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Automatic Detection of the Seizure Onset Zone based on ictal EEG

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Abstract—**In this paper we show a proof of concept for novel automatic seizure onset zone detector. The proposed approach utilizes the *Austrian Institute of Technology (*AIT*)* seizure detection system EpiScan extended by a frequency domain source localization module. EpiScan was proven to detect rhythmic epileptoform seizure activity often seen during the early phase of epileptic seizures with reasonable high sensitivity and specificity. Additionally, the core module of EpiScan provides complex coefficients and fundamental frequencies representing the rhythmic activity of the ictal EEG signal. These parameters serve as input to a frequency domain version of the Minimum Variance Beamformer to estimate the most dominant source. The position of this source is the detected seizure onset zone. The results are compared to a state of the art wavelet transformation approach based on a manually chosen frequency band. Our first results are encouraging since they coincide with those obtained with the wavelet approach and furthermore show excellent accordance with the medical report for the majority of analyzed seizures. In contrast to the wavelet approach our method has the advantage that it does not rely on a manual selection of the frequency band.**

I. Introduction

Approximatley 0.35% of the world's population suffer from drug resistant epilepsy. These patients may become seizure free after a neurosurgery where the *Seizure Onset Zone* (SOZ) is resected. In order to identify the region to be resected, the SOZ has to be determined. In addition to high resolution imaging, PET and psychological testing long term EEG recording over several days is one of the cornerstones of the presurgical workup. In order to improve the localization of the SOZ, source localization could be a valuable tool to find the neuronal sources generating the measured scalp EEG signals. Lots of research has been performed on this topic, which is summarized in comprehensive reviews [1][2]. The most common approaches are linear distributed inverse solutions, e.g. Weighted Minimum Norm approaches, applied to interictal epileptic activity [2]. Today, there are commercially available software tools [3][4] allowing for calculating the neuronal sources corresponding to the EEG signals of interest. From our point of view two major drawbacks in the context of state of the art source localization remain: 1.) There are too many user-interacts necessary to reach reasonable results and 2.) In most cases only interictal spikes are investigated [1][2].

In order to overcome the above stated problems, we propose an automatic SOZ detection system which extends the AIT seizure detection system EpiScan [5][6][7] by a frequency domain source localization approach. EpiScan was evaluated on 4300h of stored EEG-data obtained from 48 patients including 224 seizures [7] and is currently subject to clinical testing in two epilepsy centers. The advantage of extending EpiScan by a frequency domain source localization approach is that this combination is capable to work without any manual data preselection, i.e. clinicians do not have to struggle with identifying appropriate EEG segments. The number of user interaction is reduced to a minimum, namely to trigger the calculation of a realistic head model, which has to be done once for each patient. The second advantage of our system is that it exploits rhythmic ictal activity for finding the SOZ in contrast to most other approaches in literature which are based on interictal spikes not necessarily originating from the SOZ [8][9]. Localizing the neuronal sources of rhythmic activity is favorably done in frequency domain [10]. The necessary frequency transformation is inherently done by the Periodic Waveform Analysis (PWA) module, which builds the core of EpiScan. Additional advantages of frequency domain source localization are that the influence of noise is reduced due to the inherent averaging during the frequency domain transformation. For spike based source localization an averaging is also necessary to increase SNR [11]. In this case the effort is much higher, because a lot of spikes of the same origin have to be found. Additionally, it turned out that our method is especially robust against artifacts, since many artifacts lie out of the subspace of periodic signals and hence do not deteriorate the system performance.

The paper is organized as follows: In section I the entire system including the algorithms are explained. Section III gives some details of the recorded EEG data and the investigated patients. The outcome of the automatic detection of the recorded seizures in time and space is discussed in Section IV. A concluding discussion closes the paper.

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II. System and Methods

A. System Overview

Fig. 1 gives an overview of the system used. The system consists of two main building blocks. Block A represents the AIT seizure detection system EpiScan. The seizure detector is explained in detail in [6] and is fed by the raw EEG signal. The main tasks of the seizure detection system are twofold: First it temporally detects the seizure. Source localization is performed for this time point. Subsequently it performs the calculation of the complex coefficients of the most rhythmic part of this EEG sequence. In particular the complex coefficients in the vicinity of the seizure onset time and at the dominating frequency are calculated by the PWA module, which is the core module of EpiScan and is explained in more detail in Section II.B.

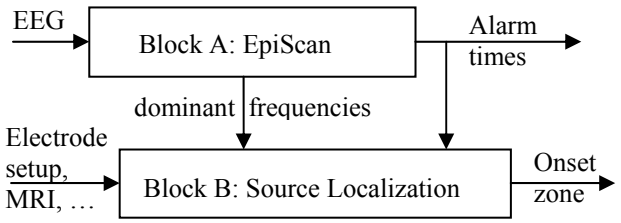

Fig 1.: System Overview

These complex coefficients are the input for the source localization in Block B. Further inputs are the electrode setup and the MRI in order to calculate the Lead Field Matrix. The result of Block B is a SOZ based on the most rhythmic components of the EEG signal.

B. EpiScan: AIT Seizure Detection System

EpiScan was developed for automatic alerting to seizures in epilepsy monitoring units. It is currently subject to clinical testing in two epilepsy centers. In this paper EpiScan is used to automatically determine the seizure onset-time. For this time instance t_0, a side product of the algorithm is exploited: EpiScan is based on a Periodic Waveform Analysis (PWA), which determines the dominant frequency f_0 of rhythmic EEG activity and calculates a complex coefficient centered at this time-frequency location,

$$c_{t_o,f_o} = \sqrt{f_o} \int_{-\infty}^{\infty} x_t \psi^*_{(t-t_o)f_o} e^{-j2\pi(t-t_o)f_o} dt.$$

The source localization algorithm requires these complex coefficients for each channel. Then, (t_0, f_0) was chosen from the PWA of the channel yielding the most distinct seizure alert.

C. Morlet Wavelets

In order to compare the source localization results based on EpiScan, we use the complex coefficients of a Morlet Wavelets frequency transformation [12] instead of the outcome of the PWA module. In contrast to the EpiScan approach, this method requires a manual selection of the dominant frequency. The EEG signals are transformed into frequency domain using Morlet Wavelets for the time instance detected by the seizure detector. An automatic selection of the strongest component of the frequency band would lead to tremendous problems in the presence of artifacts. For this reason, the dominant frequency band is manually chosen after a visual analysis of the time-frequency distribution and the resulting complex wavelet coefficients are used as input for source localization.

D. Calculation of the Lead Field Matrix

The Lead Field Matrix **L** describes the relationship between scalp potentials **e** and current density **j**: $\mathbf{e} = \mathbf{L} \cdot \mathbf{j}$.

The basis for the calculation of the Lead Field Matrix is a head model. In literature, numerous head models are discussed [1]. We chose the Boundary Element Method (BEM), because it achieves very good modeling accuracies while having tolerable computational complexity. The BEM needs the following input parameters:

- high resolution surfaces from the scalp, skull and brain; calculated from the MRI,
- electrode positions on the scalp, and
- conductivities of these compartments.

In this paper the Lead Field Matrix is calculated with the free available Neuroelectromagnetic Forward Modeling Toolbox (NFT) using a variant of BEM [13].

We calculated the electrode positions for individual MRIs according to the standard 10-10 electrode positioning rules.

The conductivities are assumed to be standard values: 0.33S/m for the brain and the scalp and 0.0132S/m for the skull [13]. The extraction of the surfaces is based on a high resolution structural MRI. A regular grid of solution points within the brain with an inter-grid distance of 7 mm is used as source space.

A complete calculation of the Lead Field Matrix lasts for approximately one hour on standard PC hardware. Note that this step has to be performed only once for each patient.

E. Source Localization Approaches

Most approaches to source localization can be divided into three categories:

- non-linear dipole fitting,
- spatial filters (adaptive and non-adaptive), and
- Bayesian approaches.

The aim of our approach is to perform source localization in a way that is robust, automatic, and fast; if possible it should be workable in real-time. Therefore, nonlinear dipole-fitting and Bayesian approaches cannot be considered: on the one hand they can run into local minima during the optimization and on the other hand they are far from real-time calculation. In addition, dipole-fitting approaches provide unreliable results, if the number of dipoles to be fitted is not exactly known beforehand. Therefore, we focus on spatial filters especially on the Minimum Variance Beamformer (MVB). The MVB belongs to the group of adaptive spatial filters [14]. The word adaptive indicates that the filter is adapted to the data. The idea behind the MVB is to minimize the interfering contributions of other voxels while fixing the contri-

bution of the interesting voxel v. This constrained minimization problem leads to the following solution for the beamforming vector:

$$\mathbf{w}_v = \left\|\mathbf{L}_v\boldsymbol{\eta}_v\right\|\mathbf{C}^{-1}\mathbf{L}_v\boldsymbol{\eta}_v\left(\boldsymbol{\eta}_v\mathbf{L}_v\mathbf{C}^{-1}\mathbf{L}_v^T\boldsymbol{\eta}_v^T\right)^{-1}$$

Here, $\mathbf{w}_v$ is the beamforming vector and $\mathbf{L}_v$ is the column sum standardized Lead Field Vector. Together with the direction of the current density $\boldsymbol{\eta}_v$ at voxel v, a matrix is built which completely describes the lead field caused by voxel v. The data covariance matrix is denoted by $\mathbf{C}$. For each point in the solution space such a beamforming vector and furthermore the current density $\mathbf{j}_v$ for voxel v can be calculated:

$$\mathbf{j}_v = \mathbf{w}_v^H\mathbf{E}_{f\,dom}$$

Here, $\mathbf{E}_{f\,dom}$ are the complex coefficients of the dominant frequency. The optimal direction for the current density vector $\boldsymbol{\eta}_v$ at voxel v is the eigenvector $\mathbf{x}_{\min}$ corresponding to the minimum eigenvalue $k_{\min}$ of the generalized eigenvalue problem:

$$\mathbf{L}_v\mathbf{C}^{-1}\mathbf{L}_v^T\mathbf{x}_{\min} = \mathbf{L}_v\mathbf{L}_v^T\mathbf{x}_{\min}k_{\min}$$

At this point the covariance matrix of the EEG data can be calculated. From the EpiScan algorithm, the complex-valued frequency domain coefficients for the most rhythmic EEG components are already known. These are the frequency component of interest, thus our estimate of the covariance matrix is based only on these coefficients:

$$\mathbf{C} = \mathbf{E}_{f\,dom}\mathbf{E}_{f\,dom}^H$$

Note that the covariance matrix has only rank one, which requires a regularization of its inversion.

III. Data and Patient Description

In our preliminary study we applied the proposed source localization method to long-term EEG recordings from 2 patients who underwent a presurgical workup due to drug resistant epilepsy. The recordings and the clinical analyses were done by medical doctors in the Epilepsy Center Kempenhaeghe, The Netherlands. Data were analyzed by medical-technical assistant to annotate seizure onsets.

In the Epilepsy Center a 64 electrode system from Stellate (Natus Inc, USA) was used. The electrodes where glued according to the standard 10-10 system including additional temporal electrodes at positions F9, F10, FT9, FT10, TP9 and TP10, SP1 and SP2. Due to the lack of knowledge of exact positions the electrodes SP1 and SP2 were excluded from source localization. The recordings of both patients were referenced to CPz. The EEG signal was sampled with 600Hz. Additionally to the EEG signals, a whole head MRIs with a spatial resolution of 1mm³ imaged with a 3 Tesla MRT using T1 weighting was performed. Furthermore, a medical report for all patients is provided. We refer to the two patients as O1 and O2 respectively. Patient O1 is a 63-year old male with temporal lobe epilepsy, probably due to mesio-temporal sclerosis of the right hippocampus. Patient O2 is a 54 old female with a left centro-temporal lesion. It was concluded from the long-term monitoring that this patient suffers from temporal seizures, which are not lateralized.

IV. Results

In this section the source localization results for the automatically detected rhythmic activity within the 5 seizures of both patients are compared for the EpiScan and the Morlet wavelet driven approaches. Additionally they are compared to the clinical findings provided by medical doctors.

EpiScan was able to detect 5 out of 6 seizures. One seizure was missed because there was no significant rhythmic seizure activity. For source localization, the EEG signal at the first seizure alarm was used. In this preliminary study false alarms were not used for localization.

We defined the position of the maximum of the current density vector as the center of the SOZ. The five seizures were analyzed and the coordinates of the centers of the SOZs for the different approaches were calculated. In order to compare the results of the different approaches, we calculate the relative distances between the source positions of both approaches (tabled in Tab 1).

Patient O1:

As described in the medical report, the first seizure starts which strong activity at SP2 (not included in the source localization) rapidly spreading to F8, F10, FT8 and FT10. The result of the source localization based on the PWA at the first alarm of the seizure detector is depicted in Fig 2.

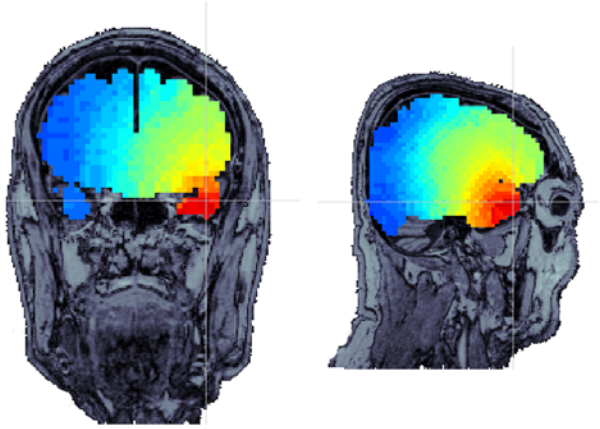

Fig 2.: Near the Onset of seizure 1 of patient O1 calculated with MVB applied to PWA coefficients.

As it can be seen in Fig 2, the onset is in the tip of the right temporal lobe. The Morlet based solution is in the right central temporal lobe (not shown). The distance between the both solutions is 29mm. Thus the PWA solution better matches with clinical findings (SP2).

Seizure 2 of patient O1 shows almost the same performance. The rhythmic activity starts at SP2 (not included in the source localization) rapidly spreading to F8, F10, FT8 and FT10. The maximum activity at the first alarm within the second seizure is in the right anterior temporal lobe for the PWA based method and in the right central-inferior temporal lobe for the Morlet based approach.

Patient O2:

As stated in the medical report, the first seizure starts with strong activity at F7 and F9. Although the onset of this seizure is left temporal, at the end of the seizure the strongest

rhythmic activity can be found at the right hemisphere on AF8, F6, F8, F10, FT8 and FT10. This propagation during the seizure described in the medical report can be confirmed by visualizing the source localization results of the whole seizure in form of a movie.

Both methods show a left frontotemporal onset zone. The PWA based method provides a more central source, compared with the Morlet solution which is more medial.

The second seizures of patient O2 show almost the same properties. The only difference is that both methods find a left anterior temporal SOZ.

For the first alarm of the third seizure the PWA based approach yields a left posterior temporal onset zone. The Morlet driven approach localizes a left parieto-occipital onset zone. This does not coincide with the results stated in the medical report (SP2). The reason for this inaccurate localization is that the used time point (first alarm) is too far from the real seizure onset.

Patient / Seizure	SOZ PWA	SOZ Morlet	Distance / mm	SOZ Medical Report
O1/1	Tip of the right temporal lobe	right central temporal lobe	29	SP2
O1/2	right anterior temporal lobe	right central-inferior temporal lobe	33	SP2
O2/1	left central fronto-temporal lobe	left medial fronto- temporal	23	F7, F9
O2/2	left anterior - temporal lobe	left anterior-temporal lobe	20	F7, F9, FT7, FT9, AF7
O2/3	left posterior temporal lobe	left parieto-occipital lobe	23	SP2

Tab 1.: Comparison of the position of maximum activity at the seizures first alarm in the vicinity of the seizure onset between the PWA and the Morlet driven source localization and the results stated in the medical report.

V. Discussion and Conclusion

Our first results for automatic SOZ detection are encouraging. In 4 of 5 cases the source localization results are in good accordance with clinical findings. Furthermore, the automatic EpiScan based method yields similar source localization results than the wavelet analysis which suffers from the drawback that one has to choose the dominant frequency manually. The remaining differences between the results of the PWA and the Morlet driven source localization may result from using different frequency segmentation resulting in small differences of the input signal for the source localization. The analysis of the propagation of the maximum activity is an additional advantage of using ictal EEG signals. For patient O2 the result of the source localization indicates a moving source during the seizure. This is also confirmed by clinical findings.

This proof of concept shows that the AIT seizure detection system is a promising preprocessor for source localization based on ictal EEG signals. In our future work we will focus on the evaluation of more patients and the improvement of the detection of the temporal onset.

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