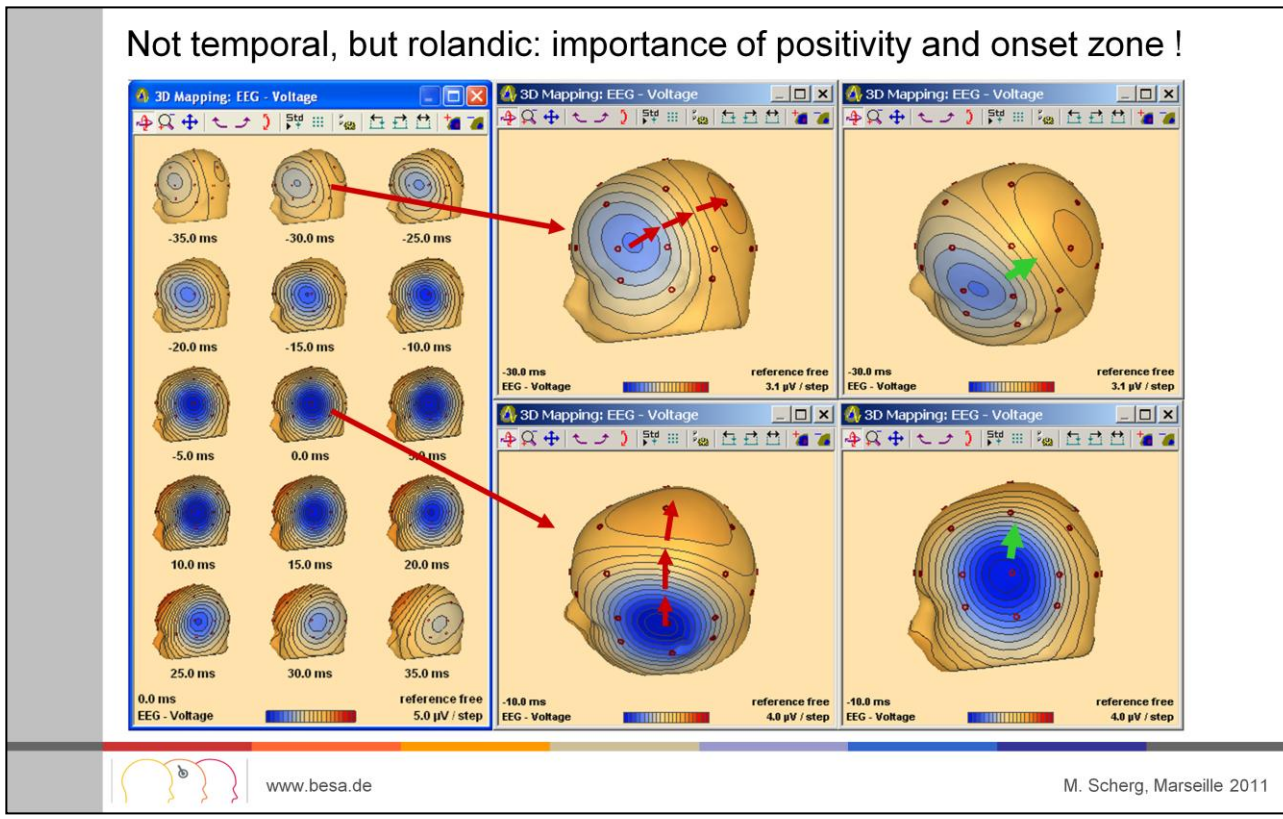


The single spikes of this child show a polarity reversal between F7-T7 and T7-P7 similar to typical temporal lobe spikes. The corresponding radial map at the spike peak has a maximum negativity over the temporal lobe.

Spike onset is unclear and varies between the single spikes. The single spike map during onset reflects mostly EEG background activity.

After averaging, the tangential topography during spike onset becomes apparent. The onset pattern shows a negativity over the frontal cortex and a more superior horizontally oriented, oblique dipolar pattern.

But, when just considering the spike peak, this seems to reflect a left temporal lobe spike. Is this correct?



Is this spike peak with an apparently radial map coming from the lateral surface of the left temporal lobe?

How can we estimate the 'approximate source location' from the maps?

Consider a line connecting the negative and positive maxima on the scalp (red arrows). This line follows the shortest connection having the highest voltage gradient (~ narrowest distance between equipotential lines).

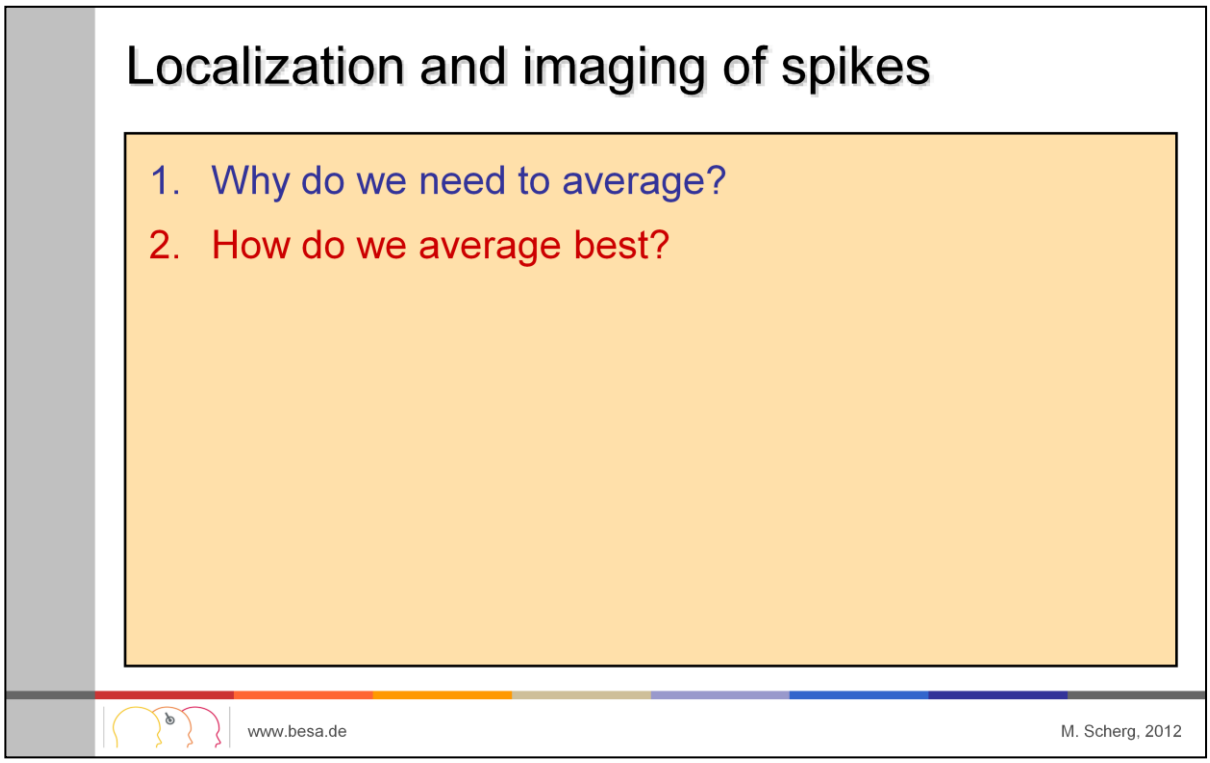
Then, find the region of highest gradients and consider the relative strengths of the positive and neagtive poles

The onset map is close-to-tangential (upper row), the equivalent location is approximately below the area of maximum gradient (green arrow).

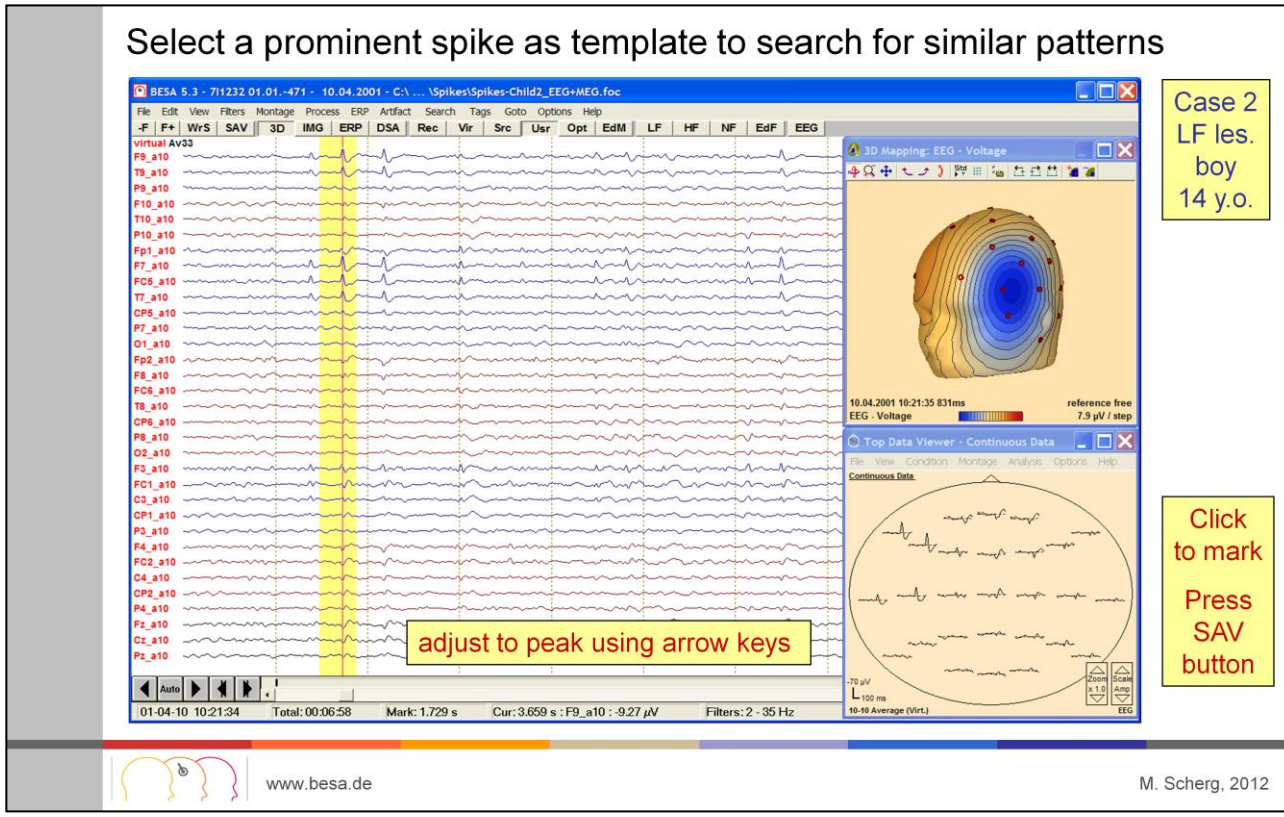
The peak map appears radial (lower row), but the center location is shifted slightly from the negative towards the positive pole along the region of largest gradient. The positive pole is not on the other side of the head, but superior!

The equivalent centers of both maps are similar and point to a circumscribed region of origin in the rolandic cortex above the Sylvian fissure. Polarity indicates that the tangential rolandic spike is likely to arise from the anterior wall of the post-cental gyrus (~face area) with ensuing propagation to the surface of the gyrus (radial map), since the tangential onset current is flowing backwards into the posterior wall of the central suclus.

Thus, it is obvious that we need to average a) to determine if there is propagation from onset to peak, and b) to be able to interpret the onset map.



Next we want to understand the practical steps involved in averaging interictal spikes.



We now illustrate how spike templates are used during the review process to detect similar spikes and obtain an averaged signal allowing for the evaluation of the spike onset topography in comparion to the peak.

Pressing **F4**, we obtain an optimized montage for detecting spikes in the on-going EEG. This sets the virtual average reference montage AV33 including the inferior electrodes F9/10, T9/10, P9/10, and intermediate electrodes, e.g. FC1, FC5, CP1, CP5...

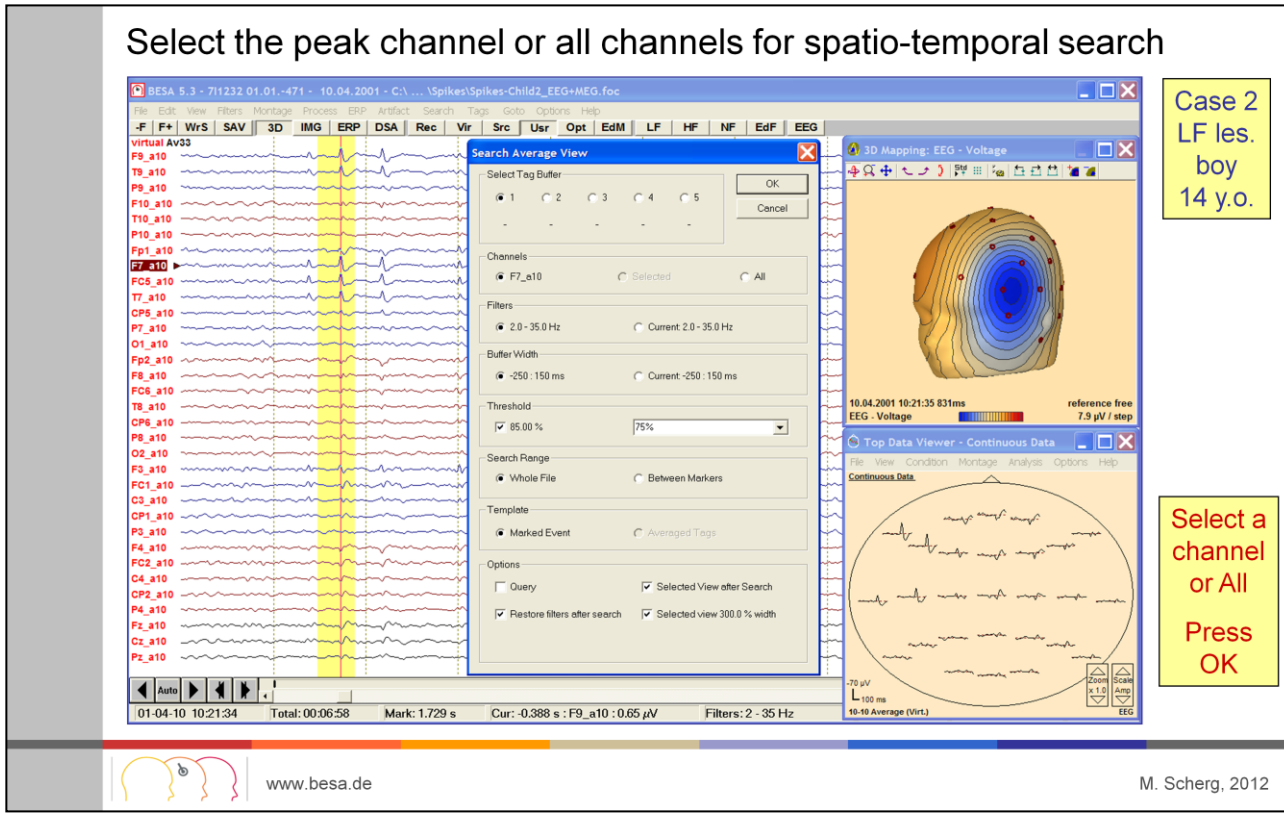
Spikes, including inferior-temporal patterns, are better visible by using

1) this **virtual montage** with 33 electrodes that covers the whole head by extrapolating to intermediate and inferior sites even in the absence of such electrodes,
2) the **grouping of channels** in three longitudinal rows (e.g. the denser Fp1, F7, FC5, T7, CP5, P7, O1 row), and
3) an **optimized filter band (2 – 35 Hz)** that suppresses slow EEG activities and renders spikes riding on slow EEG activity more vísible. At the same time, the high filter removes a sufficient amount of EMG activity to enhance the visibility of spikes.

We page through the EEG and look for a prominent spike that has a flat, undisturbed onset epoch (marked yellow block). This presents an ideal template for pattern search

Click on the spike and adjust to the spike maximum in the map using the arrow keys.

Press button SAV to obtain the search-average-view dialog box.



The SAV-box provides preset optimized values and the option to modify these for the pattern search. This starts when pressing OK.

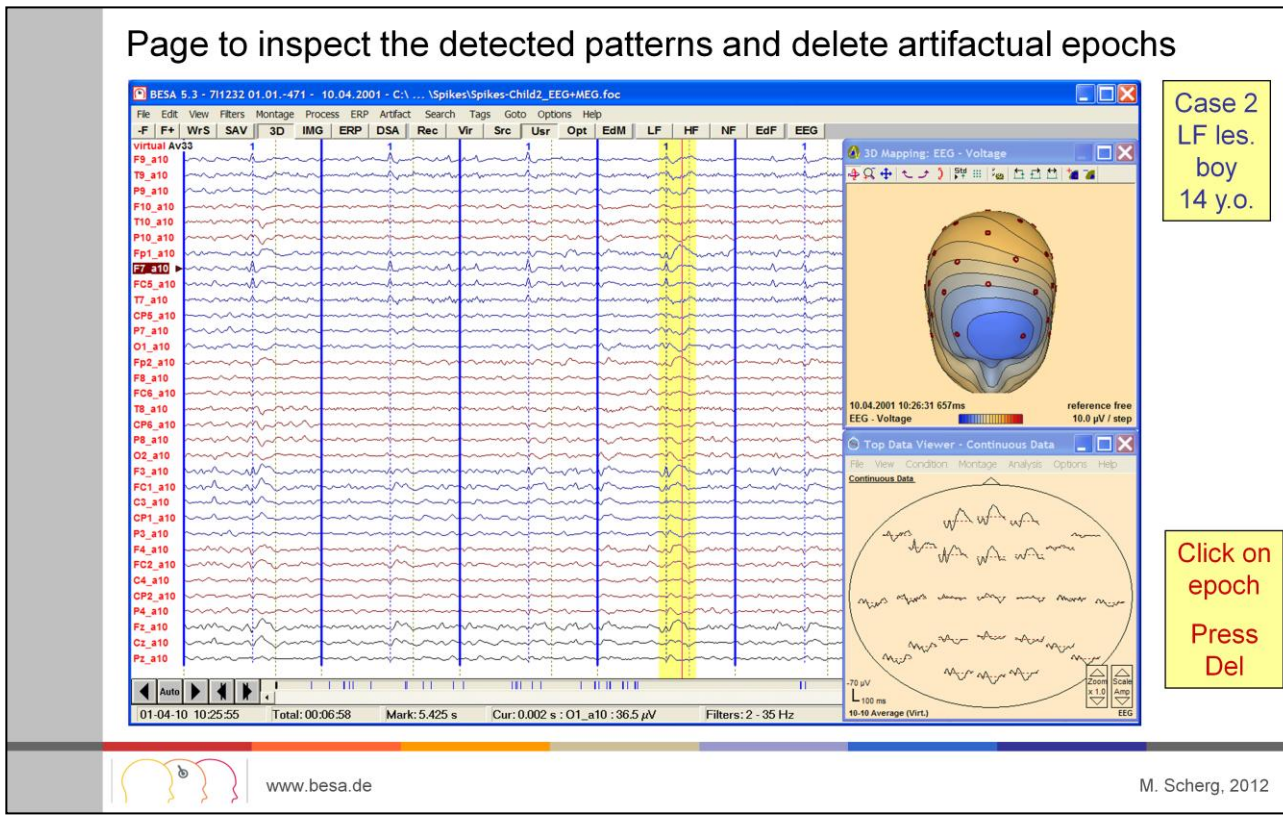
The largest spike channel is identified and marked automatically, and one may choose either this channel, manually selected channel(s), or all displayed channel for template search. When using the average reference montage and a clear spike patterrn, it is recommended to use the **All** channels template. With a source montage, the **largest spike channel** can be used as proposed automatically.

Optionally, several channels showing a clear spike pattern can be marked for template search (e.g. F9, T9, F7, FC5, T7) prior to pressing SAV.

If only one channel is selected, the marked pattern of this channel is shifted along the whole on-going EEG and correlation is assessed at peaks.

If the selected threshold is exceeded, a detection marker will be created at the time when the template best matches the recorded EEG pattern. Thus, spikes are aligned optimally in time.

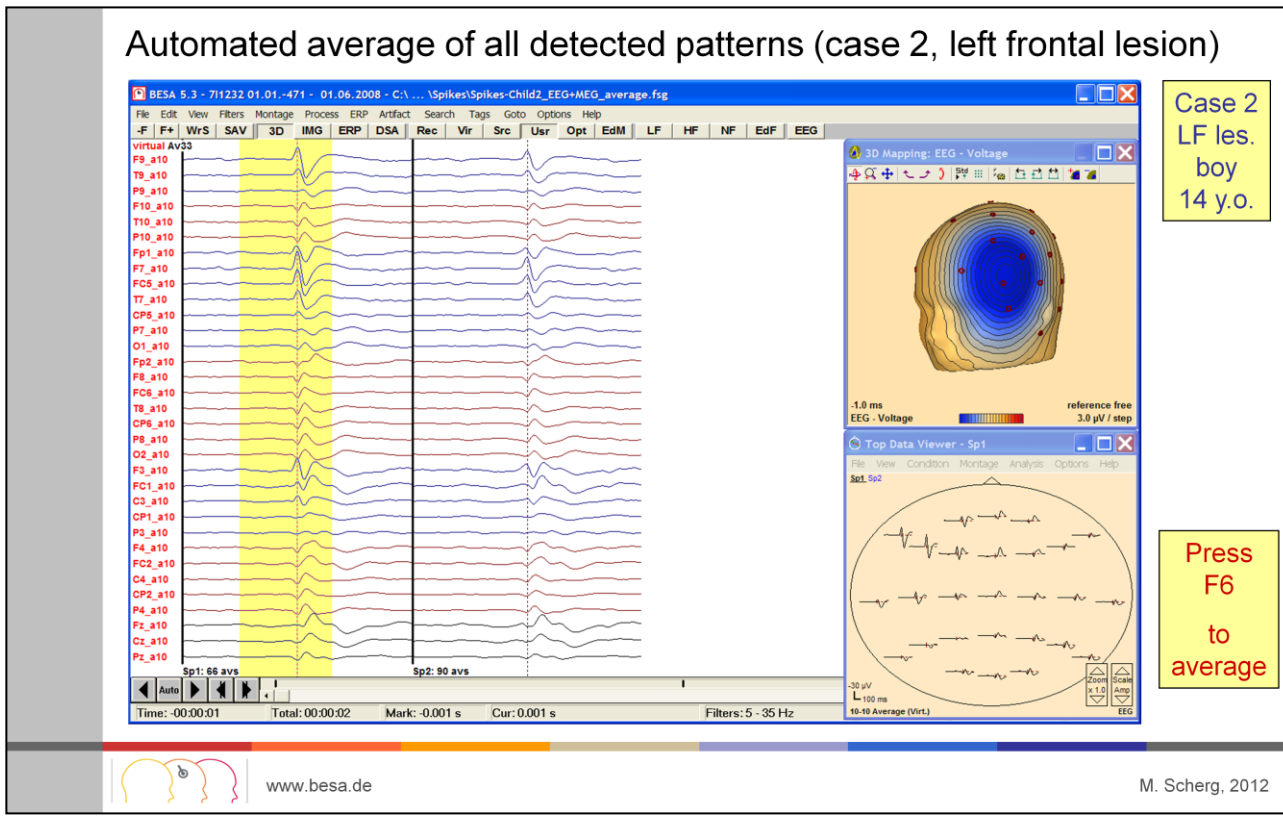
If several or all channels are selected, a spatio-temporal template is calculated and aligned with all selected traces. I.e. if there are delays in the peaks between channels, the pattern search will look for similar delays in the EEG intrinsically.



After the pattern search is completed, the detected patterns are displayed automatically. We inspect these patterns using the paging functions and delete detected events where the spike is blurred by background noise or artifact. Simply **click** onto a noisy spike segment and **press** the **D** or **Del** key.

Thus, you may control the events that are included in the final average.

The preliminary average can be viewed (menu: View / Average Buffers) and used as an improved template if desired.

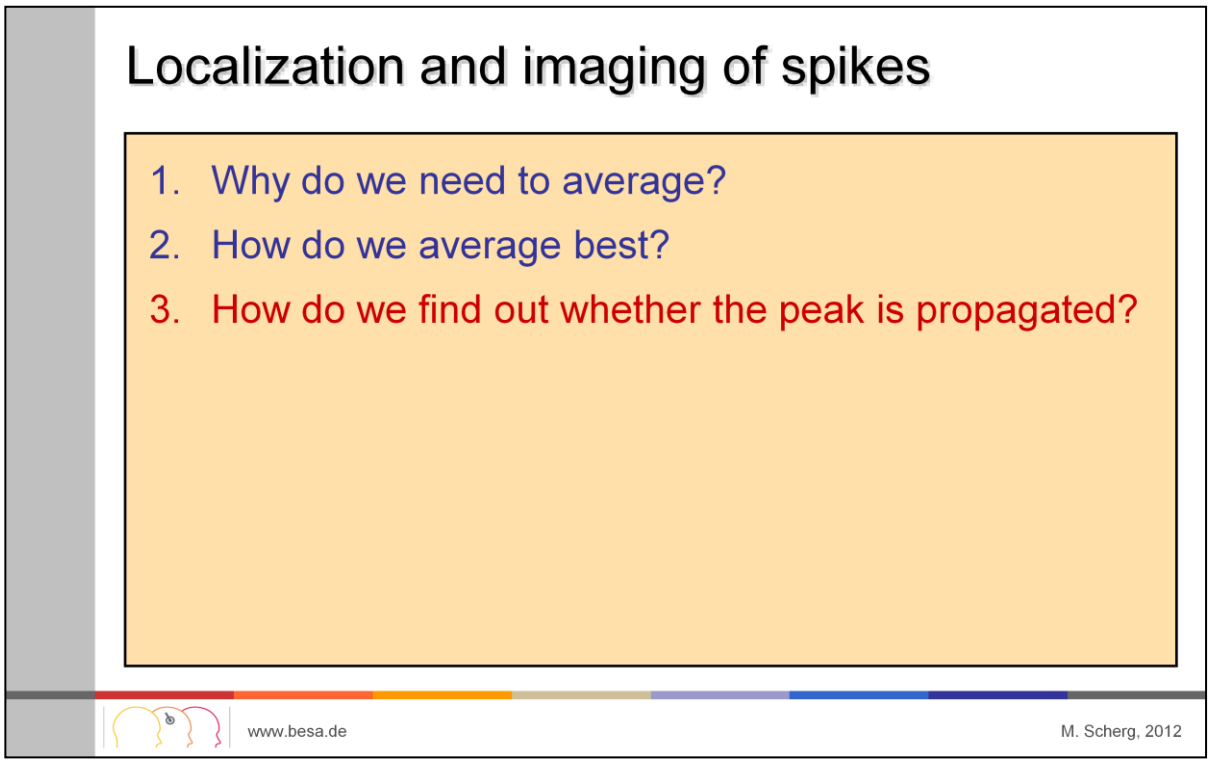


After inspection of the detected spike epochs, we press **button F6** to obtain the averaged signals for all marked tags (up to 5 different pattern types).

The underlying batch process converts the tags 1-5 into triggers 41-45, saves these events into an ASCII file, reads and averages the segments from the original EEG file, and creates an averaged file that is displayed automatically.

Next, filters are set optimally for the analysis of the spike onset (5 Hz low filter, forward characterisic corresponding to a time constant of 30 ms; 35 Hz high filter). This creates an optimal baseline for the analysis of spike onset and removes unwanted EMG.

We may click onto the spike and inspect the 3D maps to localize onset and peak visually. Use the arrow keys to change latency.

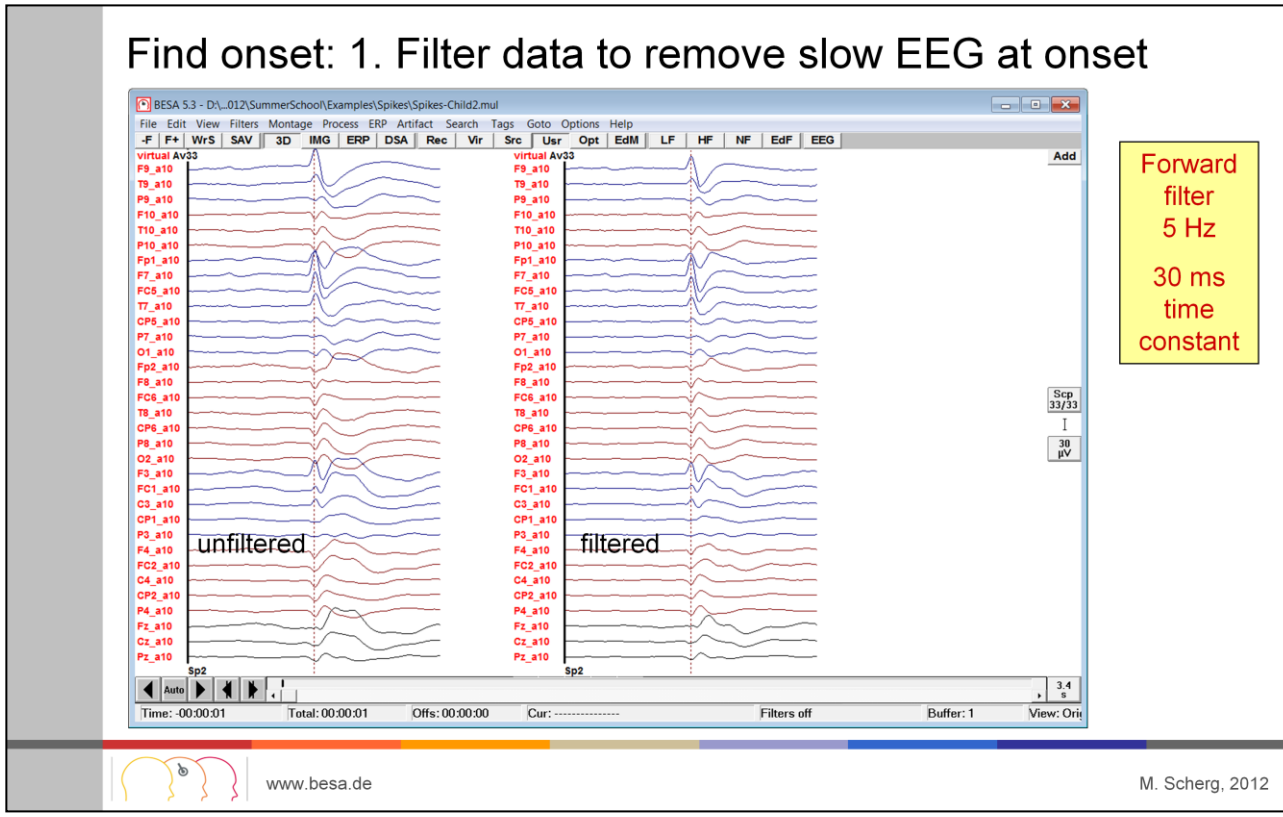


Before localizing we should use several methods to inspect the onset-peak interval of the averaged spike. The aim is to determine if the onset is different from the peak.

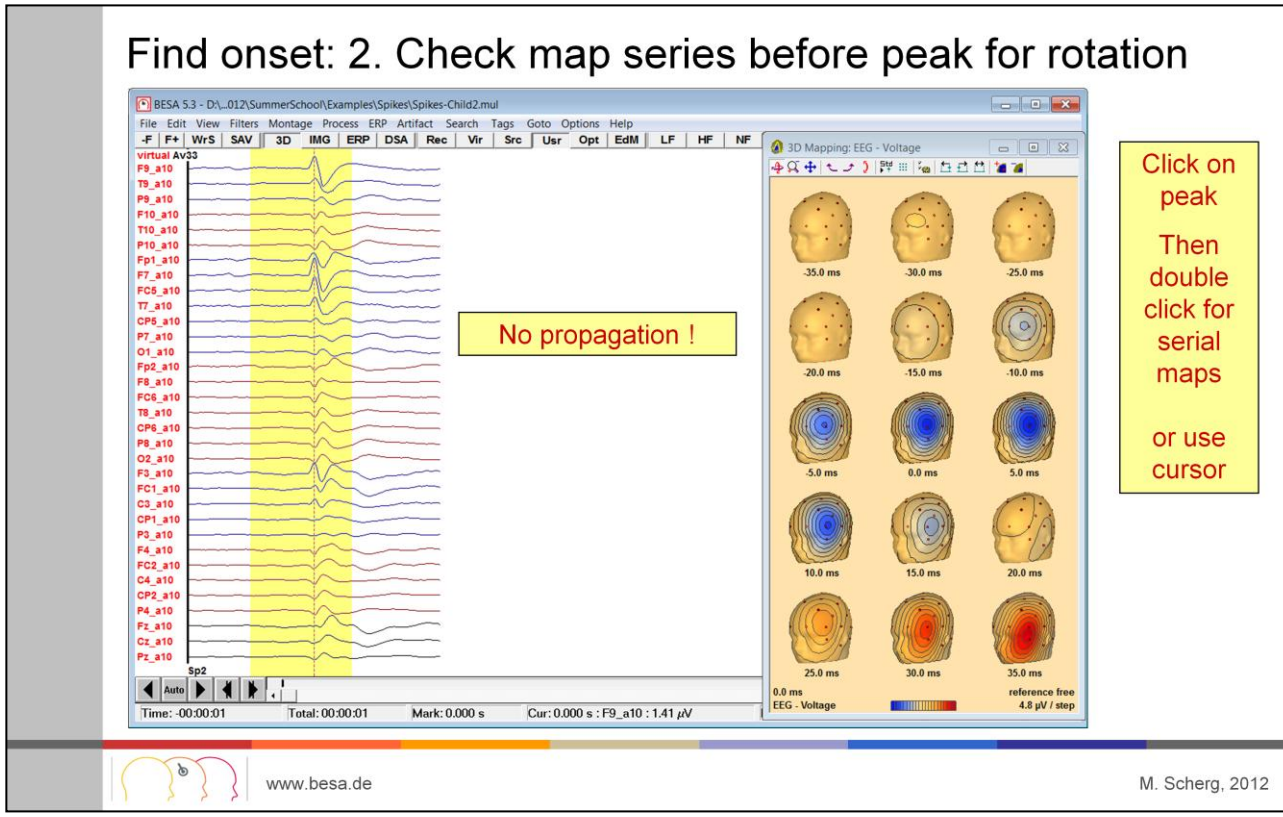
First, we need to filter the data for optimal analysis of the onset.

Second, we compare the onset and peak maps and localize their centers visually to check for propagation.

Third, we will perform a principal components analysis (PCA) to see if different spatial patterns exist in the onset-peak interval and to determine the onset interval using the earliest stable topographic pattern.



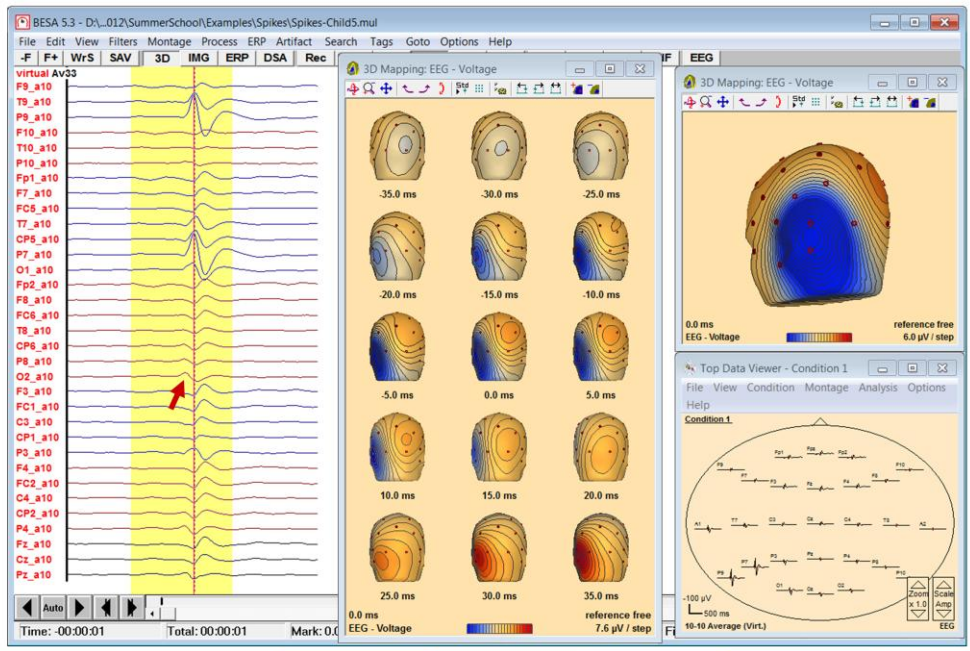
In the above example of an averaged spike (child2), we can observe the effect of a forward filter to remove slow EEG noise from the baseline. Such noise remains even after averaging and dominates the maps at onset. Thus, we need to use a sufficiently high filter (~short time constant) to enhance the onset signal over the noise (5 or 10 Hz forward low cutoff filter).



When mapping the filtered averaged spike during the onset-peak interval we check if the pattern is substantially different in the onset period and if it is rotating as a consequence of overlapping topographies. Here, we merely observe an onset of a pattern similar to the peak with subsequent attenuation and inversion. The basic pattern remains the same throughout the onset-peak interval.

Thus, no substantial propagation is seen in the serial maps of child 2 during this interval. Furthermore, the peaks in all channels of the AV33 montage appear at the same latency.

Propagation seen in serial maps of filtered data of child5



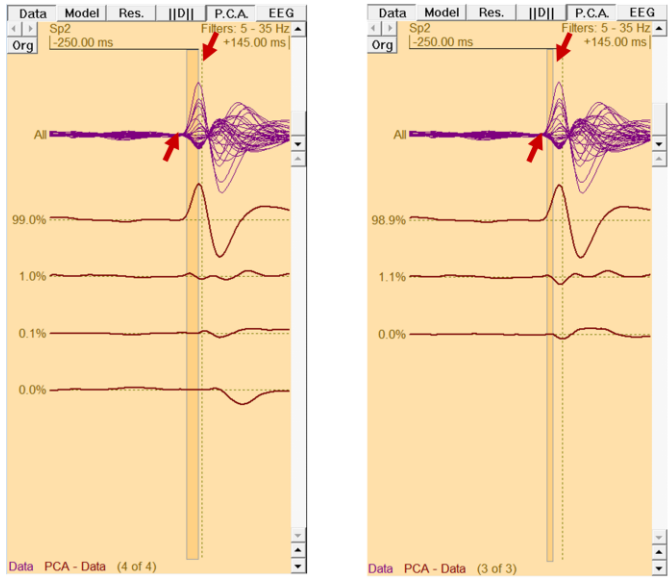
1. Data have been filtered at 5 Hz

2. Serial maps show different initial pattern and rotation

In contrast, the serial maps of child 5 show a large change from the onset to the peak pattern with a rotation of the negativity from occipital to left inferior-temporal.

A small preceding peak is seen at right posterior channels (arrow: O2, P8).

Find onset: 3. Check principal components in onset interval



whole onset interval 1st half

Child 2:

1 dominant component in onset interval

Same as in first half of onset interval

No propagation !

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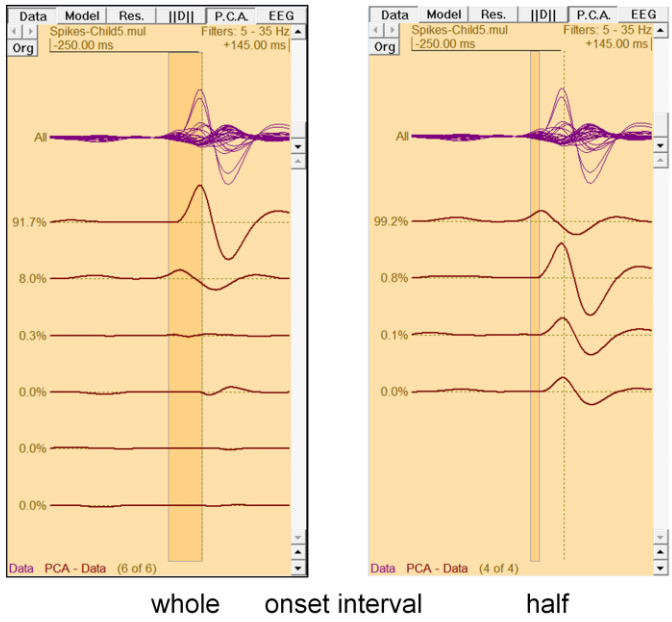
Principal components analysis of the whole versus the first half of the onset-peak interval does not show a large difference. Apparently, one spatial component (topography) dominates the onset.

Also, the spike peaks in the butterfly plot over the different (average-reference) channels all align at the same latency.

Thus, there is no sign of propagation in these data of child2.

Propagation: 3. Different PCA components seen in child5



whole onset interval half

Child 5:

2 components appear in whole onset interval.

Second component dominates in the onset interval.

Propagation !

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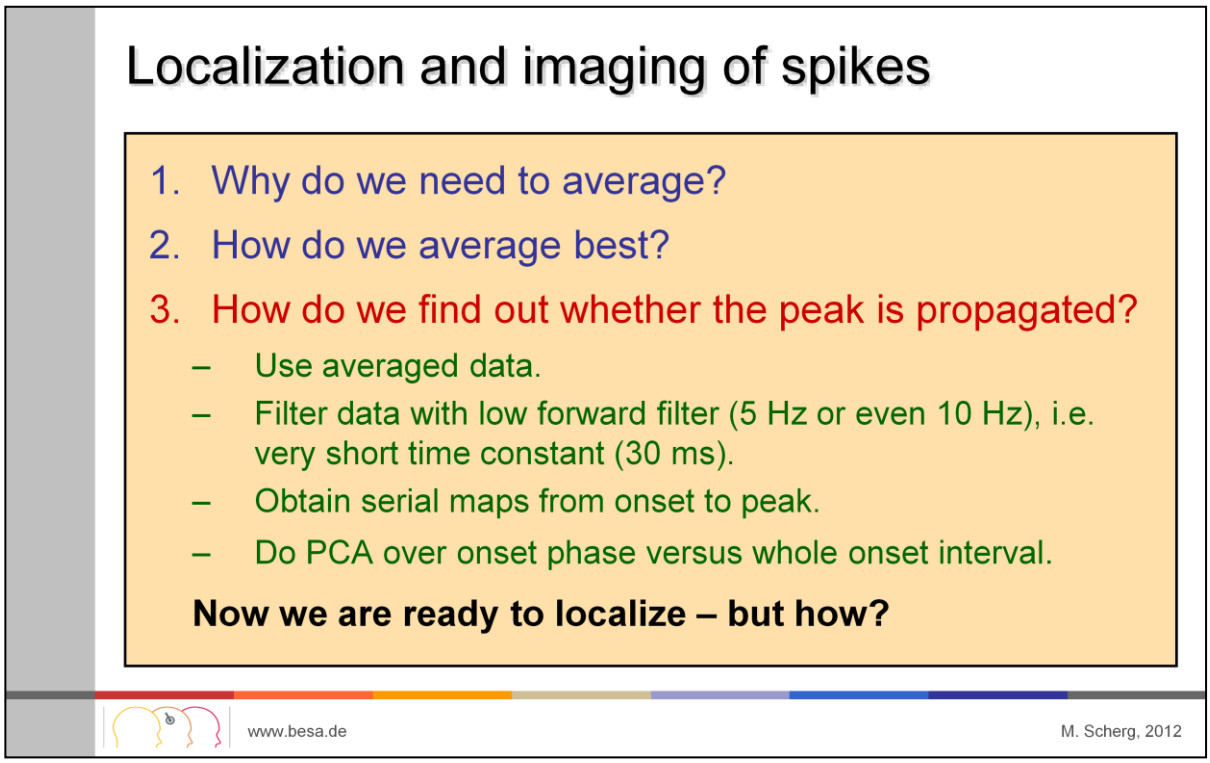
Principal components analysis of the whole onset-peak interval reveals two major components (left). The second component (8% of the total variance) shows a clearly earlier pattern that is also obvious in the onset period of the butterfly plot.

When PCA is restricted to this onset interval (right), it can be seen that the earlier component dominates in this interval (99%). Thus, we can adjust the onset interval to maximize the PCA output for this component. Now, the dominant component at the peak (left) is in second place since it already evolves with a small activity (0.8%) in the marked onset period (right).

Peaks in the butterfly plot are no longer aligned and seem grouped into an earlier and later pattern according to the amount of activity the related channel picks up from the earlier and later generators.

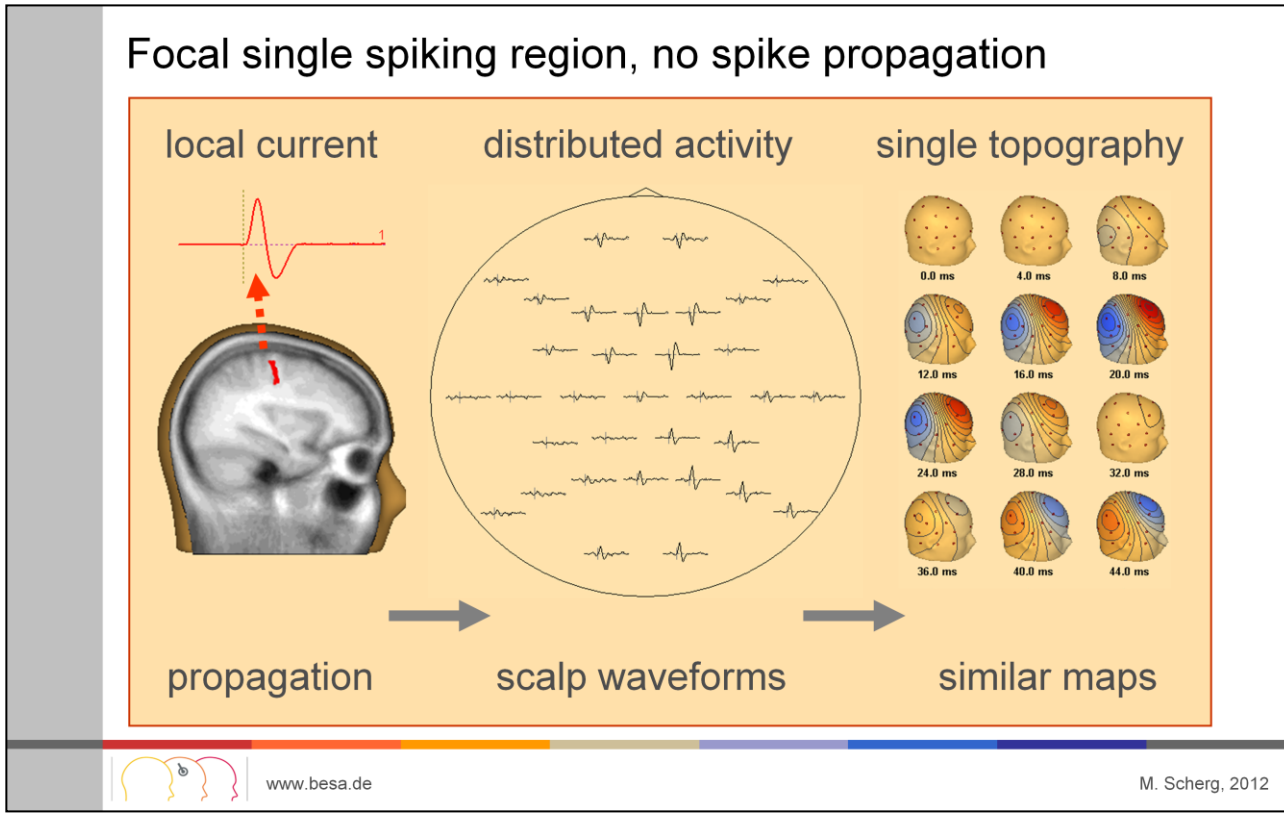
Thus, there are clear sign of propagation in these data of child5.



Above, the necessary steps for data preparation prior to localization are summarized again.

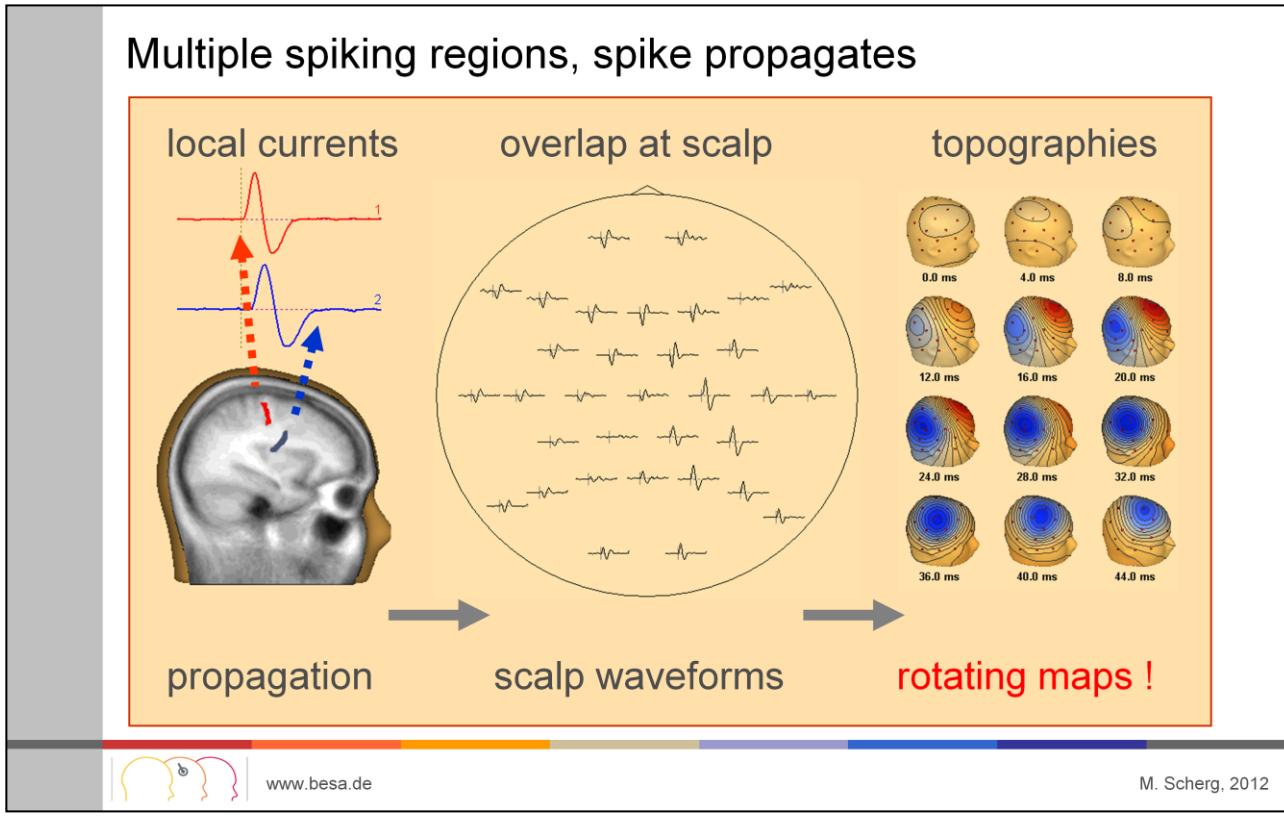
Also, we have obtained the first ideas about localization and propagation by inspecting the onset to peak maps of the averaged spike.

What else will we learn, if we perform spike localization and/or imaging using the scalp EEG data with the indiviual MRI and a realistic head model, if avallable?



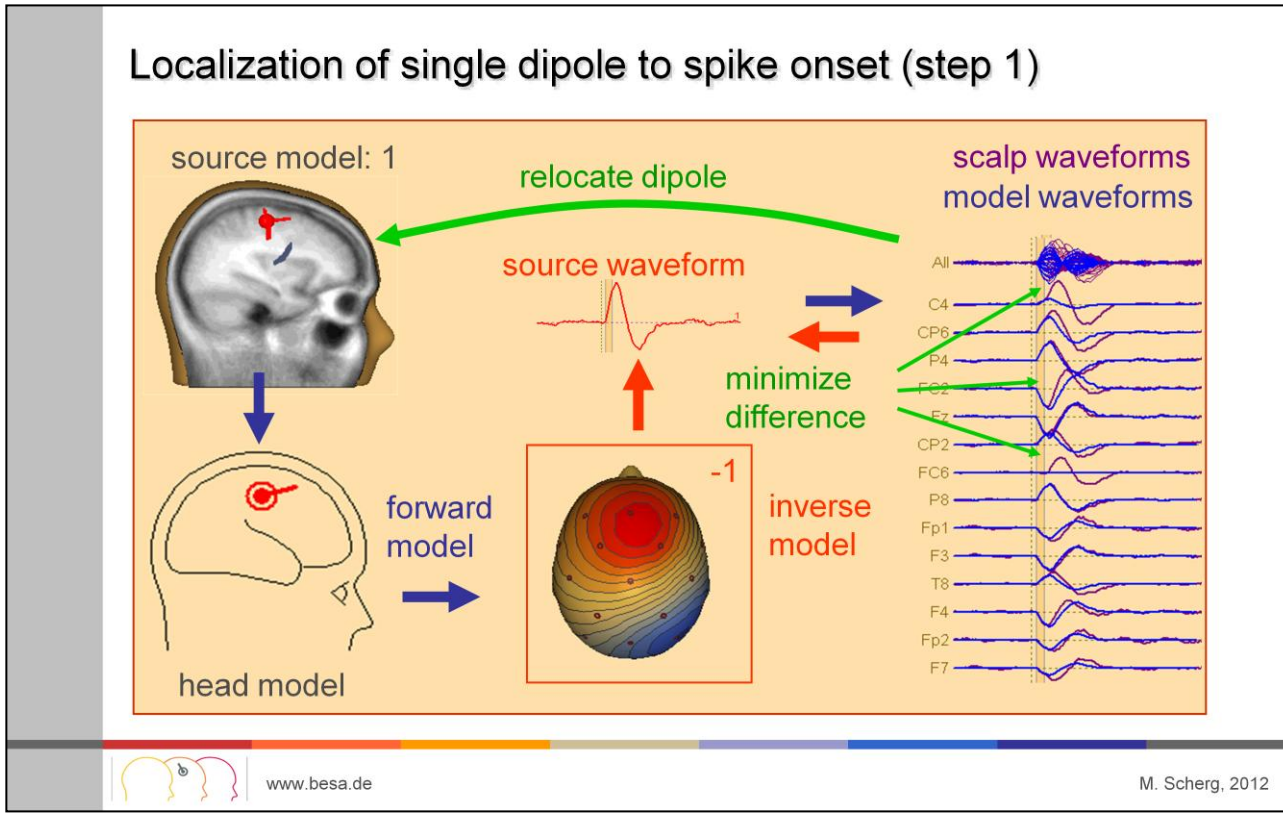
First, we want to learn the principles of localization by considering a simulated example.

We start with a single sheet of cortex spiking with a biphasic pattern that is volume conducted (propagated) to the scalp. The scalp maps show the waxing and waning of the same pattern with polarity reversing.



Next, consider the situation of two brain regions separated by about 3 cm and activated within a few milliseconds. Each of the areas has a biphasic pattern with onset, peak, and polarity reversal. The two patches have different orientations. This is the main cause for their very different scalp topographies. Due to the time difference in activation their maps overlap with continuously changing magnitudes according to the instantaneous strength of the 2 compound currents. This results in an apparent rotation of the maps over time, and it becomes difficult to identify and separate the two sources by mere visual inspection.

However, at the onset we may expect the pattern of the initial source to be dominant. Thus, at the onset there is a chance to localize a focal pattern.

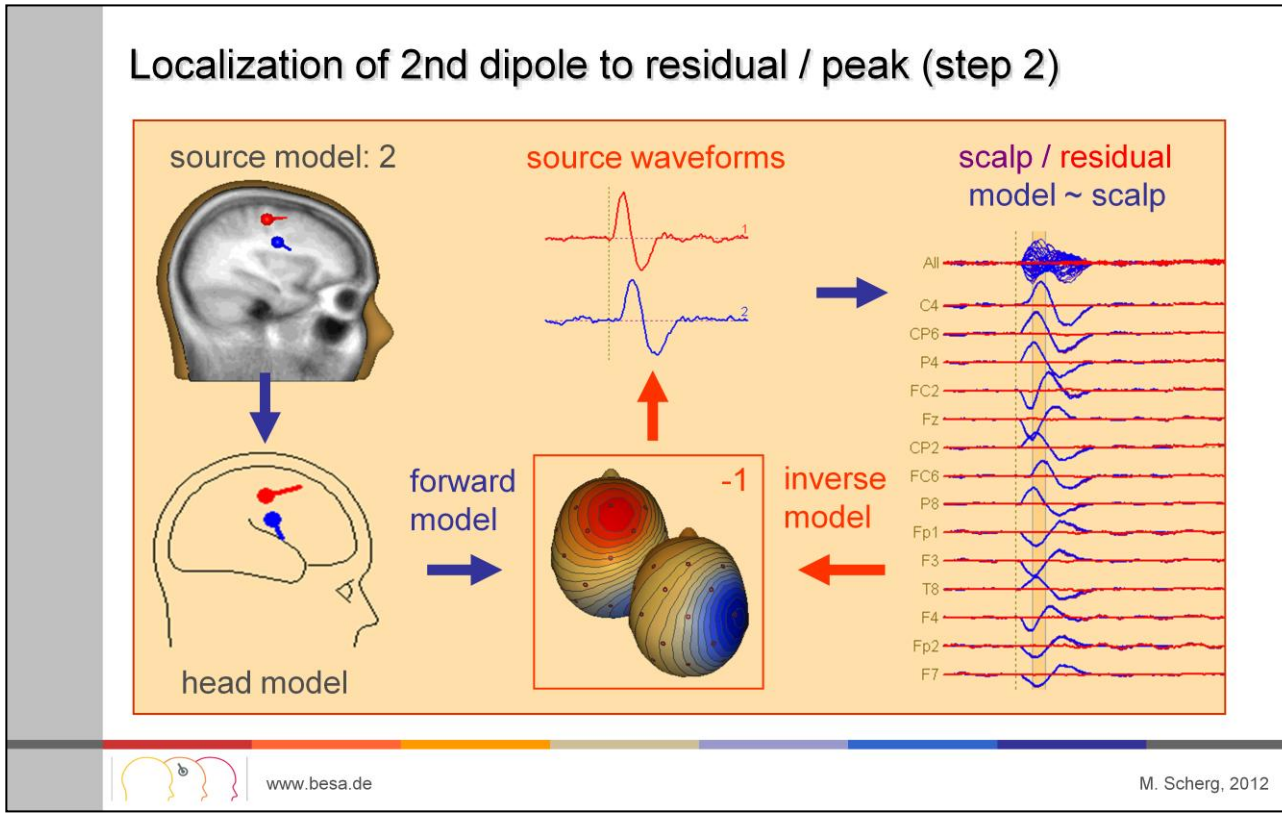


The fit procedure:

We assume that a single dipole will explain the early onset phase when only one focal cortical sheet is active. Using the head model the forward model topography is estimated. The inverse of the topography matrix is applied to the data to estimate the source waveform. The source waveform is projected back to the scalp using the forward coefficients of the map to estimate the model signals (blue). Measured and modeled data are subtracted to estimate the residual waves. In an interactive process, dipole location and orientation are adjusted and the calculation process is repeated until the residual difference between scalp and model waveforms is minimized. The equivalent dipole locates in or near the active cortex if the single source hypothesis, the head model, and data are sufficiently accurate.

Fitting strategy for multiple activities – step 1:

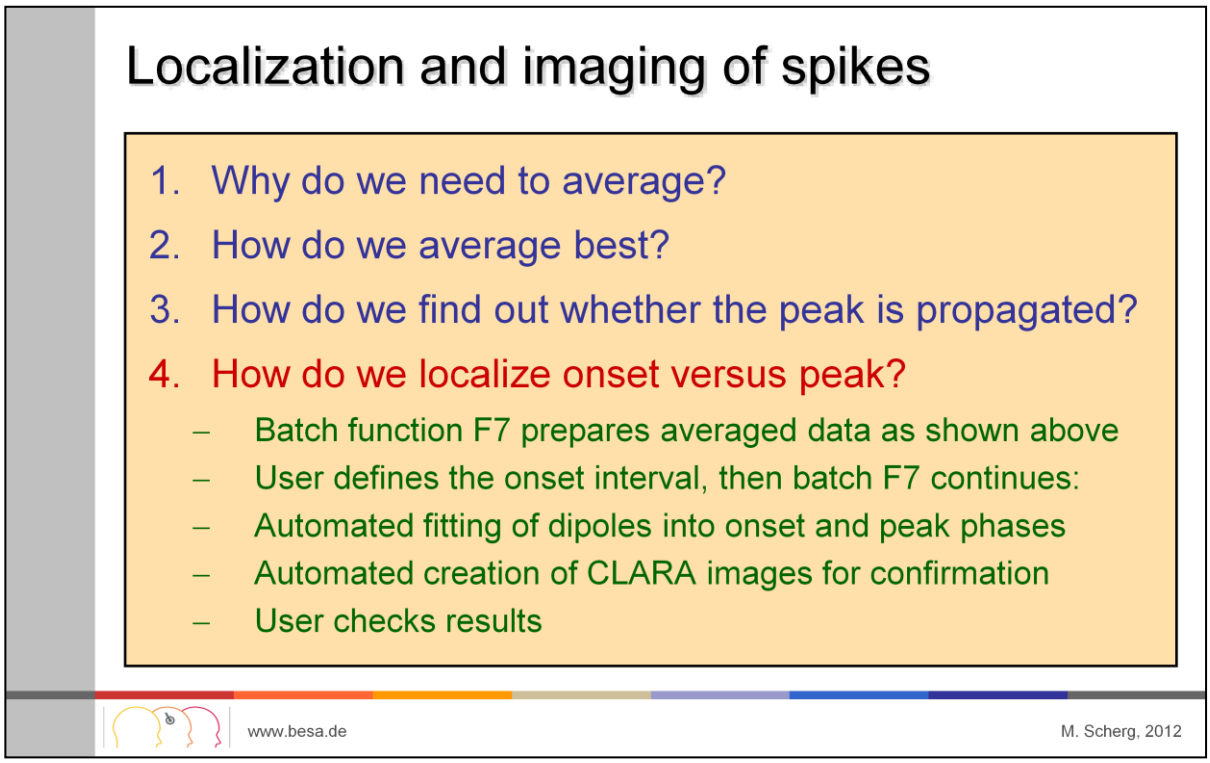
Use the 3D maps to define the fit interval from the time when a clear dipole field emerges until it starts changing. Performing a principal components analysis over this interval should show one dominant component. The percentage of variance it explains should decrease, if the interval is extended further. Fit the first dipole over this interval.



Fitting strategy for multiple sources – step 2:

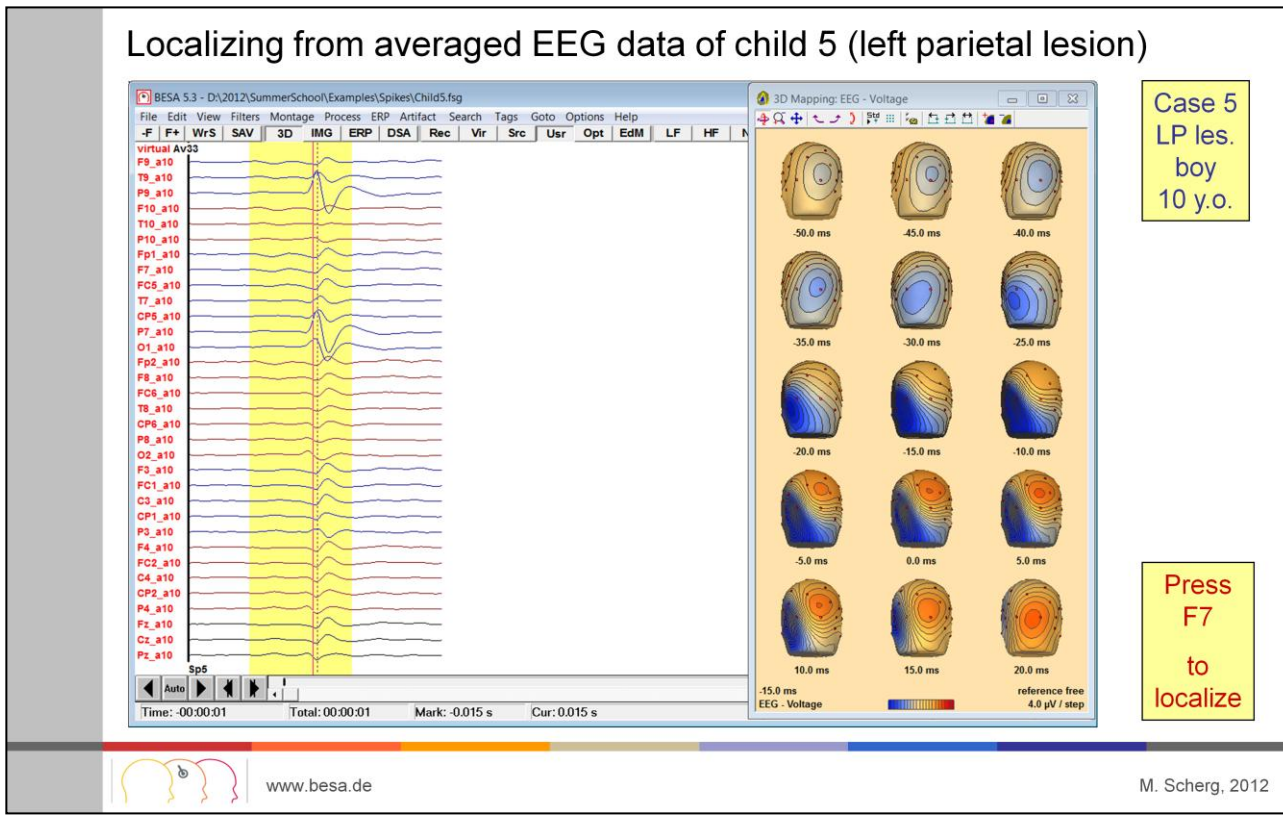
Display the residual waves and maps. Perform a PCA on the residual waves and repeat the same procedure to mark the next onset interval in the residual data. Fit a second dipole to this interval while keeping the first dipole fixed in location and orientation. The model now contains two sources: the fixed source modeling the onset activity (that does not stop!) and the source to be fitted to explain the additional activity at the peak.

In the simulated example with good signal-to-noise, this results in the separation of the underlying two active areas and their source waveforms.



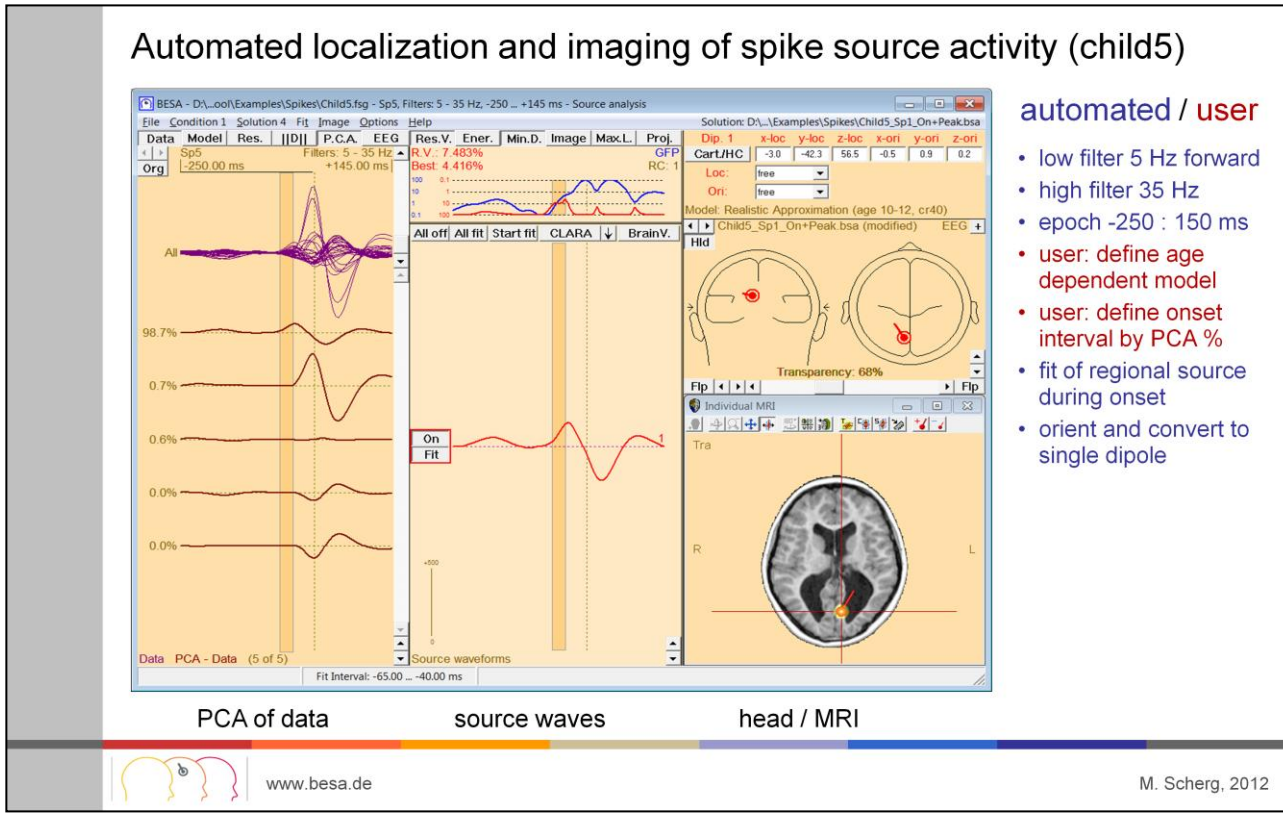
Since there are many steps involved in preparing and fitting averaged interictal spikes, these steps have been implemented into an automated batch process (associated with function key F7 in BESA Research 5.3).

Thus, the user will be able to concentrate on selecting the appropriate head model and defining the onset interval before finally checking the automatically obtained results without any further user-dependent interference.



Localization starts by opening the averaged spike file and pressing F7.

This will filter the data to reduce noise at onset (5-35 Hz) and open the source analysis window with the request to select the realistic head model appropriate to the age of the subject.



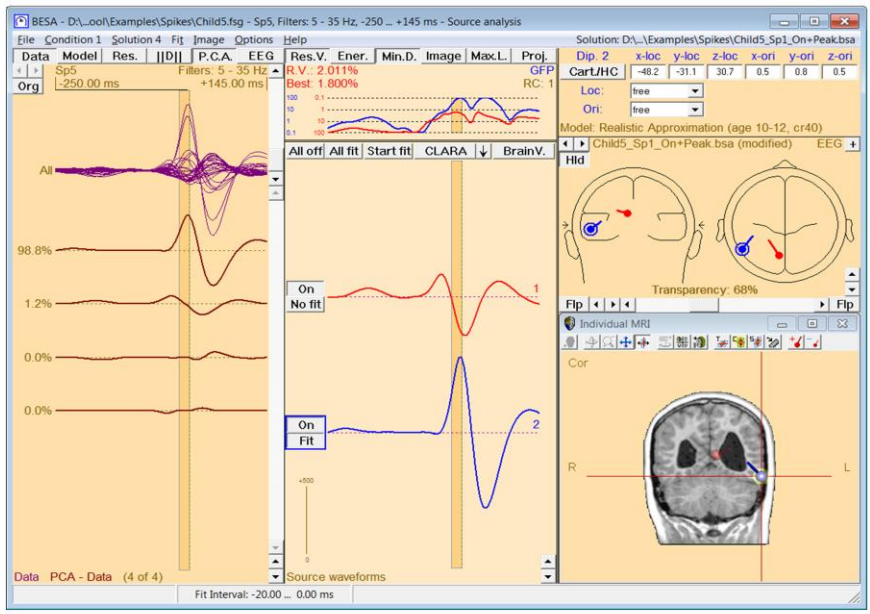
The batch function associated with the **F7 button** performs automated steps and stops occasionally to request user input. A list of the automated settings and analysis steps performed by this batch function is shown above on the right in blue. The required user actions are marked in red.

After the source analysis window opens, the user first needs to **select the head model** for the EEG to match the age of the subject. Then, the batch control proposes to the user to mark the onset interval graphically. This step is helped by a visual comparison of the automatically calculated principal components analysis (**PCA** – displayed on the left) with the butterfly overplot showing all recorded channels in average reference (displayed above).

The onset interval is defined by finding the initial interval that exhibits **one dominant principal component** (accounting for a data variance of more than 90-95%). Its prominent waveform (here: 98.8%) is compared to the wings in the butterfly plot to assess, whether it comprises the peak or an earlier activity. Inspection of the following PCA components shows no significant other activities in the onset interval of child5.

Next, the batch fits a **regional source** into the onset epoch and rotates the 3 underlying orthogonal dipoles such that the first **dipole** is oriented to explain all the activity at the maximum of the onset interval. Only the first dipole of the regional source is retained (above, right). It shows the center location and orientation of the initial activity implicitly assumed to be uni-focal.

Automated localization and imaging of spike source activity (child5)



PCA of data source waves head / MRI

automated / user

- low filter 5 Hz forward
- high filter 35 Hz
- epoch -250 : 150 ms
- user: define age dependent model
- user: define onset interval by PCA %
- fit of regional source during onset
- orient and convert to single dipole
- fit of 2nd source at peak interval (-20:0)
- user: compare onset to peak sources

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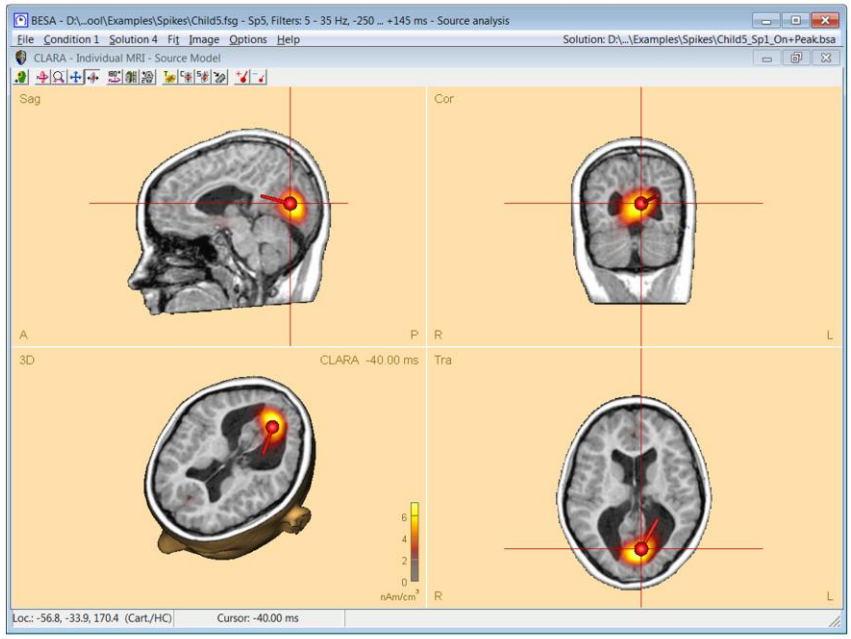
Next, the batch fits a **regional source** into the peak epoch (-20:0 ms) while the onset dipole is present in the 2-source model to avoid contamination of the peak activity by on-going activity in the onset area.

The user can now compare onset (red) and peak (blue) sources. The source waveforms are clearly separated in time and the activity appears to have propagated from a midline occipital area to lateral inferior-temporal.

Automated localization and imaging of spike source activity (child5)



automated / user

- low filter 5 Hz forward
- high filter 35 Hz
- epoch -250 : 150 ms
- user: define age dependent model
- user: define onset interval by PCA %
- fit of regional source during onset
- orient and convert to single dipole
- fit of 2nd source at peak interval (-20:0)
- user: compare onset to peak sources
- user: compare with the CLARA (LORETA) image at the maximum in the onset interval

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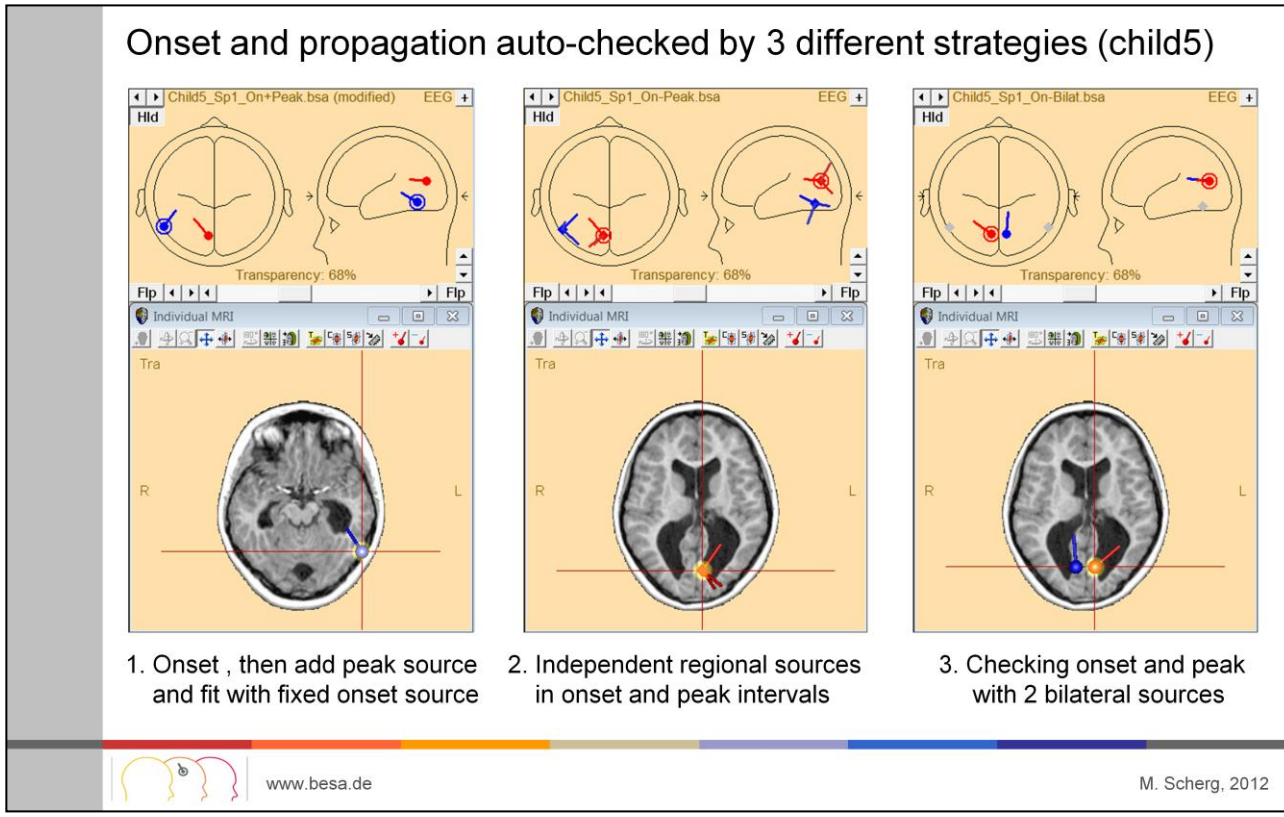
If available, the individual MRI is loaded and a CLARA image (more details further below) is computed for comparison.

At onset (-40 ms), the CLARA image and dipole localization coincide. The proximity to the midline does not allow for lateralization based on the image or dipole location alone.

Considering the orientation of the dipole, however, the spike activity points into the left occipital cortex indicating that the mesial surface of the left occipital cortex near the interhemispheric cleft is spiking. Hence, propagation occured within the left hemisphere from midline occipital cortex to the lateral inferior temporal-occipital region (cf. previous slide). The posterior horn of the ventricle on this side was enlarged.

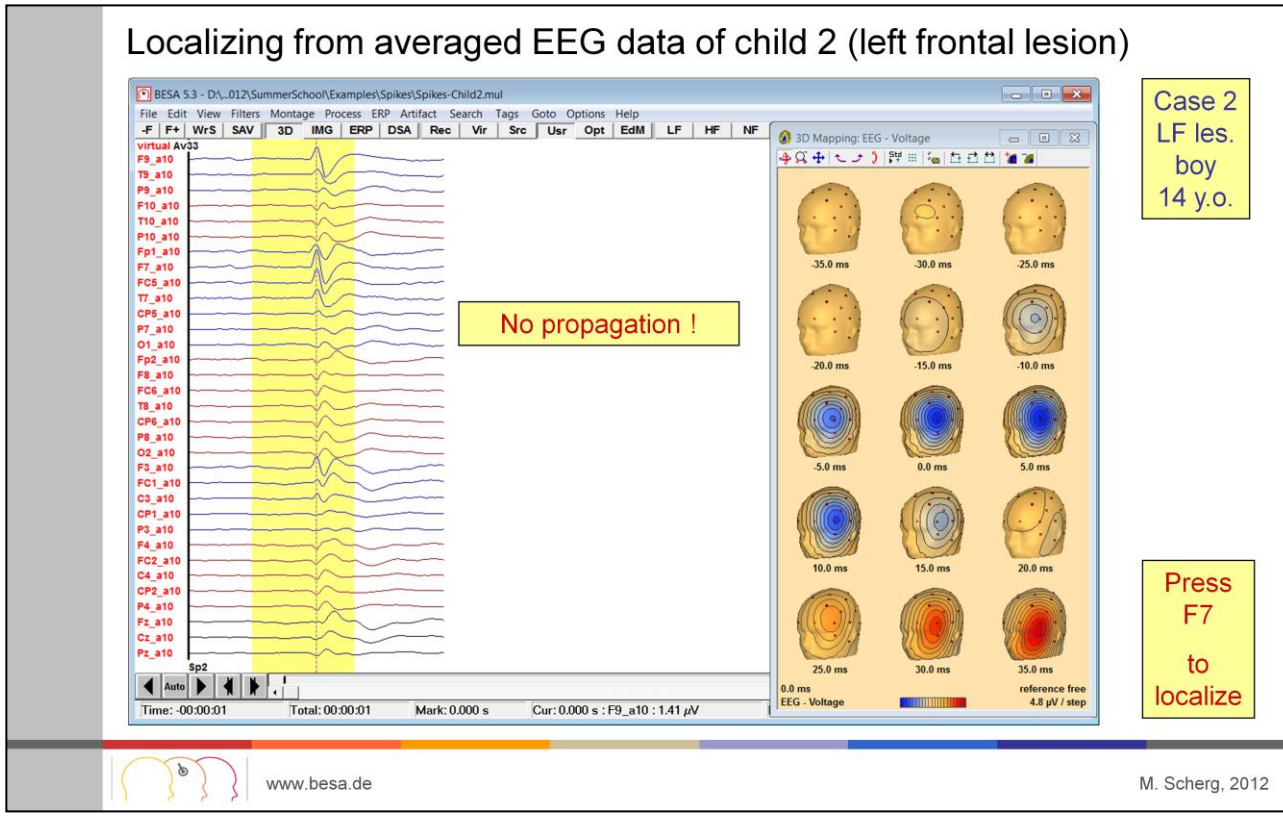


Using the batch F7, several hypotheses are tested automatically to confirm a difference between onset and peak localization and to check for the presence of bilateral onset:

Strategy 1 (On+Peak): The onset dipole source (red) is kept in the model and an additional source is fitted in the peak interval (-20 : 0 ms). This is the physiologically most plausible and prefered solution assuming focal onset and overlap of the later part of the onset activity with the rising peak activity.

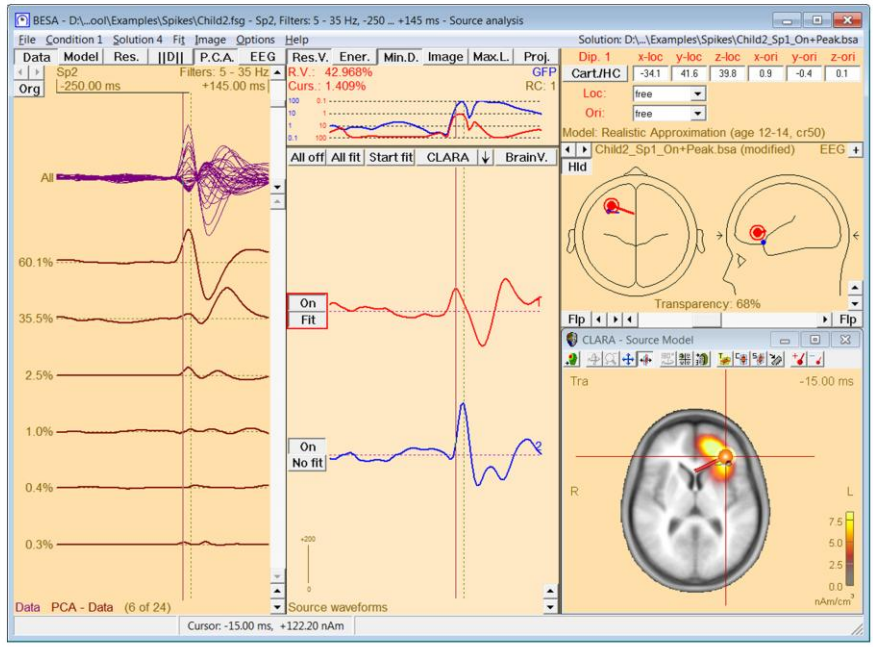
Strategy 2 (On-Peak): Regional sources are fitted independently in the user / PCA defined onset interval and in the peak interval. The onset source locataion is the same as in strategy 1, but the peak solution is simplified assuming a single source independent of the onset. The difference between onset and peak can thus be confirmed in cases that show interference when both sources are fitted together.

Strategy 3 (On-Bilateral): A pair of symmetric regional sources is fitted in the onset interval to test whether a near midline activity is indeed coming from the cortical areas near the interhemispheric cleft (here: yes), or whether the onset occurs synchronously in both hemispheres. This test is important, especially for source activities oriented along the interhemispheric cleft, since such activity can be modeled very accurately by one midline source even when coming from both hemispheres.



Let us check the same automated localization procedure for the non-propagating case of the averaged spikes of child2. Remember the stability of the map pattern and the lack of rotation, if the data are properly prepared with the low forward filter of 5 Hz.

Automated localization and imaging of spike source activity (child2)



automated / user

- low filter 5 Hz forward
- high filter 35 Hz
- epoch -250 : 150 ms
- user: define age dependent model
- user: define onset interval by PCA %
- fit of regional source during onset
- orient and convert to single dipole
- fit of 2nd source at peak interval (-20:0)
- user: compare onset to peak sources
- user: compare with the CLARA (LORETA) image at the maximum in the onset interval

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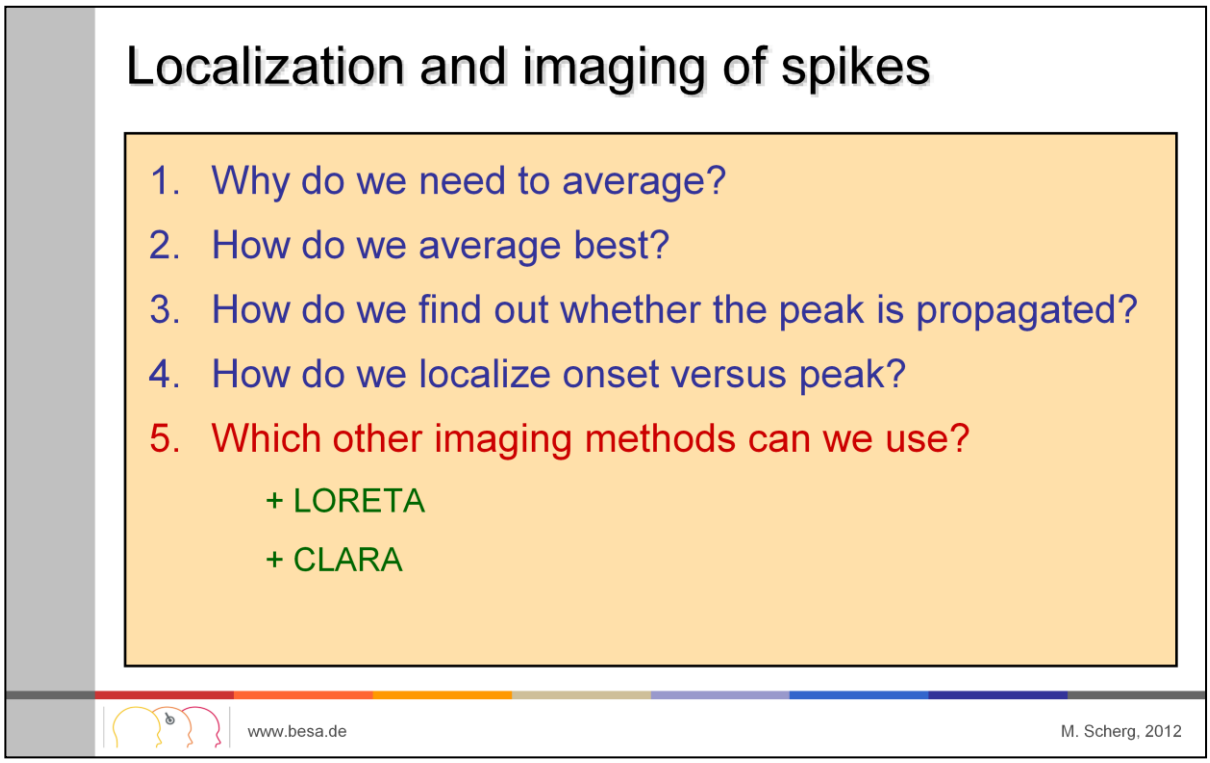
Onset and peak dipoles localize in the same region with similar orientations. In this case, the individual MRI was not available and a CLARA image (more details further below) was computed using the standard head for comparison with the dipole localization.

The image and dipole localization coincided at onset. Thus, the center of the region of onset was defined consistently in the left lateral frontal cortex. There is only a small change in orientation but no clear difference in localization.

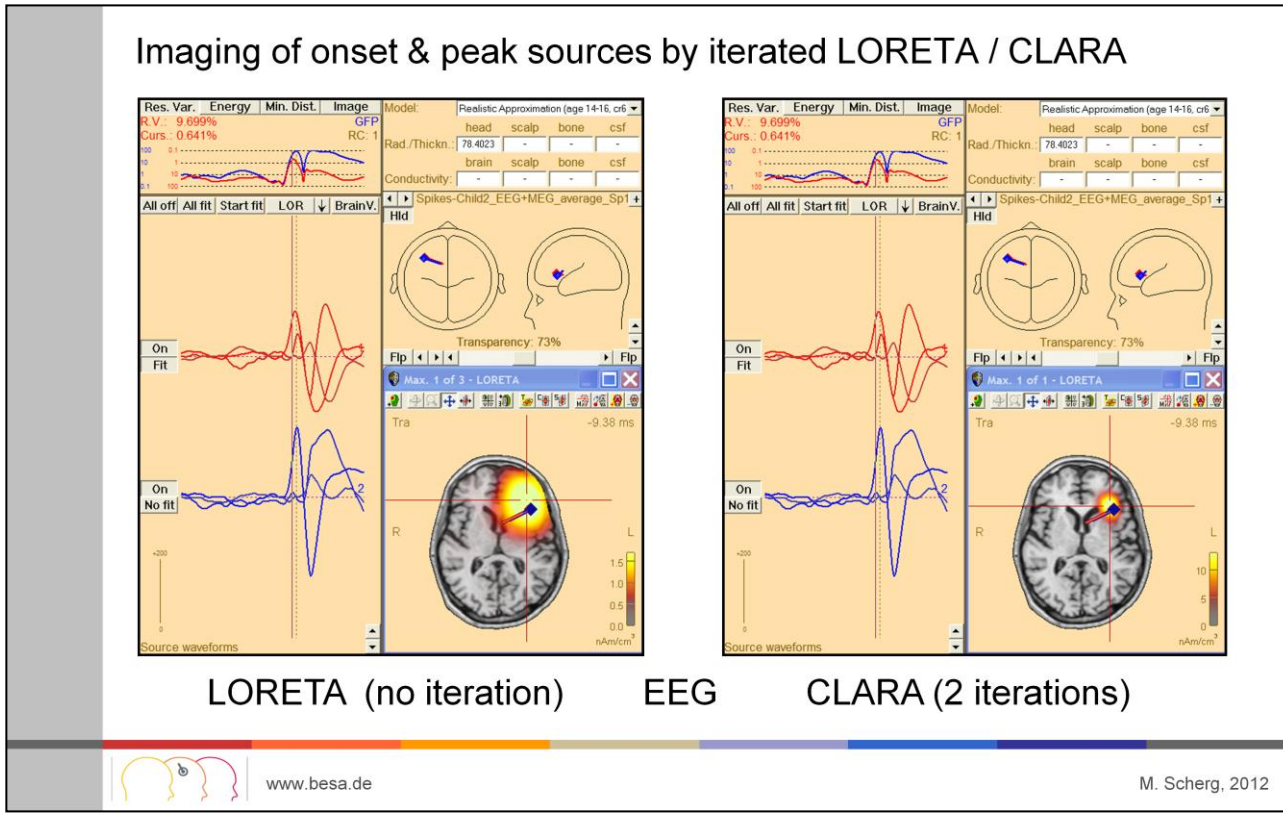
Note that neither method displays the extent of the activated zone – this information is not availabe from the scalp EEG. The extent of the image indicates the intrinsic smoothing of the CLARA/LORETA method and the limited resolution of the scalp EEG (here: 33 channels).



In the previous cases, a comparison of dipole localization with another imaging method has already been shown.

The basic aim of this comparison is to find consistency between onset localization using dipole fitting and an independent imaging method based on a distributed source model with a strong smoothing constraint.

If the results point to the same brain region, more stability of the solution can be assumed. Furthermore, by combining the point-like center solution of an equivalent dipole with a smeared distributed source image, overinterpretation of the precision of localization is avoided.

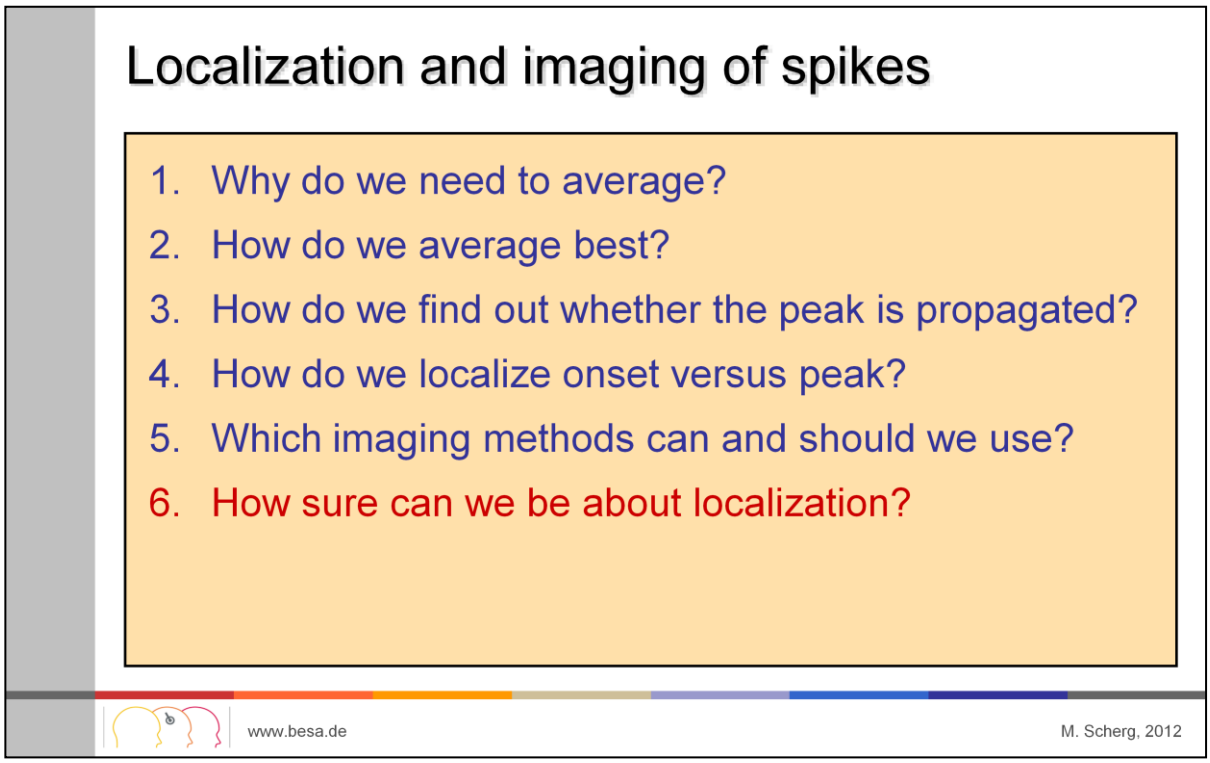


This automated analysis of the averaged spikes of child 2 presents the onset source (fit interval -25 : -9.4 ms, red) and compares it with the peak source (fit interval -20 : 0 ms, blue). Both sources almost coincide in location and exhibit only a small difference in orientation. If both sources are activated together, their source waveforms (left) share the activity and are similar.

On the left, a comparison with a LORETA (Low Resolution Electromagnetic Tomography, Pascual-Marqui et al. 1994) image at the onset maximum (-9.4 ms) is depicted. The tradeoff between resolution and smoothing has been optimized such that a mirror source in the other hemisphere can be separated in the LORETA image (the result above shows that there was no such mirror source on the right).

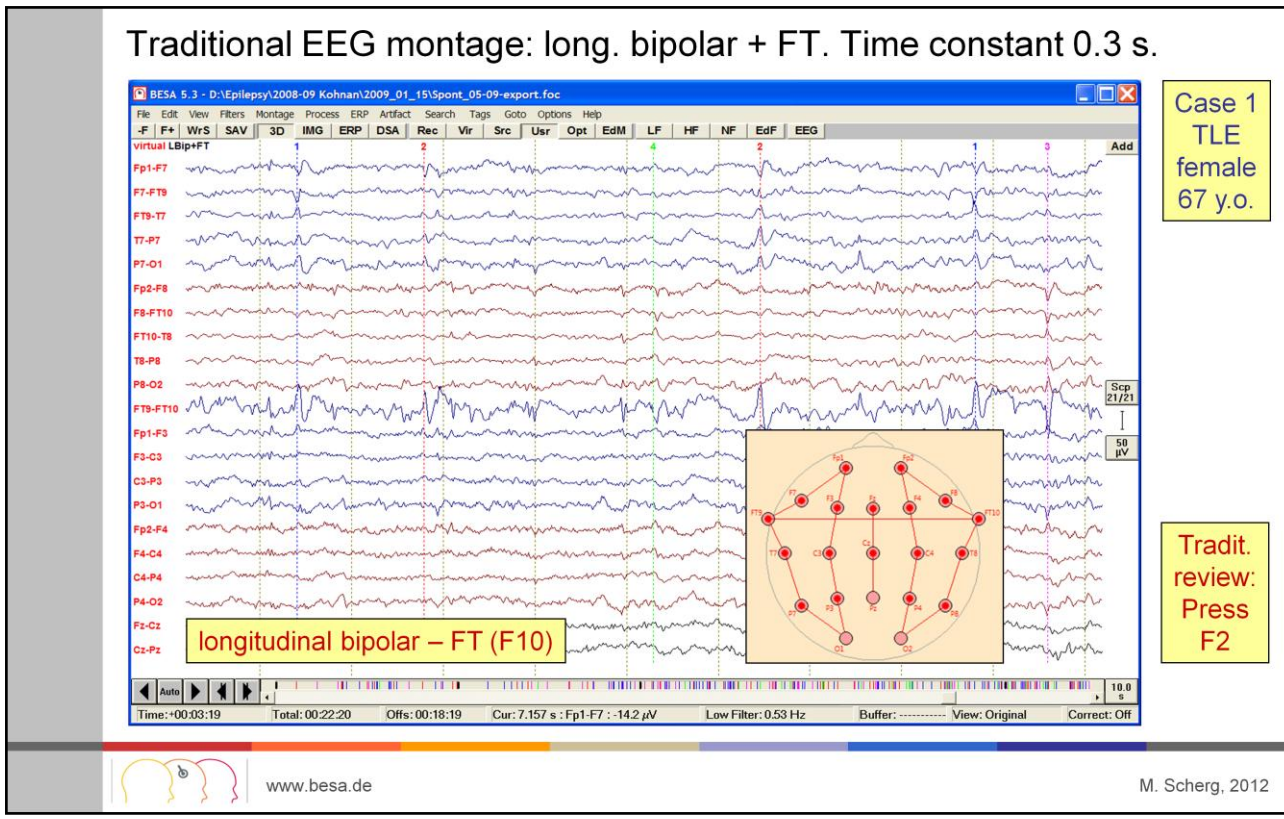
Separation and resolution can be enhanced by iterating LORETA twice with regularization constants appropriate for EEG and MEG, respectively, as seen on the right in the CLARA image (Classical Loreta Recursively Applied).

Other distributed imaging methods, for example sLORETA (standardized LORETA), lead to more smearing in the presence of bilateral or multiple sources. Therefore, they are not further considered in this talk.



As already explained above, the combination of dipole fitting with an independent imaging method like CLARA can provide more certainty about source localization of spike onset.

In the following, we want to inspect a few more cases of averaged interictal spikes to understand the benefits and limits of localization when combining the two methods. Furthermore, we will compare their results to the visual localization derived from scalp maps of properly preprocessed EEG data.



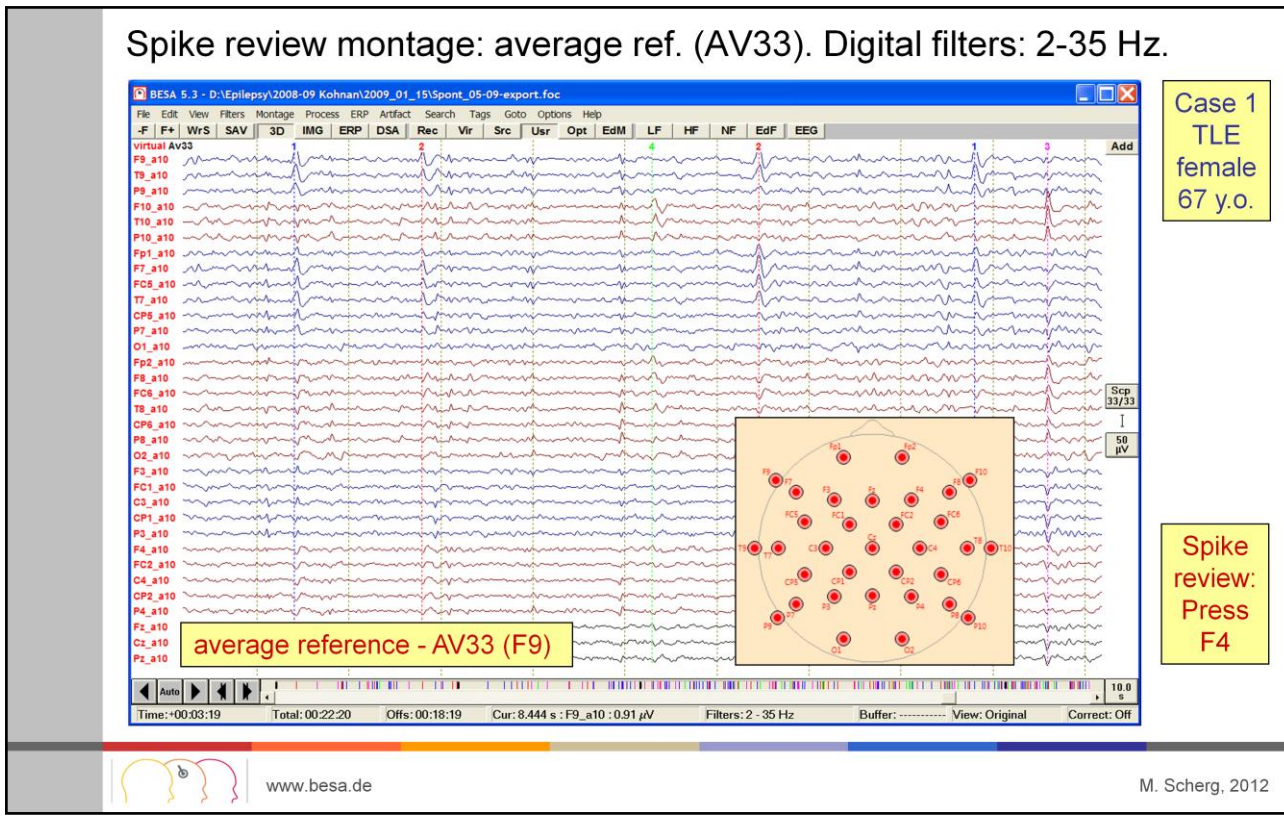
As a first example, we will use the EEG data of a patient with temporal lobe epilepsy to understand how improved montages and filter settings can enhance the perception of interictal spikes in the EEG. We will inspect a 10-sec page of EEG with different standard montages and filter settings.

Pressing **F2**, we obtain a standard EEG display with a longitudinal bipolar montage that is extended to inferior and has an additional transverse FT9-FT10 channel (Lueders montage). A standard EEG review filter is set: time constant of 0.3 sec, i.e. a low forward filter of 0.53 Hz; no high filter.

Polarity reversal can be seen over the left hemisphere between F7-P7 showing 4 spikes (marked by tags 1 & 2) and on the right between F8-P8 showing 2 spikes (tags 3 & 4).

The tags have been set by pattern search using the temporal lobe source montage described below.

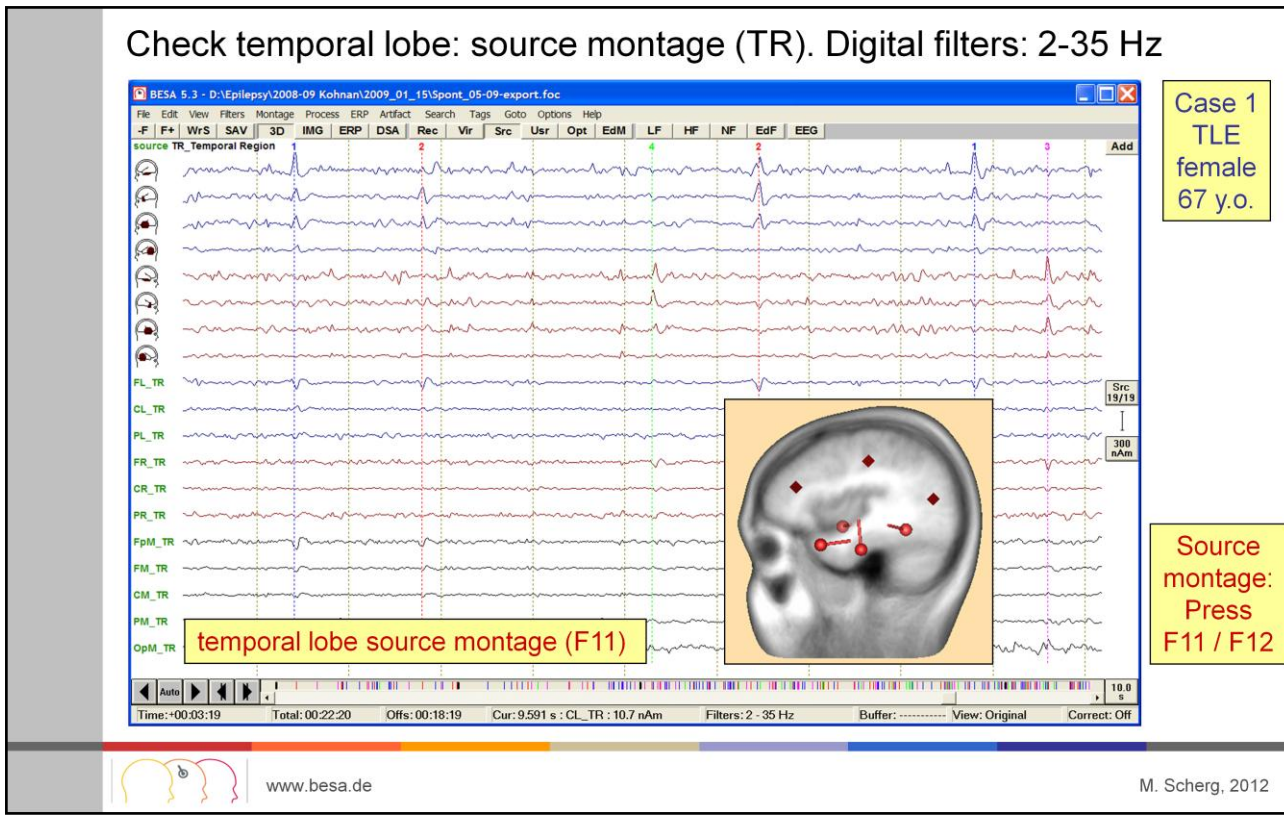
Instead of using the recorded channels, the displayed montage uses virtual channels, i.e. the EEG signals are interpolated at standard 10-20 and 10-10 locations on the scalp. This reduces local muscle artifact and allows to interpolate missing or bad channels and to extrapolate to more inferior sites, e.g. FT9 / FT10 in cases where only the standard 10-20 electrods are used. Thus, the EEG display always shows a consistent set of channels that makes reviewing more easy and reliable.



Pressing **F4**, we obtain the virtual average reference montage AV33 with inferior electrodes F9/10, T9/10, P9/10. These electrodes allow for some differentiation of spikes with tag 1/3 (spike signal largest at T9/10, present also at P9/P10) from spikes tag with tag 2/4 (spike signal largest at F9/10, not present at P9/P10).

Spikes, including inferior-temporal patterns, are better visible by using

1) a **virtual montage** that covers the whole head by extrapolating to intermediate and inferior sites even in the absence of inferior electrodes,
2) the **grouping of channels** in three longitudinal rows (e.g. the denser Fp1, F7, FC5, T7, CP5, P7, O1 row), and
3) an **optimized filter band (2 – 35 Hz)** that suppresses slow EEG activities and renders spikes riding on slow EEG activity more vísible. At the same time, the high filter removes a sufficient amount of EMG activity to enhance the visibility of spikes.



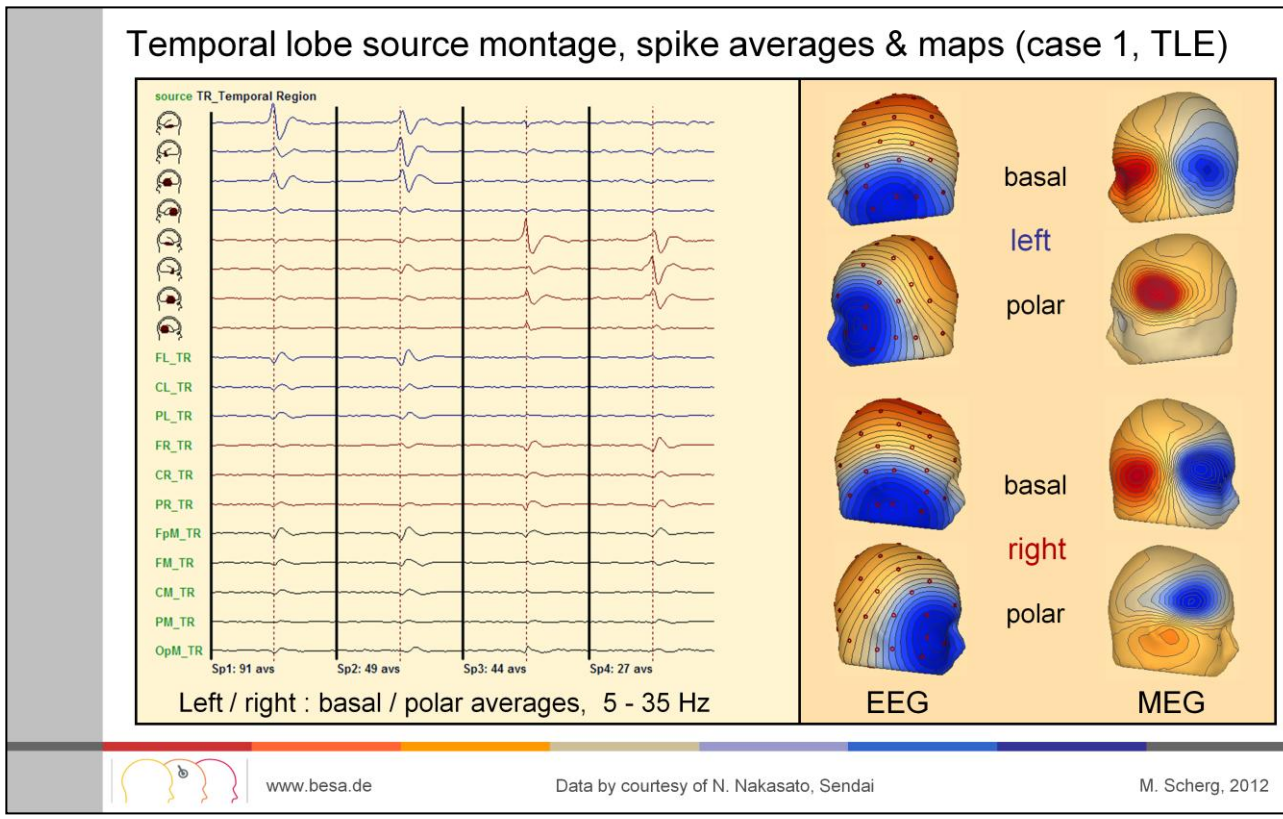
Pressing **F11**, we obtain the temporal-region source montage that estimates the activity at 4 different aspects of the temporal lobe. The EEG activity is projected onto the various brain regions using the potential distribution of all scalp electrodes in an inverse model. Thus, the left (upper 4 traces, blue) and right (next 4 traces, red) temporal lobe activities can be separated to a large degree from each other and from the activities in other brain regions (below).

The 4 temporal lobe aspects from top to bottom in each of the left and right groups are:

- temporal-basal
- temporal-polar
- temporal-anterior lateral
- temporal-posterior lateral

Spikes with tags 1/3 show the largest and earliest activity at the temporal base, while spikes with tags 2/4 show a leading temporal-polar activity.

Based on this distinction, obvious only in this specific source montage, we were able to search for and average similar spikes of these basal and polar types in the left (tags 1 & 2) and in the right temporal lobe (tags 3 & 4). The displayed EEG page shows typical detections that were found using a clear template for each spike type in the appropriate source channel.



First, we want to analyze the different spike types in the EEG and simultaneous MEG of this patient with bilateral temporal lobe epilepsy. The averaged EEG spikes are shown using the temporal lobe source montage.

Only the peak maps are shown to characterize the different detected spike types:

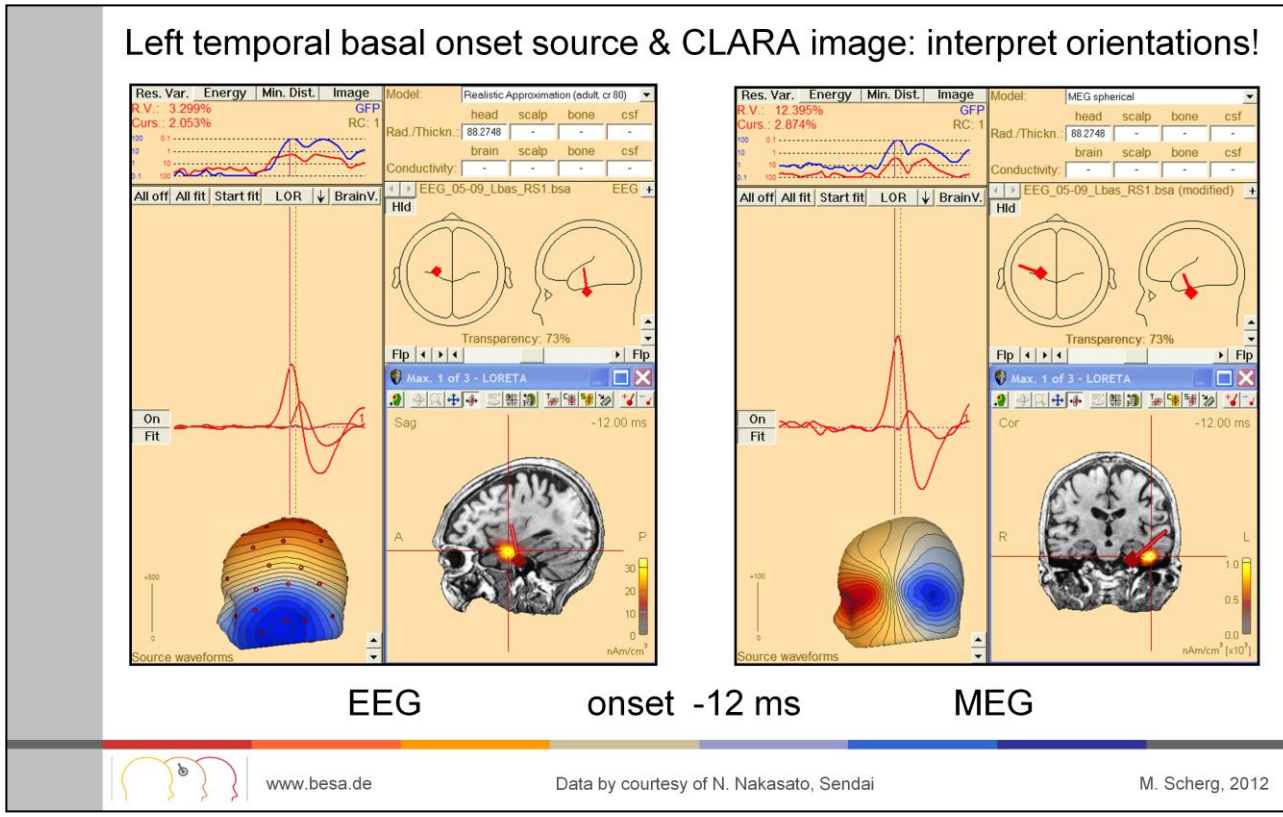
Sp1: left basal - EEG vertical map, the MEG shows the corresponding horizontal map, same center in left temporal lobe (91 averages)

Sp2: left polar - EEG oblique map with negative maximum over the eye, MEG map with reduced inferior negativity, pointing to the same more anterior center (49 averages)

Sp3: right basal - EEG vertical map, the MEG shows the corresponding horizontal map, same center in right temporal lobe (44 averages)

Sp4: right polar - EEG oblique map with negative maximum over the eye, corresponding orthogonal MEG map, pointing to the same more anterior center (49 averages)

In each hemipshere, 4 dipoles have been used to estimate the activity at the basal, polar, antero-lateral and postero-lateral aspects of the temporal lobe (left: traces 1-4, right: traces 5-8). The leading signal at the temporal base can be seen in the basal source channels (traces 1 & 4) in the averages Sp1 & Sp3; the leading signal at the temporal pole can be seen in the polar channels in the averages Sp2 & Sp4 below the basal channels (traces 2 & 5).



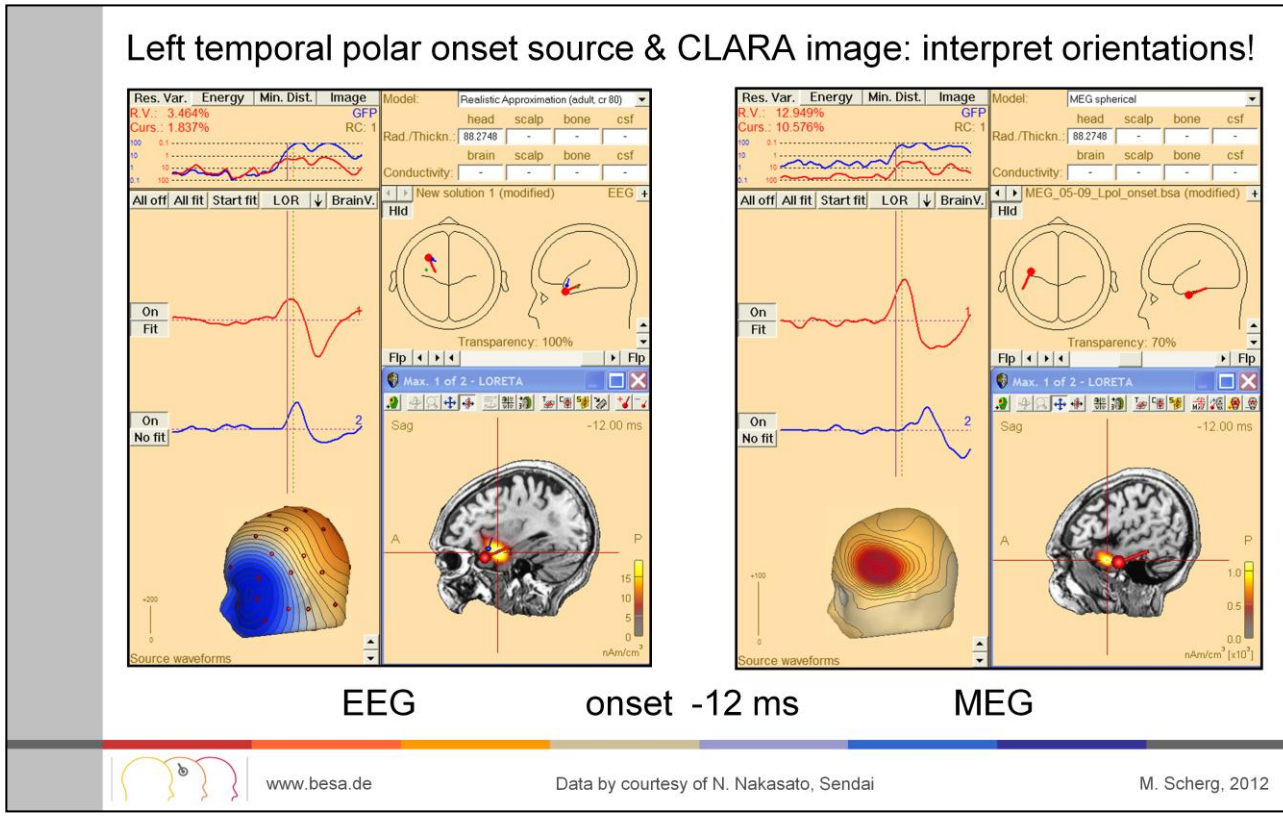
Pressing **F7**, we started the EEG source analysis and defined the onset interval of Sp1, i.e. the average of the 91 left spikes with basal onset. The red onset and blue peak sources were then fitted automatically and overlayed with a CLARA image (left). The peak source was removed in order to show when the EEG signal starts deviating from the onset signal (onset of 2nd dipole source waveform of the red regional source). Then, using a separate batch, the MEG solution at the maximum of the onset interval was computed (right).

Both the EEG and MEG source localizations and the CLARA image of the MEG point to the left basal temporal lobe as origin. In the EEG, the vertical orientation of the onset source supports this interpretation while the CLARA image simply highlights the anterior left temporal lobe without certainty about which surface is involved. This can only be assessed by the orientation of the EEG dipole.

The extent of the basal activation cannot be estimated from EEG or MEG.

Furthermore, depth should be interpreted with caution, because the equivalent vertical dipole can easily be shifted 1-2 cm deeper or laterally and still explain the data very well. Hence, orientation is the main cue to identify which surface is involved.

MEG source orientation is tangential to the spherical head model and, therefore, appears oblique in the coronal plane since the model sphere center is on the AC-PC line 16 mm behind AC. Thus, MEG dipole localizations and orientations should not be misinterpreted as pointing to the hippocampal region or showing the true current orientation. In fact, at least a major portion of the anterior parahippocampal gyrus has to be active to produce the clear basal onset signals in the scalp EEG and in MEG.

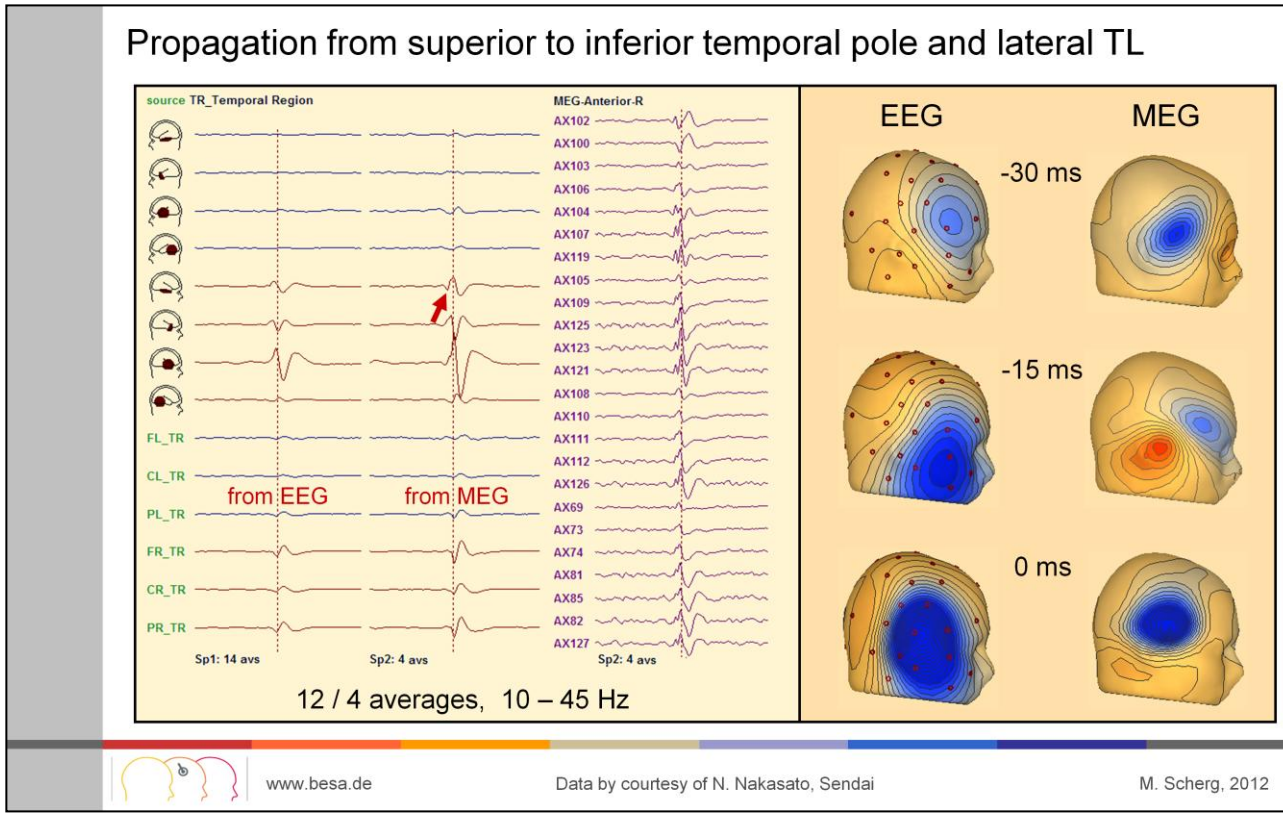


The average of the 49 spikes with left temporal polar onset in the source montage was analyzed using the corresponding batch for spike type 2 (Sp2). To better illustrate the evolution at the onset, the onset source was separated into 2 dipoles (red = onset dipole 1, blue = onset dipole 2 of the regional source).

The red onset source is oriented backwards in EEG and MEG and points to the left polar surface as origin. This is supported by the CLARA image of the MEG while the EEG image – as in the basal spikes – is unspecific with respect to which cortical surface is involved.

However, since EEG represents the true current vector orientations as opposed to the tangential projection of the MEG dipoles, it can be seen from the orientation of the 2nd onset dipole (blue) that a rapid propagation occured to the lateral polar part that was not visible in MEG due to the radial orientation of this activity. The 2nd EEG dipole could even be localized at an equivalent location within the polar region with the location again being unspecific with respect to the surfaces involved.

The key information on the spreading involvement of the different surfaces of the anterior temporal lobe is provided by the orientations and source waveforms of both EEG dipoles. They show that the initial tangential polar spikes (red) are rapidly getting overlapped by activity propagating to the lateral-anterior convexity - as seen in the delayed onset of the near-to-radial 2nd EEG dipole (blue). Since the MEG cannot see this radial activity, the 2nd MEG dipole does not show a large activity during this later part of the onset interval (-12 : 0 ms). It shows only propagated activity at a posterior portion of the temporal basal region much later on (right, blue dipole activity).



This example of a right temporal spike in another patient shows the activation of yet another surface in the polar temporal region and a considerable propagation. Here, we analyzed 4 spikes averaged from a sharp transient in the MEG.

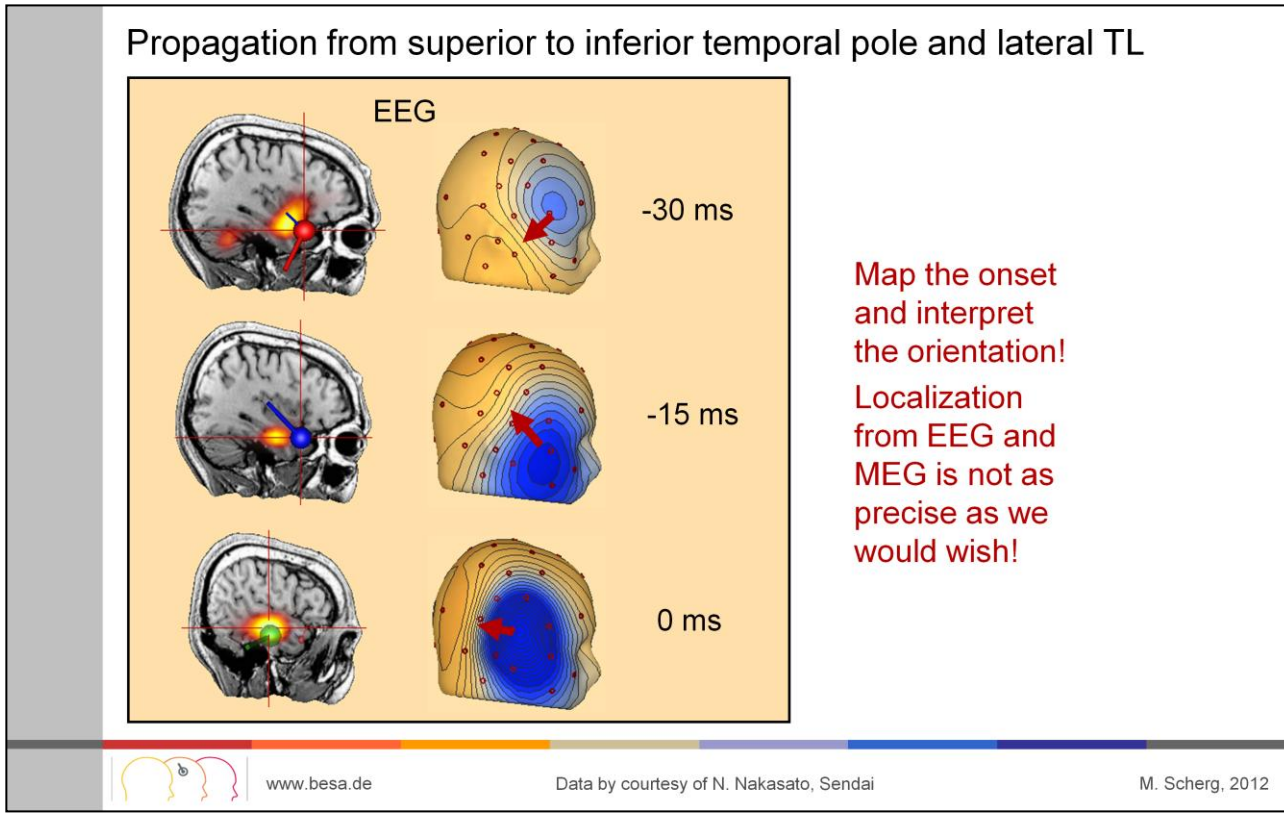
Note that the initial EEG dipole map at -30 ms shows a frontal negativity. When considering the accompanying inferior positivity and the gradients of the equipotential lines, it becomes evident that the underlying center is more inferior and corresponds to an oblique equivalent dipole pointing down and inwards.

The initial downward component is confirmed by the MEG map at -30 ms.

15 ms before the peak we observe a typical right temporal polar pattern, while superficial lateral activity with partly posterior orientation dominates at the peak (0 ms). Again, the polar current is confirmed by the MEG maps.

Thus, we might conclude that the spikes are initiated at the superior and lateral surface of the right temporal pole within the Sylvian fissure. This interpretation is supported by the small downward spike in the right temporal basal source waveform. This signal is constructed using a vertical dipole in the right basal temporal region within a multiple source model covering the other aspects of the right temporal brain region, the corresponding regions on the left and all other brain regions by regional sources. Thus, the basal source waveform will pick up spikes in the supratemporal plane as well, but with inverse, downward polarity.

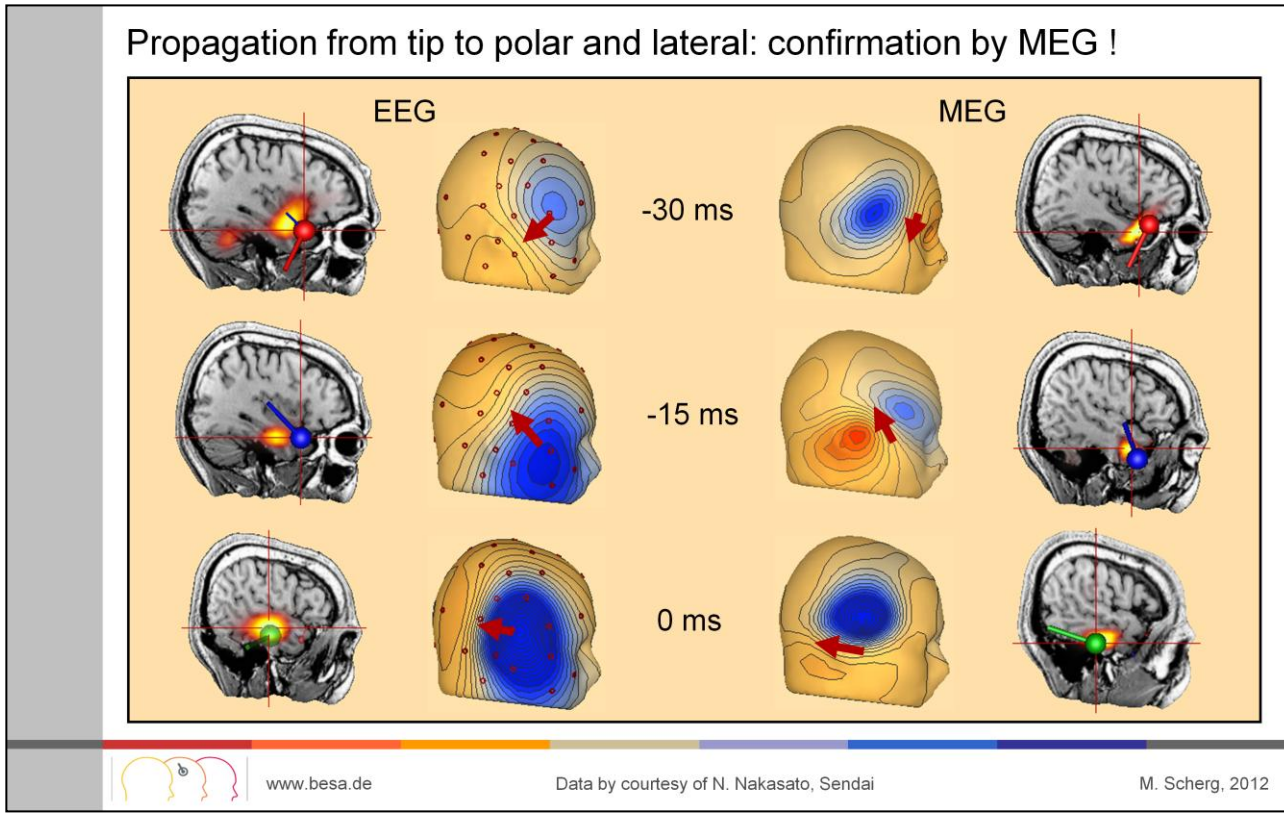
After this short initial superior spike, the typical propagation to the polar and further on to lateral regions was seen in the right temporal polar and lateral source waveforms.



This slide illustrates that the interpretation of the 3D EEG maps was confirmed by source imaging and dipole localization – using orientation as key information as well. The 3D maps by themselves already allowed for the correct interpretation of onset and propagation:

Based on the rules of finding an equivalent center in a (predominantly) dipolar map, the downward activity at -30 ms was identifiable in both the EEG and MEG maps. Considering the fact that epileptic spikes are cortical surface negative, the only candiate for the origin of a downward-posterior current can be the upper surface of the temporal lobe within the Sylvian fissure. The anterior location and the subsequent propagation to the inferior and lateral part of the temporal pole suggest the upper surface of the temporal pole as origin.

The polar maps at -15 ms are quite typical for temporal-polar spikes and easy to interpret. The stronger negativity and oblique, backward orientation of the EEG polar map indicates anterior, inferior and lateral involvement of the polar region.



In contrast to the EEG, the MEG is dominated by the polar and basal activity and blind to the radial part. At the peak, the MEG map was more complicated and not clearly dipolar. The strong radial dipole of the lateral anterior temporal surface is only seen in the EEG. Where the MEG localizes, will strongly depend on which fissural aspects generate the predominant signals within a relatively widespread spiking zone involving the lateral and inferior cortical convexity of the temporal lobe.

MEG localization appeared a little more confined, but far from being able to identify precisely which part of the anterior temporal lobe was spiking. Here as well, the orientation was needed to dissociate the superior surface of the temporal tip from the basal polar surface.

Conclusions

1. Voltage mapping of spikes improves non-invasive EEG diagnosis.
2. Most often, interpretation of 3D maps is sufficient.
3. Averaging is needed to identify spike onset and propagation.
4. Only in some, complex cases, more careful analysis is required using dipole localization and imaging techniques.
5. The combination of dipole localization using different hypothesis and CLARA images enhanced reliability.
6. A good equidistant electrode coverage with inferior electrodes is important (min. 25 / 33 recommended).

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- Andrea Ostendorf, BESA GmbH, Gräfelfing / Munich
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More lectures and tutorials showing the analysis of epileptic spikes and seizures can be found along with recommended electrode settings on:

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