Automated interictal source localisation based on high-density EEG

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ABSTRACT

Purpose: To study the accuracy of automated interictal EEG source localisation based on high-density EEG, and to compare it to low-density EEG.

Methods: Thirty patients operated for pharmacoresistant focal epilepsy were retrospectively examined. Twelve months after resective brain surgery, 18 were seizure-free or had ‘auras’ only, while 12 had persistence of disabling seizures. Presurgical 257-channel EEG lasting 3–20 h was down-sampled to 25, 40, and 204 channels for separate analyses. For each electrode setup, interictal spikes were detected, clustered, and averaged automatically before validation by an expert reviewer. An individual 6-layer finite difference head model and the standardised low-resolution electromagnetic tomography were used to localise the maximum source activity of the most prevalent spike. Sublobar concordance with the resected brain area was visually assessed and related to favourable vs. unfavourable postsurgical outcome.

Results: Depending on the EEG setup, epileptic spikes were detected in 21-24 patients (70-80%). The median number of single spikes per average was 470 (range 17–15,066). Diagnostic sensitivity of EEG source localisation was 58-75%, specificity was 50-67%, and overall accuracy was 55-71%. There were no significant differences between low- and high-density EEG setups with 25 to 257 electrodes.

Conclusion: Automated high-density EEG source localisation provides meaningful information in the majority of cases. With hundreds of single spikes averaged, diagnostic accuracy is similar in high- and low-density EEG. Therefore, low-density EEG may be sufficient for interictal EEG source localisation if high numbers of spikes are available.

Abbreviations

Abbreviations:
CI confidence interval
ESL EEG source localisation
FDM finite difference model
FN false negative
FP false positive
IFCN International Federation of Clinical Neurophysiology
ILAE International League Against Epilepsy
IQR interquartile range
sLORETA standardised low-resolution electromagnetic tomography
OR odds ratio

TN true negative
TP true positive

1. Introduction

Pharmacoresistant focal epilepsy can be cured by surgical removal of the epileptogenic zone, i.e., the specific area of the brain which is indispensable for the generation of epileptic seizures [24]. Prior to such surgery, potentially eligible patients undergo a thorough multimodal diagnostic workup, first, to delineate the epileptogenic zone with maximum possible precision, and second, to define functional brain areas which must remain untouched to avoid neurological
was recorded using 257 electrodes (Philips EGI, now Magstim EGI, surgery, for at least 3 h during daytime or overnight, high-density EEG lent to Engel IA and IB) or unfavourable outcome if disabling seizures persisted (ILAE class 3 or higher). Favourable postsurgical outcome in presurgical patients with focal epilepsy [2, 33]. However, the respective studies were based on conventional low-density EEG with 25–31 electrodes. High-density EEG using at least 64 electrodes has been reported to yield more accurate ESL results than low-density EEG in comparative studies [5, 13, 30] although this finding could not be confirmed in a recent meta-analysis [29]. The accuracy of automated high-density ESL has not yet been assessed. Therefore, the study presented here retrospectively evaluated automated interictal ESL based on presurgical 257-channel EEG, validated by subsequent resective brain surgery and 12-month postsurgical seizure outcome. Via spatial down-sampling of the full 257-channel EEG, the accuracy of spike detection and ESL was compared between two high-density and two low-density EEG setups.

2. Methods

2.1. Patients and recordings

The high-density EEG database of the EEG and Epilepsy Unit at the University Hospitals Geneva was retrospectively screened, up to 31 July 2020, for patients meeting the following criteria: (a) 257-channel EEG recording with a minimum duration of 3 h (to achieve a sufficiently high number of spikes); (b) subsequent first resective brain surgery to treat pharmaco-resistant focal epilepsy; (c) presurgical high-resolution structural MRI available; (d) postsurgical brain imaging and 12-month postsurgical seizure outcome available. Following the International League Against Epilepsy (ILAE) criteria [37], patients were classified as having favourable 12-month postsurgical outcome if they were seizure-free or had ‘auras’ only since surgery (ILAE class 1 or 2, equivalent to Engel IA and IB) or unfavourable outcome if disabling seizures persisted (ILAE class 3 or higher). Favourable postsurgical outcome indicates that the epileptogenic zone was correctly identified. Prior to surgery, for at least 3 h during daytime or overnight, high-density EEG was recorded using 257 electrodes (Philips EGI, now Magstim EGI, Eugene, Oregon, USA), unfiltered acquisition, at 500–1000 Hz sampling rate. For the head model, individual high-resolution structural T1 or MPRAGE MRI without contrast medium was used. The study was approved by the local ethics committee of the province (canton) of Geneva. Since clinical routine data were reused and individuals cannot be identified, the need for written informed consent was waived.

2.2. EEG setups

To allow comparison of different electrode setups representing low- and high-density EEG, the original 257-channel EEG was spatially down-sampled to three other setups (Fig. 1, supplementary figure 1). The first contains 25 channels as recommended as a minimum for clinical routine low-density EEG by the International Federation of Clinical Neurophysiology (IFCN). It represents the classical 10–20 setup with an additional three basal temporal electrodes on either side, namely F9/10, T9/10, and P9/10 [27]. As an example for a setup typically used in presurgical epilepsy evaluation, the second array consists of 40 channels as used in the ongoing ‘Prospective Multicenter Study on Localization Accuracy and Clinical Utility of Automated Electric Source Imaging in Presurgical Evaluation’ [4]. As a high-density alternative to the full 257-channel array, the third down-sampled setup contains 204 channels as used in a previous study of ours [35]. It does not include the electrodes F9/10 and T9/10, but the electrode row 5% more cranial is preserved (Fig. 1, supplementary figure 1).

2.3. Automated EEG source localisation

Fig. 2 gives an overview of the processing steps. De-identified raw hd-EEG and MRI data were processed by Epilog NV (Ghent, Belgium), blinded for clinical information including site of surgery and outcome. For each EEG setup, electrodes overlapping with the classical 10–20 montage were pinpointed and renamed. These were all channels of the 25- and the 40-channel setup, 76 for the 204-channel setup and 84 for the 257-channel setup (supplementary figure 2). Continuously noisy channels were visually identified and excluded from further analysis.

Using the Persyst Spike Detector P14 (Persyst, San Diego, California, USA), the EEG was band-pass filtered between 0.5 and 30 Hz. All detected events with a spike-probability higher than 0.5 were automatically selected for further analysis, and a two-second epoch centred around the peak was generated for each of them. Epochs containing possible corrupted channels (i.e., channels with a standard deviation that exceeds five times the median standard deviation of all channels) were excluded, and the remaining channels were average-referenced and baseline-corrected. Based on the topographical maximum, i.e., the channel with the highest amplitude at the peak, the single event epochs were grouped into clusters and merged if the scalp topography at the peak had a correlation higher than 0.9. Clusters with less than 15 single events were excluded. Eventually, those four clusters with the highest numbers of single events were subjected to ESL analysis.

The patient’s T1 or MPRAGE MRI sequences were used to construct an individual head model with a 1 mm cubic resolution and six different
tissues: scalp, skull, cerebrospinal fluid, grey matter, white matter, and air [17, 31]. For tissue segmentation, the Statistical Parametric Mapping software version 12 (Wellcome Centre for Human Neuroimaging, University College London Queen Square Institute of Neurology, London, UK) automatically estimated each tissue probability map. The maps were smoothed and then combined to generate the head model, with manual adjustments if necessary. The EEG electrodes were manually co-registered to the head model. Dipoles were distributed in a regular 3-dimensional grid with 4 mm spacing throughout the grey matter, excluding thalamus and basal ganglia. The lead-fields were computed using the finite difference method as forward solution [11]. The standardised low-resolution electromagnetic tomography (sLORETA) served as inverse solution. For each spike cluster, the maximum (crosshairs) of the source activation was visualised in the three orthogonal planes of the MRI at the onset, half-rise, and peak of the average spike. The source maximum was later compared to the postsurgical MRI.

2.4. Evaluation

To distinguish genuine spike clusters from other EEG patterns, an EEG-certified neurologist (B. J. V., aware of clinical information) visually reviewed 2-second epochs of the 20 most representative single events per cluster in bipolar and average montage, based on 18 EEG channels for visual simplicity. Artefacts and physiological EEG patterns were discarded. Polyphasic epileptiform patterns such as polyspikes or fast rhythms were not further analysed either, because the detection algorithm chooses the peak of maximum amplitude and not the first apparent deflection, and the respective source may be subject to propagation. “Mixed” clusters that consisted of both genuine spikes and artefacts were taken as artefact clusters. Sensitivity of spike detection was defined as the proportion of genuine spike clusters amongst all clusters. Success rate was defined as the proportion of EEGs with at least one genuine spike cluster. For each genuine spike cluster, source maxima at the onset, half-rise, and peak of the average spike were visually compared to the postsurgical MRI. The grey matter was divided into 19 ‘sublobes’ per hemisphere [35] based on the Lausanne parcellation atlas [6]. Two subcortical ‘sublobes’ belonging to the atlas were not included in the source space (thalamus and basal ganglia; supplementary table S1). Source maxima were compared to sublobe(s), lobe(s) and hemisphere affected by resective surgery, and to the borders of the resection itself. Sublobar concordance at the most prevalent genuine spike’s half-rise was the study’s primary outcome parameter. Secondary outcome parameters were the source maximum being inside the resected area, sublobar concordance at spike onset and peak, and sublobar concordance using other spike clusters than the most prevalent one.

Concordance in patients with favourable outcome (ILAE 1-2) was considered true positive (TP), and discordance in patients with unfavourable outcome (ILAE ≥ 3) was considered true negative (TN). By analogy, sublobar concordance in case of unfavourable outcome was considered false positive (FP), and discordance in favourable outcome was considered false negative (FN). Sensitivity was calculated as TP / (TP+FN), and specificity as TN / (TN+FP). Please note that TP and sensitivity are more reliably defined than TN and specificity [23]. Overall accuracy was calculated as (TP+TN) / (TP+TN+FP+FN). The
diagnostic odds ratio (OR) of favourable postsurgical outcome in case of concordant ESL results was calculated as \((\text{TP} \times \text{TN}) / (\text{FP} \times \text{FN})\). The 95%-confidence interval (95%-CI) of the parameters sensitivity, specificity, and overall accuracy was calculated as \(\text{parameter} \pm 1.96 \times \sqrt{\frac{1}{\text{sample size}} \left( \frac{\text{parameter} - \text{true parameter}}{\text{true parameter}} \right)^2} \). The 95%-CI of the diagnostic OR was calculated as \(e^{(\text{ln(OR)} \pm 1.96 \times \text{SE})} \). These definitions were specified before analysing the data.

2.5. Statistical analyses

Statistical analyses were performed using SPSS 25 (IBM, Armonk, US-NY). Data are given as percent or as median and interquartile range (IQR). Dichotomous data from more than two dependent samples were subjected to Cochran Q tests; nominal (including dichotomous) data from independent samples were subjected to \(\chi^2\) tests. Ordinal or continuous data from two independent samples were subjected to Mann-Whitney U tests. Continuous data from > 2 dependent samples were subjected to Friedman tests, followed by pairwise Wilcoxon tests. Correlations of continuous data were compared using Spearman’s \(\rho\). All tests were two-sided, \(p < 0.05\) was considered statistically significant. Repeated pairwise testing of the same parameter was corrected for using the Benjamini-Hochberg procedure [12]. However, to not inflate the risk of type-II errors, the testing of multiple parameters was not corrected for. Besides favourable vs. unfavourable outcome, no further patient subgroup analyses (e.g., temporal vs. extratemporal cases, MRI-positive vs. MRI-negative cases) were performed because of the low numbers of patients.

3. Results

3.1. Patient cohort

A total of 357 hd-EEG recordings dating from 2008 to 2020 were screened, of which 47 were recorded with 257 channels and had a duration of at least 3 h. Eight patients did not undergo resective surgery, three had previous brain surgery, and one had a skull defect. In three patients, the EEG files were irreparably corrupted, and another two had relevant clinical data missing. With these 17 cases excluded, 30 were eventually analysed.

Table 1 gives an overview of the study cohort; individual details can be found in table S2. Twelve months after surgery, 17 patients were seizure-free (ILAE 1), and one had aware non-motor seizures (‘auras’) only (ILAE 2). These 18 were counted as having favourable postsurgical seizure outcome. The remaining 12 patients had persisting disabling seizures and were counted as unfavourable outcome (ILAE 3–5).

3.2. Spike detection

The median duration of hd-EEG recordings was 15 h and 15 min (range 3 h and 20 min to 20 h and 40 min). The median proportion of continuously corrupted channels ranged from 0% (IQR 0–4%) in the 25-channel setup to 2.7% (IQR 1.2–5.8%) in the 257-channel setup (corrected \(p > 0.07\); Friedman’s test). Except for two setups in different patients, the automated spike detection found four clusters of supposed epileptic spikes with at least 15 single events in every EEG setup and patient. Following expert review, 38% of these were genuine interictal epileptic discharges, i.e., spikes or sharp waves. Another 6% were epileptic polyspikes or fast rhythms which were not considered further because of their polyphasic configuration limiting ESL, 11% were classified as physiological EEG patterns such as wicket spikes or K complexes, and 45% were classified as technical or biological artefacts like ECG or eyelink artefacts. Detection accuracy did not significantly differ across EEG setups (\(p = 0.41\); \(\chi^2\) test; Fig. 3).

The average detection sensitivity decreased from 57% in the most prevalent cluster to 23% in the fourth most prevalent cluster (Fig. 4A). The average success rate to detect at least one genuine spike cluster per EEG study increased from 57%, when considering the most prevalent cluster only, to 73%, when considering all four most prevalent clusters (Fig. 4B). Depending on the EEG setup, between 21 and 24 out of all 30 patients had at least one genuine spike cluster amongst the four most prevalent clusters. Of these patients, 12–14 had a favourable outcome and 9–10 had an unfavourable outcome. Four patients had no genuine spike cluster detected with any EEG setup. One of these four patients had polyspikes only; two others were known from clinical evaluation to have genuine spikes which were not identified by the methodology used here despite more than 15 h of EEG recording; the fourth patient was known to have very rare spikes. The median number of single events per genuine spike cluster was 470 (IQR 106–1340, range 17–15,066) with the number of single spikes correlating with the duration of the EEG recording (Spearman’s \(\rho = 0.62\); \(p < 0.001\)).

3.3. Source localisation

For each patient and EEG setup, the genuine spike cluster with the highest number of single discharges was evaluated to assess ESL accuracy. An overview of the levels of concordance (sublobar, lobar, hemispheric, or contralateral) between ESL maximum and the resected brain area in patients with favourable vs. unfavourable postsurgical seizure outcome is given in supplementary figure 2. Sublobar concordance, the study’s main outcome parameter, was achieved in 58–75% of cases with favourable postsurgical seizures outcome as compared to 33–50% of cases with unfavourable seizure outcome (corrected \(p > 0.10\)). The respective sensitivities, specificities, and overall diagnostic accuracies of ESL achieved with the different EEG setups are detailed in Fig. 5A, together with their 95%-CIs. Across all setups, the average sensitivity was 68%, the average specificity was 61%, and the average diagnostic accuracy was 73%. Table 1

| Parameter | All patients | Favourable outcome (ILAE 1-2) | Unfavourable outcome (ILAE 3-5) |
|-----------|--------------|-----------------------------|-------------------------------|
| Group size | 30 (67%) | 18 (61%) | 12 (75%) |
| Sex Male | 10 (33%) | 7 (39%) | 3 (25%) |
| Age at onset (years) | 16 [5–25] | 16 [4–25] | 17 [5–25] |
| Age at surgery (years) | 29 [19–39] | 28 [15–39] | 29 [20–43] |
| Localisation TLE | 18 (60%) | 13 (72%) | 5 (42%) |
| ETLE | 12 (40%) | 5 (28%) | 7 (58%) |
| Hemisphere Left | 15 (50%) | 9 (50%) | 6 (50%) |
| Right | 15 (50%) | 9 (50%) | 6 (50%) |
| Structural MRI Lesional | 26 (87%) | 17 (94%) | 9 (75%) |
| Non-lesional | 4 (13%) | 1 (6%) | 3 (25%) |
| Duration of EEG (hours) | 15 [9–16] | 15 [6–17] | 15 [12–16] |
accuracy was 65%. There were no statistically significant differences between the electrode setups (0.69 < \( p \) < 0.86). The diagnostic OR ranged from 1.4 (95%-CI 1.1–9.0) with the 204-channel setup to 6.0 (5.1–46.3) with 257 channels.

Across the time course of the spike, the average sensitivity based on sublobar concordance increased from 50% at onset to 72% at the peak, while the average specificity decreased from 65% to 50% (supplementary figure 3). The average overall accuracy was lower both at the spike’s onset (57%) and at the peak (62%) than at its half-rise (65%). However, differences across the different time points were not statistically significant. All diagnostic parameters together with their 95%-CIs are detailed in supplementary table S3. The number of single spikes per average spike was similar in accurate (TP or TN) vs. non-accurate (FP or FN) tests (\( p = 1 \); corrected Mann-Whitney U tests).

In a second, more rigorous validation approach, localisation was considered positive only with the source maximum being located inside the resected zone. In that case, average ESL sensitivity was 60% and average specificity was 74%, together with an average overall accuracy of 66% (Fig. 5B).

A ‘second most prevalent’ genuine spike cluster was detected in 54 setup analyses of 18 patients. Here, based on sublobar concordance of ESL maximum and the resected brain area at the spike average’s half rise, average sensitivity, specificity, and overall accuracy were 48%, 61%, and 54% (supplementary figure 4). With concordance defined by the source maximum being located inside the resected brain area, average sensitivity, specificity, and overall accuracy based on the second most prevalent genuine spike were 22%, 61%, and 39%. A ‘third’ and ‘fourth most prevalent’ genuine spike cluster were detected in 29 and 10 setup analyses, respectively. These were not further analysed due to the low numbers.

### 4. Discussion

With this study, we show that automated spike detection can identify...
genuine epileptic spikes in two thirds of cases both from high- and low-density EEG. We further demonstrate that if spikes are successfully detected, ESL localises the epileptogenic zone correctly in two thirds of cases, again irrespective of high- or low-density EEG.

4.1. Spike detection

On a cluster level, the sensitivity of automated spike detection ranged from 57% in the most prevalent cluster to 23% in the fourth most prevalent cluster, with an average of 38%. For comparison, on a single spike level and in a different study cohort, the same spike detector as used here had a sensitivity of 44% [26], while other algorithms had similar sensitivities of 44–47% [30, 32]. Experienced human EEG readers were found to have pairwise sensitivities of 40–52% for each other’s spike markings [26]. Most recently, an artificial intelligence-based algorithm was reported to detect single epileptic spikes with a sensitivity of 82% [9]. In our approach, assessing the sensitivity of spike detection on a single discharge level was not possible. However, the low sensitivity of 38% on a cluster level is at least partly due to the liberal settings of the spike detection algorithm with a pre-specified spike probability of 0.5.

On an EEG analysis level, this liberal approach together with the use of up to four discharge clusters led to successful spike detection in 70–80% of patients. For comparison, 93% of the patients were known from clinical evaluation to have epileptic spikes in their EEG. This means that spikes were missed in 13–23% of evaluated patients, most likely because our approach was based on evaluating the four most prevalent EEG patterns only, and infrequent spikes could be missed. On the other hand, in comparison to manual marking and averaging of spikes, visual validation of automatically detected spike clusters based on exemplary epochs was time-efficient and convenient.

4.2. Source localisation

Validated by sublobar concordance with the resected brain area and 12-month surgical seizure outcome, we found that automated ESL had diagnostic sensitivities of 58–75% and overall accuracies of 54–71%. This is in the range of our earlier ESL studies [2, 33, 35] and those of
others, e.g., [7, 28]. We previously published two articles on automated ESL based on low-density EEG. In 32 operated patients (24 of those with favourable outcome), ESL at the peak of the spike average led to a sensitivity of 70% and an overall diagnostic accuracy of 77% [33]. In a second study on 41 operated patients (25 with favourable outcome), ‘semi-automated’ ESL provided a sensitivity of 88% alongside with an overall accuracy of 78% [2]. ‘Semi-automated’ meant that the reviewer could choose other spike clusters and other time points than those suggested by default, depending on the clinical context.

According to a meta-analysis including 515 patients from 19 studies published before June 2018, the reported sensitivity of interictal ESL is 81% (95%-CI 76-95%) and the reported overall accuracy 74% (70-78%) [29]. Sensitivities and accuracies achieved in the current study are slightly lower, but within the same range. Interestingly, in our study, ESL based on high-density EEG with 204–257 channels did not perform better than low-density EEG with 25–40 channels, whereas earlier comparative studies using 13–55 spikes per patient reported high-density EEG to lead to higher ESL accuracy than low-density EEG [5, 8, 13]. Nevertheless, in the above-mentioned meta-analysis, high- and low-diagnostic sensitivities and accuracies [29]. We speculate that for localising average spikes with a smooth spatial distribution, based on a high number of single events, low-density EEG is sufficient. On the other hand, high-density EEG may be beneficial for localising spike averages with a low signal-to-noise ratio (due to low numbers of single spikes, low amplitude, or background noise) or single spikes, for source connectivity analyses, and for visual spike analyses in the sensor space.

In another recent study on interictal ESL, we found that spatial down-sampling of the 257-channel array to 204 channels by removing the inferior channels over cheek and neck improved ESL accuracy [35]. Surprisingly, we could not replicate this finding in the current study where the 204-channel setup tended to perform worse than the full 257-channel setup. This discrepancy may result from the use of different head models: Other than a simplified realistic 3-shell head model as in the previous study, a realistic six-layer finite difference model was used in this study, which particularly accounts for the anatomy of the skull base. Therefore, inclusion of inferior channels might reduce ESL accuracy in the simplified head model but not in the more sophisticated model.

In our study, ESL at the half-rise of the average spike was more accurate than at its onset or peak. This is in line with previous findings of ourselves [35], but higher accuracies at very early time points [20] or the peak [33] have also been found. Interictal spike sources at late time points may be influenced by propagation [3, 14, 16, 21], but the signal-to-noise ratio at a spike’s onset is much lower than at the peak [3, 22, 36]. Therefore, in most cases, the half-rise of the spike can be the ‘happy medium’ to balance the effects of propagation and signal-to-noise ratio.

4.3. Limitations and outlook

As a limitation of this study, visual review of the automatically labelled discharges was performed by a single EEG expert and based on 20 examples per cluster. Therefore, post-hoc inclusion or exclusion of single discharges was not possible. The study results come with large 95%-confidence intervals, and most differences between the groups were not statistically significant. This is because the study cohort was limited to 30 patients, due to the strict inclusion criteria. As another limitation, the vast majority of patients had a potentially epileptogenic lesion on MRI. Concordance of interictal ESL and MRI results is a good predictor of favourable surgical outcome [15] which underlines the usefulness of ESL also in MRI-positive cases. However, automated ESL needs to be assessed in a larger population of MRI-negative cases. For the future, prospective, adequately powered and, for that purpose, multicentre studies are necessary to better delineate the usefulness of high-density EEG for interictal source localisation.

5. Conclusion

Automated spike detection from high-density EEG captures interictal epileptic spikes in three out of four cases. Expert review of the putative spike clusters is essential to distinguish genuine spikes from other EEG patterns. The automated approach appears particularly useful in patients with frequent spikes. Here, diagnostic accuracies of automated high- and low-density ESL appear comparable.

CRediT authorship contribution statement

Bernd J. Vorderwülbecke: Conceptualization, Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. Amir G. Baroumand: Investigation, Formal analysis, Validation, Writing – original draft, Writing – review & editing. Laurent Spinelli: Funding acquisition, Data curation, Writing – review & editing. Margitta Seeck: Resources, Supervision, Writing – review & editing. Pieter van Mierlo: Conceptualization, Resources, Supervision, Writing – review & editing. Serge Vulliémoz: Funding acquisition, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

A. G. Baroumand is employee of epilogue NV (Ghent, BE); P. Mierlo is co-founder and shareholder of epilogue NV; M. Seeck and S. Vulliémoz are shareholders and advisors of epilogue NV. B. J. Vorderwülbecke and L. Spinelli have no conflicts of interest to report.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.seizure.2021.09.020.

References

[1] Abdallah C, Maillard LG, Ricik E, Jonas J, Thiriaux A, Gavaret M, et al. Localizing value of electrical source imaging: frontal lobe, malformations of cortical development and negative MRI related epilepsies are the best candidates. Neuroimage Clin 2017:16:319–29. https://doi.org/10.1016/j.nicl.2017.08.009 [doi];S2213-1582(17)30019-7 [pii].
[2] Baroumand AG, van Mierlo P, Strobbe G, Pinborg LH, Fabricius M, Rubboli G, et al. Automated EEG source imaging: a retrospective, blinded clinical validation study. Clin Neurophysiol 2018. https://doi.org/10.1016/j.clinph.2018.09.015.
[3] Bast T, Boppel T, Rupp A, HARTING I, Hacheetetter K, Fauner S, et al. Noninvasive source localization of interictal EEG spikes: effects of signal-to-noise ratio and averaging. J Clin Neurophysiol 2006;23(6):487–97. https://doi.org/10.1097/01.JCN.0000222028.14060.e7.
[4] Benický S. Clinical Utility of Automated Electric Source Imaging in Presurgical Evaluation. (PROMAESIS) 2020. https://clinicaltrials.gov/ct2/show/NC1T04218812 [Accessed 09.06.2021 2021].
[5] Brodbbeck V, Spinelli L, Luscano AM, Wissemeier M, Vargas MI, Vulliémoz S, et al. Electroencephalographic source imaging: a prospective study of 152 operated epileptic patients. Brain 2011;134:2887–97. Pt 10awr243 [pii];10.1093/brain/awr243 [doi].
[6] Daducci A, Gerhard S, Grillis A, Lemkaddem A, Cammoun L, Gigandet X, et al. The connectome mapper: an open-source processing pipeline to map connections with MRI. PLoS ONE 2012;7(12):e48121. https://doi.org/10.1371/journal. pone.0048121.
[7] Feng R, Hu J, Pan L, Wu J, Lang L, Jiang S, et al. Application of 256-channel dense array electroencephalographic source imaging in presurgical workup of temporal
