Ictal EEG Source Imaging for Presurgical Evaluation of Refractory Focal Epilepsy

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Ictal EEG Source Imaging for Presurgical Evaluation of Refractory Focal Epilepsy

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Key Words: Ictal EEG; Interictal EEG; Source Imaging; Source Localization; Epilepsy
Abbreviations and Acronyms:

BEM: Boundary Element Method

dSPM: Dynamical Statistical Parametric Mapping

EEG: Electroencephalogram

ESI: EEG Source Imaging

fMRI: functional Magnetic Resonance Imaging

FOV: Field of View

FSPGR: Fast Spoiled Gradient-Recalled

GFP: Global Field Power

MEG: Magnetoencephalography

MRI: Magnetic Resonance Imaging

OSEM: Ordered Subset Expectation Maximisation

SEEG: Stereoelectroencephalography

sLORETA: Standardized low resolution brain electromagnetic tomography

SNR: Signal to Noise Ratio

SPECT: Single Photon Emission Computed Tomography

TE: Echo Time

TR: Repetition Time

wMNE: weighted Minimum Norm Estimate
Abstract

BACKGROUND: EEG source imaging (ESI) is a promising tool for localizing the cortical sources of both ictal and interictal epileptic activities. Many studies have shown the clinical usefulness of interictal ESI but very few have investigated the utility of ictal ESI. The aim of this article is to examine the clinical usefulness of ictal ESI for epileptic focus localization in patients with refractory focal epilepsy, especially extratemporal lobe epilepsy.

METHODS: Both ictal and interictal ESI have been performed by using patient specific realistic forward models and three different linear distributed inverse models. Lateralization as well as concordance between ESI estimated focuses and Single Photon Emission Computed Tomography (SPECT) focuses have been assessed.

RESULTS: All the ESI-focuses (both ictal and interictal) have been found lateralized to the same hemisphere as ictal SPECT-focuses. Lateralization results are also in agreement with the Magnetic Resonance Imaging (MRI) lesion sides. Ictal ESI results, obtained from the best performing inverse model, are fully concordant to the same cortical lobe as SPECT-focuses whereas the corresponding concordance rate is 87.50% in case of interictal ESI.

CONCLUSIONS: Our findings show that ictal ESI gives fully lateralized and highly concordant results with ictal SPECT and may provide a cost effective substitute for ictal SPECT.

Introduction

Focal epilepsy is the most common form of epilepsy (~60% of all epilepsy) and around 15% of all focal epilepsy are uncontrolled or of the refractory type (8, 29). Approximately half of the patients with refractory focal epilepsy, i.e. ~4.5% of all patients with epilepsy, are
potential candidates for surgical resection (8, 29). The goal of epilepsy surgery is to resect or disconnect the epileptogenic zone completely (5) and precise localization of this zone is obligatory for producing seizure freedom.

Different diagnostic techniques, such as non-invasive scalp electroencephalogram (EEG), invasive EEG, magnetoencephalography (MEG), MRI, functional magnetic resonance imaging (fMRI), ictal and interictal SPECT are used to measure the ‘epileptogenic zone’ which refers to a cortical region of the brain that, when stimulated, produces spontaneous seizure or aura (23). Among these techniques, EEG is the most commonly used. Traditionally, EEG recordings are analysed through visual inspection, but simple visual analysis is not adequate for precise localization of the epileptogenic zone. EEG source imaging (ESI) is comparatively a new model-based computational technique that can localize and depict the possible cortical sources of EEG activities (15). It works by solving the so-called forward and inverse problems. The forward problem is solved by finding the scalp potentials at the electrodes that would result from a given cortical source configuration. The process of identifying the sources of the measured surface potentials is called the inverse problem and its solution involves one or several repeated solutions of the forward problem with a priori assumptions of the source and the volume conductor. Both ictal and interictal scalp EEG can be utilized for localizing the epileptogenic zone.

Several clinical studies have examined the feasibility and accuracy of interictal ESI and their findings are summarized in a recent review of Kaiboriboon (15). This review showed that interictal ESI had a high positive predictive value and could provide useful information about the cortical origins of interictal spikes. These spike origins can be separate from the
epileptogenic zone (29) because of the fast propagation of interictal epileptiform activity (32). On the other hand, ictal EEG is believed to be more reliable than interictal EEG in localizing the epileptogenic focus (13), but comparatively difficult to analyse by using ESI because of the low Signal to Noise Ratio (SNR) and undetectable low strength of ictal events before being spread considerably (15). Therefore very few studies (1-4, 7, 12, 14, 16-18, 21, 22, 24, 33) evaluated the performance of ictal ESI. More than one-third of the reviewed articles (1, 2, 14, 18, 24) used multilayer spherical head models whereas four other studies (3, 12, 17, 33) used template MRI based realistic head models for estimating the epileptic focus. Actual patient’s head and such generalized head model have significant anatomical differences. Therefore, from the surgical point of view, it is obvious that such strategies of ESI do not necessarily provide correct solutions. Only five (4, 7, 16, 21, 22) out of fourteen articles on ictal ESI used patient specific realistic head models for their studies, although the sensitivity of ESI can be increased by using patient specific realistic head models (5).

In comparison with extratemporal lobe epilepsy, ictal events in temporal lobe epilepsy are mostly examined in the ictal ESI studies. Thirteen (1-4, 7, 12, 14, 16, 18, 21, 22, 24, 33) out of fourteen reviewed articles on ictal ESI have investigated the ictal events in temporal lobe epilepsy while eight (4, 7, 12, 16, 21, 22, 24, 33) of those thirteen articles have extended their investigations for extratemporal lobe epilepsy patients. One recent article (17) on ictal ESI inspected the ictal events in frontal lobe epilepsy only, but highlighted the importance of the presurgical evaluation in extratemporal lobe epilepsy.

A more recent study by Kovac et al. (17) investigated whether ictal ESI, using low density EEG recording of eight patients, leads to improved lateralization compared with visual
analysis. However, a major limitation is in the use of template MRI based finite element head model. Patient specific realistic head models were used in five ictal ESI studies (4, 7, 16, 21, 22) and most of these studies (4, 16, 21, 22) validated their ictal ESI results against stereoelectroencephalography (SEEG) and postsurgical outcomes. Although, SEEG can estimate the epileptic focus more precisely than visual analysis of scalp EEG, this invasive modality has several surgical constraints as well. Since ESI is a noninvasive modality for epileptic source localization, it is logical to compare its results with an equivalent modality such as SPECT. Ding et al. (7) analysed seizures from five epilepsy patients and their ictal ESI results were consistent with either MRI lesions or SPECT scans. They proposed a novel but complicated method based upon a combination of the subspace source localization technique and the spectrum-based causal interaction estimation technique. Beniczky et al. (3) used conventional method for conducting ictal ESI study and validated the results against corresponding SPECT results. They also performed interictal ESI in the same group of patients as ictal ESI and presented there interrelations. Using template MRI based BEM model is the major limitation of their study. A reliable clinical study that uses realistic head models, standard medical EEG records and conventional ictal ESI techniques for the noninvasive evaluation of both temporal and extratemporal lobe epilepsy, still remain a principle research challenge.

In this context, this study evaluates the usefulness of ictal ESI as a noninvasive diagnostic modality for localizing the epileptogenic focus in patients with refractory focal epilepsy, especially extratemporal lobe epilepsy. Both ictal and interictal ESI have been performed by using low resolution EEG data, commonly used ESI techniques (1-3, 12, 16, 17, 24), patient specific realistic BEM head models and three different inverse models namely weighted minimum norm estimate (wMNE), dynamical statistical parametric mapping (dSPM) and
standardized low resolution brain electromagnetic tomography (sLORETA). The results obtained are validated against MRI lesions and ictal SPECT. Performance of ictal ESI is compared with that of interictal ESI. Effects of three different inverse modelling algorithms on ictal ESI have also been investigated.

Materials and Methods

Patients

This study was conducted using anonymized retrospective data and the study protocols were approved by the University of Malaya Research Ethics Committee (UMREC) of the University of Malaya, Malaysia.

Fifteen patients, who suffered from pharmacoresistant focal epilepsy and underwent presurgical evaluation by means of clinical semiology, MRI, ictal SPECT and long-term video-EEG (both ictal and interictal) monitoring, were primarily selected from the database of the University of Malaya Medical Centre (UMMC). Eight patients, whose ictal SPECTs were found concordant with the clinical semiology were finally selected in this study. The patients’ demographics and clinical characteristics are summarized in Table 1. Five out of these eight patients had extratemporal lobe epilepsy whereas the three patients, namely patient #5, patient #7 and patient #8, had temporal lobe epilepsy.

Anatomical Data Acquisition

Anatomical details of every patient’s head were obtained from their corresponding MRI scans. Those details were used for pre-surgical evaluation as well as for generating patient
specific head models for ESI analysis. All patients’ structural MRI scans were performed with a Signa HDxt 3.0T scanner (General Electric Healthcare, USA). Three dimensional Coronal T1-weighted fast spoiled gradient-recalled (FSPGR) images were acquired with these imaging parameters; slice thickness: 1.4mm, field of view (FOV): 350mm, echo time (TE): 1.8ms, repetition time (TR): 6.8ms. Axial and sagittal images were reconstructed for review. In six patients, the structural MRI showed a focal abnormality indicating an epileptogenic lesion; the other two patients (patient #4 and patient #6) had normal MRI.

**Functional Data Acquisition**

Functional states of patients’ brains were recorded through long-term video-EEG. Recording was performed on all patients with standard clinical EEG setups according to the international 10–20 system with additional 2 electrodes at T1 and T2. All the recordings were captured with NicoletOne EEG/LTM system (Natus Medical Inc., USA). Electrode impedances were kept below 10kΩ and sampling rate was set to 512Hz (with one exception: 256Hz for patient #6). The long-term EEG recordings captured between 2 and 8 seizures across all patients.

**Nuclear Image Acquisition**

Regional cerebral blood flow was measured by SPECT using a brain-dedicated gamma camera, Brightview XCT (Philips Electronics N.V.), equipped with low energy high resolution collimators. Imaging was acquired within 60 minutes of the intravenous radiopharmaceutical administration of 25 millicurie of 99mTc-HMPAO (Ceretec, GE Healthcare, UK). An ictal scan was performed by injecting the radiotracer within 30 seconds from the onset of seizure. Datasets were acquired in a 128 x 128 byte matrix (Q matrix) over
360 degrees, with 120 views obtained at 3 degree intervals for 40 seconds per view (energy setting of 140 keV). Images were reconstructed using Astonish advanced reconstruction algorithm with an iterative 3D-Ordered Subset Expectation Maximisation (OSEM) algorithm and built-in corrections for resolution recovery, scatter correction and attenuation correction. Images of SPECT were coregistered to MRI FSPGR images (when available). Reconstructed transversal, sagittal and coronal images were visually evaluated blinded to the results of EEG findings.

Electroencephalographic Source Analysis

a. Data Pre-processing

Automated quantitative analysis techniques, such as ESI, are negatively influenced by the signal intensity inhomogeneity or bias field effect in MRI. Such inhomogeneity of all the MRI scans was corrected with the Freesurfer image analysis suite (http://surfer.nmr.mgh.harvard.edu/). Moreover the software was also used for obtaining uniform voxel size (1mm X 1mm X 1mm) and orientation (RAS) by revising the raw MRI scans.

One of the major difficulties of source modeling through surface ictal EEG is the inevitable presence of various artifacts. Since most of the ictal rhythmic events are of 3-29Hz (10, 14), a narrow bandpass filter of 1Hz to 30Hz was used to minimize these obscuring artifacts and thus improved the SNR. No such extra bandpass filter was used for pre-processing the interictal EEG records because the epochs having significant artifacts were excluded from the interictal analysis. With the help of power density spectrum and visual inspection, individual channels (T6 for patient #2, Fp1 & Fp2 for patient #3, C4 for patient #4 and P4 for patient
Having excessive artifacts, were identified and then eliminated from both ictal and interictal source analysis.

b. Epoching and Averaging

The time points of interictal spikes and ictal onset rhythms or spikes, as classified by Foldvary et al. (9), were determined by an experienced epileptologist through visual inspection of scalp-recorded video-EEGs and their filtered outputs respectively. At least 10 interictal spikes (70ms) or sharp waves (200ms), that were isolated (i.e. no similar discharge within ±500ms), were selected and marked for each patient’s interictal analysis. Epochs of ±100ms (15, 16) around those marked time points were used for interictal analysis. Ictal epochs of each patient were acquired from the EEG segment which was recorded during seizure, had evolution of ictal rhythms and in which the radioactive tracer for SPECT was injected. The channel with ictal rhythms (or spikes) and maximum power density around the rhythm frequencies was considered as the prominent channel. At least 10 non-overlapping 200ms epochs were included in each patient’s ictal analysis so that the centre time point of each epoch holds the negative maximum peak of an ictal event of the prominent channel. Figure 1(a) illustrates the ictal EEG of patient #2. The EEG segment within the green box is the region of interest. Ictal events were selected from this region. Power spectrum density of each channel, measured throughout the region of interest, is shown in Figure 1(b). Ictal rhythm frequency within the region of interest was around six and the channel T5 showed the highest power at 6Hz, therefore T5 was considered as the prominent channel for this patient. Figure 1(c) is the magnified view of the region of interest. The vertical lines represent the centre time points of the selected ictal events. For the improvement of the SNR, averaging of
every selected group of epochs was performed separately (i.e. one average ictal epoch and one average interictal epoch for each patient).

c. **Head Modelling**

Estimation and imaging of the sources of brain electrical activities comprises the so called forward modelling and inverse modelling. A known model of head is required for forward modelling. Patient specific realistic head models, namely three layer boundary element method (BEM) head models, were used in this study (3, 16). Necessary segmentation from bias field corrected MRI scans and thus extraction of scalp, outer-skull, inner-skull, grey matter and white matter surfaces were performed by using BrainSuite 14a (30). Obtained surfaces of scalp, outer-skull and inner-skull were further processed by Brainstorm 3.2 (31) for generating non-intersecting BEM meshes with 1922 vertices per layer. Known dipole sources were located in two different source spaces (surface and volumetric) separately. Standard geometrical positions of electrodes, available in Brainstorm software, were used after manual inspections and necessary alterations according to individual patient’s scalp surface. Based on these geometrical descriptions of BEM meshes, source spaces and the channel positions, two separate forward models (with surface source space and volumetric source space) were computed for each patient with the help of OpenMEEG software (11).

d. **Source Localization**

Estimation of the unknown sources corresponding to the measured scalp EEG is referred to as inverse modelling. Different inverse modelling approaches were proposed and all of those approaches have some relative merits and drawbacks (15). Three linear distributed inverse models, known as wMNE (20), dSPM (6) and sLORETA (26), were used in this study.
Brainstorm-implementations of these algorithms were used without any dipole orientation constraint. Source analysis was performed on the average maps of both ictal rhythms (9) and interictal spikes or sharp waves. The time point at which the source analysis was performed was termed as examination time point ($t_0$). For ictal and interictal analysis $t_0$ represented the time point at which the peak and the 50% rising phase (28) of the global field power (GFP) occur respectively. Figure 2 illustrates the examination time points on the average maps of selected ictal and interictal events of patient #1. Ictal events can be oscillatory-type and spike-type as well (9). The ictal event of Figure 2 is a spike-type ictal event which is selected for the better visualisation of various time points.

e. Stability of Estimated ESI Results

Cortical source of EEG can be estimated for every single time point. An obtained source on a single time point may not be considered as true source unless the result remain stable for a certain duration, because unstable localization can appear in the case of inadequate SNR. Therefore, it is expected that the examination time point and its adjacent time points would estimate the sources in the same or nearby cortical regions. The durations of stable results have been measured around the examination time point.

In the average maps of Figure 2 the highlighted signals hold the highest amplitude. The time points, $t_1$ and $t_2$, of every average map represent two adjacent local minima of the highlighted signal (around $t_0$). The time duration from $t_1$ to $t_2$ is considered as the event duration. Sources have been estimated for every time points starting from $t_0$ until $t_1'$ and $t_2'$ (where $t_1' \geq t_1$ and $t_2' \leq t_2$) so that all the estimated sources remain in the same lobe. Besides, the time points next to
t_{1}' and t_{2}' estimate the source in different lobe. The time duration from t_{1}' to t_{2}' is considered as the duration of stable results.

\textit{f. Performance Measure}

All the estimated ESI-focuses were compared with the corresponding SPECT-focuses. ESI results were considered to be concordant with SPECT results if both ESI-focus and SPECT-focus were located in the same lobe. Concordance rate was measured as the percentage of concordant results in the total number of considered results. If an estimated ESI-focus and the corresponding SPECT-focus were found in the same hemisphere, then the estimated result was considered as lateralized.

\textbf{Results}

Figure 3 illustrates the SPECT results and corresponding ESI results of two patients (patient \#2 and patient \#3). These two sets of results are selected so that all the ESI results of one patient (patient \#2) are fully concordant with SPECT result whereas the ESI results of the other patient (patient \#3) are not in all cases concordant with SPECT result. All the ESI results and the SPECT result of patient \#2 shows that the epileptic focus is located in the left occipital lobe. Therefore, all the ESI results of patient \#2 are considered concordant with the SPECT result. According to the SPECT result of patient \#3 the epileptic focus is located in the right parietal lobe. Obtained ESI results show that only ictal analysis through dSPM estimates the focus in the same lobe.
The sLORETA analysis of ictal events which estimates the focus in the lateral sulcus of Sylvius of the same hemisphere is also considered concordant. Other ESI results of patient #3, although estimate the focus in the adjacent lobe (temporal lobe and insular cortex), are not considered concordant with SPECT result. The volume of ESI-focus is threshold dependent. Different threshold values are chosen for different ESI results for better visualization and easier localization of the regions with maximum current density. Therefore, the volumes of ESI-focuses, highlighted with red color in Figure 3, do not provide information on the extent of epileptogenic zone. These highlighted regions represent the brain volumes that contain the maximum current density sources.

Cortical locations of all the eight patients’ electroencephalographic sources along with the positions of their corresponding SPECT-focuses and MRI lesions are listed in Table 2. ESI with surface source space and volumetric source space estimated the sources in the same sublobe. The only difference was that the surface source space based analysis always estimated the sources on the grey matters while the volumetric source space based ESI often found the sources in the white matters of the corresponding sublobe. Therefore the results obtained for surface source space and volumetric source space have not been listed separately in Table 2.

Based on the results listed in Table 2, concordance and discordance of the obtained ESI results with SPECT results are summarized in Table 3. Ictal analysis results show that dSPM and sLORETA can locate the ESI-focus and the SPECT-focus in the same lobe for all of the 8 patients (concordance rate 100%) whereas wMNE results is not concordant for patient #3 (concordance rate 87.50%). On the other hand the results obtained from interictal analysis
show that wMNE and sLORETA estimate concordant results for seven (except patient #3) out of eight patients (concordance rate 87.50%) while the dSPM fails for patients #1, #3 & #7 (concordance rate 62.50%). Among the three distributed inverse models sLORETA gives the highest concordance rate for both ictal and interictal analysis, whereas for individual inverse model the number of concordant results of ictal ESI is either equal to or higher than that of interictal ESI. All the ESI results are lateralized correctly because all estimated ESI sources are found in the same hemisphere as their corresponding SPECT sources and MRI lesions (see Table 2).

The durations (in milliseconds) of stable results around the corresponding examination time points are listed in Table 2 for all the ESI analysis. These durations indicate that the ictal analysis through sLORETA produces the results with the longest average duration of stability and it is 50ms (median: 37.5ms, range: 18 – 134ms). The results obtained for ictal analysis through wMNE remain stable for the shortest average duration and it is 43.75ms (median: 25.5ms, range: 14 – 138ms). Analysis results through rest of the methods of both ictal and interictal analysis remain stable for average duration of 46.13ms to 49.38ms. Overall average duration for ictal analysis results (4.71ms) has been found slightly (1.13ms) longer than that of interictal analysis results (4.58ms) and it supports the acceptability of ictal analysis results. However, longer average duration of stable ictal analysis results is expected, because the event duration \( (t_2 - t_1) \) of ictal events are usually longer than that of interictal events.

**Discussion**

This study demonstrates that all the estimated ictal ESI-focuses and the corresponding clinically evaluated seizure focuses are lateralized to the same brain hemisphere.
Furthermore, all the ictal ESI results, except one wMNE analysis result, are concordant with the results of at least two other diagnostic modalities (MRI and SPECT). These ESI analyses have been conducted using MRI scans and EEG data that were acquired within a standard clinical setup for presurgical evaluation of epilepsy. These findings also support the argument that ictal ESI can be considered as a potential noninvasive diagnostic tool for the presurgical evaluation of focal epilepsy.

Kovac et al. (17) reported that ictal ESI, through dipole modelling, gave lateralizing results in 8 out of 17 seizures (47%). Significantly improved results of ictal ESI are obtained in this current study and such improvements are rationalised through the use of patient specific realistic head models. The highest concordance rate previously reported (16) was 90% which is in agreement with the obtained results of this study. The only article that compared the performance of ictal and interictal ESIs (3), reported a better concordance rate of ictal ESI over interictal ESI which further support the higher concordance rate of ictal ESI obtained in this study.

The evidence in support of interictal ESI (19, 28) show the source estimation time point at the 50% rising phase of GFP. However, to the best of our knowledge there is no such study that recommends the best examination time point for ictal source estimation. Koessler et al. (16) analyzed all the time points of each selected ictal event and the source with the highest amplitude across time and space was chosen, i.e., the examination time point was not fixed. For ease of analysis, a generalized examination time point, which is the time point at the peak of GFP has been used in this study for ictal source estimation with reasonable stability (see Table2).
The importance of ictal ESI is highlighted in next three subsections. A major limitation to this study is its sample size. Future studies on ictal ESI will need a larger patient population in order to verify these results.

**Advantages of Ictal ESI over Ictal SPECT**

Another noninvasive diagnostic tool used for the presurgical evaluation of refractory focal epilepsy is ictal SPECT. When acquiring ictal SPECT, a costly radioactive tracer is injected during the onset of seizure. In reality, there is always a latency (3–260 seconds) from seizure commencement to injection (25) and the tracer takes around 30 seconds to circulate to the region of interest (9). This circulatory delay allows the ictal activity to spreads to the other regions, i.e., ipsilateral basal ganglia and the motor cortex. Therefore the area of hyperperfusion on ictal SPECT doesn’t always represent the seizure focus. Besides, an ictal SPECT scan captures one seizure only and has poor temporal resolution (14). In contrast, ictal ESI can easily cover multiple seizures and has greater temporal resolution, which can localize the source for every instant (limited by the sampling rate of EEG recordings) of ictal EEG records. Ictal ESI is thought to be able to distinguish the primary source from the secondary source due to its high temporal resolution (7). Moreover, obtaining successful SPECT result demands careful monitoring, trained staff for the early injection of radioactive tracer and specially trained nuclear medicine technologist for acquiring the SPECT scans. Ictal ESI does not need these supportive measures and thus remains less expensive.
Advantages of Ictal ESI over Visual Inspection of EEG

Traditional methods of interpreting scalp EEG through visual inspection are often misleading, because they follow the simplistic principle that the electrodes recording the clearest epileptic event overlie the seizure focus (1) and do not consider the volume conduction effect. In contrast, multilayer head model based ESI solutions consider different conductivity for different head layers. Visual interpretation of EEG provides coarse approximation of the underlying cortical sources, whereas ESI can provide more refined sublobar prediction of seizure origin (1, 16). Furthermore, ESI can provide information on corticocortical propagation during the short period of an interictal spike or seizure onset that is not easily obtained from the traditional visual inspection of the EEG waveforms.

Advantages of Ictal ESI over MEG-Based Source Imaging

The principles of source imaging for EEG apply just as equally to the MEG-based source imaging (27). Although, MEG has better immunity to field distortion by volume conductor effects and superior spatial resolution than EEG, the use of ictal ESI has a higher advantage over MEG-based ictal source imaging. A good quality MEG recording requires patients to stay motionless making it inappropriate for pediatric and ictal studies. Hence, long-term MEG monitoring is unrealistic. MEG is also insensitive to radially oriented sources, where only superficial sources can be detected through MEG analysis (27). These limitations and its high cost infer that MEG-based source imaging is less useful than ESI.
Conclusion

The result of ictal ESI and ictal SPECT are fully lateralized and highly concordant with all three different inverse models. The use of ictal ESI is shown to be feasible in a conventional clinical setup and is able to estimate epileptogenic focuses more concordantly than interictal ESI. Therefore, this study will form a basis for future studies evaluating the value of ictal ESI as a cost effective substitute for ictal SPECT.

Acknowledgement

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References:


Figure Legends

**Figure 1:** Ictal epochs acquisition. (a) Ictal EEG of patient #2, (b) Power spectrum density in the region of interest, (c) EEG segment of interest with centre time points of selected epochs. The channel highlighted in red color is the prominent channel.

**Figure 2:** Average maps of selected ictal (a) and interictal (b) EEG events of patient #1. Highlighted channel holds the highest amplitude and the time duration from \( t_1 \) to \( t_2 \) is considered as the event duration. Estimated source at \( t_0 \) has been used for final result analysis while stable results have been obtained for all the time points between \( t_1 \) and \( t_2 \).
Figure 3: SPECT results and corresponding ESI results of two patients (patient #2 and patient #3). ESI sources, estimated by using volumetric source space and surface source space, have been presented on MRIs and simulated cortical surfaces respectively. Cortical regions with red color represent the estimated epileptic focuses.
Table 1: Demographics and Clinical Characteristics

<table>
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<tr>
<th>#</th>
<th>Gender</th>
<th>Age at Onset</th>
<th>Age at evaluation</th>
<th>Histopathology (based on MRI/HPE)</th>
<th>Surgical Resection</th>
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<td>M</td>
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<td>HS</td>
<td>Yes</td>
<td>R selective amygdalo-hippocampectomy</td>
<td>I</td>
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<td>8</td>
<td>M</td>
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<td>48</td>
<td>HS</td>
<td>Yes</td>
<td>L selective amygdalo-hippocampectomy</td>
<td>I</td>
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</table>

#: Patient Number, M: Male, F: Female, L: Left, R: Right; FCD: Focal cortical dysplasia; HS: Hippocampal Sclerosis; HPE: Histopathological examination; Engel Class I: Seizure free after surgery; Engel Class II: Decrease of seizures of more than 80% after resection.
Table 2: Cortical locations of MRI lesions, SPECT-focuses and the ESI-focuses of all the patients.

<table>
<thead>
<tr>
<th>#</th>
<th>MRI lesion</th>
<th>SPECT</th>
<th>Ictal ESI</th>
<th>Interictal ESI</th>
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<tbody>
<tr>
<td></td>
<td></td>
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<td>wMNE</td>
<td>dSPM</td>
</tr>
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<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
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<td>sLORETA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
<tr>
<td>#</td>
<td></td>
<td></td>
<td>wMNE</td>
<td>dSPM</td>
</tr>
<tr>
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<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
<tr>
<td></td>
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<td>dSPM</td>
<td>sLORETA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
</tbody>
</table>

**EEG ictal pattern: Spikes**
1. L Postcentral G L superior parietal Lo (23ms) L superior parietal Lo (23ms) L superior parietal Lo (39ms) L superior parietal Lo (27ms) L superior parietal Lo (27ms)
2. L parieto-occipital S L parieto-occipital S L parieto-occipital S (24ms) L lateral occipitotemporal G (24ms) L preoccipital notch (47ms) L preoccipital notch (50ms) L lateral occipitotemporal G (28ms) L lateral occipitotemporal G (28ms)
3. R paracentral Lo R inferior Parietal Lo R middle temporal G (14ms) R Inferior Parietal Lo (42ms) R lateral S of Sylvius (20ms) R middle temporal G (16ms) R insular cortex (10ms) R insular cortex (10ms)
4. No lesion R occipital Lo R occipital P (24ms) R cuneus (28ms) R medial occipitotemporal G (12ms) R occipital P (40ms) R occipital P (40ms) R lateral occipitotemporal G (22ms) R lateral occipitotemporal G (22ms)
5. L middle temporal G L superior temporal G L temporal P (60ms) L temporal P (42ms) L temporal P (78ms) L temporal P (64ms) L temporal P (64ms) L temporal P (68ms)
6. No lesion R inferior parietal Lo R inferior parietal Lo (42ms) R intraparietal S (80ms) R intraparietal S (80ms) R inferior parietal Lo (20ms) R intraparietal S (30ms) R inferior parietal Lo (22ms) R inferior parietal Lo (22ms)
7. R medial temporal P R temporal P (138ms) R temporal P (136ms) R temporal P (134ms) R temporal P (70ms) R basal ganglia (50ms) R temporal P (122ms) R temporal P (122ms)

#: Patient Number, L: Left, R: Right, G: Gyrus, S: Sulcus, P: Pole, Lo: Lobe/Lobule, t₂ – t₁: duration of stable results

# Table 2: Cortical locations of MRI lesions, SPECT-focuses and the ESI-focuses of all the patients.

<table>
<thead>
<tr>
<th>#</th>
<th>MRI lesion</th>
<th>SPECT</th>
<th>Ictal ESI</th>
<th>Interictal ESI</th>
</tr>
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<tbody>
<tr>
<td></td>
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<td>dSPM</td>
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<tr>
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<td></td>
<td></td>
<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
<tr>
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<td></td>
<td>dSPM</td>
<td>sLORETA</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
<tr>
<td>#</td>
<td></td>
<td></td>
<td>wMNE</td>
<td>dSPM</td>
</tr>
<tr>
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<td></td>
<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
<tr>
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<td></td>
<td>dSPM</td>
<td>sLORETA</td>
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<tr>
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<td></td>
<td></td>
<td>(t₂ – t₁)</td>
<td>(t₂ – t₁)</td>
</tr>
</tbody>
</table>

**EEG ictal pattern: Rhythmic activity**
3. R paracentral Lo R inferior Parietal Lo R middle temporal G (14ms) R Inferior Parietal Lo (42ms) R lateral S of Sylvius (20ms) R middle temporal G (16ms) R insular cortex (10ms) R insular cortex (10ms)
4. No lesion R occipital Lo R occipital P (24ms) R cuneus (28ms) R medial occipitotemporal G (12ms) R occipital P (40ms) R occipital P (40ms) R lateral occipitotemporal G (22ms) R lateral occipitotemporal G (22ms)
5. L middle temporal G L superior temporal G L temporal P (60ms) L temporal P (42ms) L temporal P (78ms) L temporal P (64ms) L temporal P (64ms) L temporal P (68ms)
6. No lesion R inferior parietal Lo R inferior parietal Lo (42ms) R intraparietal S (80ms) R intraparietal S (80ms) R inferior parietal Lo (20ms) R intraparietal S (30ms) R inferior parietal Lo (22ms) R inferior parietal Lo (22ms)
7. R medial temporal P R temporal P (138ms) R temporal P (136ms) R temporal P (134ms) R temporal P (70ms) R basal ganglia (50ms) R temporal P (122ms) R temporal P (122ms)

#: Patient Number, L: Left, R: Right, G: Gyrus, S: Sulcus, P: Pole, Lo: Lobe/Lobule, t₂ – t₁: duration of stable results
Table 3: Concordance or discordance of ESI results with ictal SPECT.

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Ictal ESI</th>
<th>Interictal ESI</th>
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<td>dSPM sLORETA</td>
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<td>YES YES</td>
</tr>
<tr>
<td>2</td>
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<td>YES YES</td>
</tr>
<tr>
<td>3</td>
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<td>YES YES</td>
</tr>
<tr>
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<td>YES YES</td>
</tr>
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<td>YES YES</td>
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<td>7</td>
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<td>YES YES</td>
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<td>8</td>
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<td>YES YES</td>
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</table>

YES: Concordant, -: Discordant
<table>
<thead>
<tr>
<th>Results on</th>
<th>MRI</th>
<th>Cortical Surface</th>
<th>MRI</th>
<th>Cortical Surface</th>
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</tr>
</tbody>
</table>

Results of Patient #2 (Best Case) vs Results of Patient #3 (Worst Case)
Highlights:

- Although ictal EEG is believed to be more reliable than interictal EEG in localizing the epileptogenic focus, ictal EEG based source localization (by using computational methods) is less explored because of the low Signal to Noise Ratio (SNR) and undetectable low strength of ictal events before being spread considerably.
- Some studies used ictal EEG for epileptic focus localization, but they followed complex and uncommon methods or used infrequent high density EEG data or inefficient head models.
- This study used standard low density EEG records, subject specific realistic head models (obtained from MRI scans), conventional computation techniques for ictal EEG based epileptic focus localization.
- Fully lateralized and highly concordant results of ictal EEG based source localization, without any special clinical setup, support that ictal EEG based source localization can be used as a readily available supplement to epilepsy presurgical evaluation.