Spatial Relationship of Source Localizations in Patients with Focal Epilepsy: Comparison of MEG and EEG with a Three Spherical Shells and a Boundary Element Volume Conductor Model

Gabriela Scheler,* Michael J.M. Fischer, Alexandra Genow,
Cornelia Hummel, Stefan Rampp, Andrea Paulini,
Rüdiger Hopfengärtner, Martin Kaltenhäuser, and Hermann Stefan

*Epilepsy and Neurocenter, Department of Neurology, University of Erlangen-Nürnberg,
Erlangen, Germany*

Abstract: Epilepsy surgery is an option for patients with pharmacoresistant focal epilepsies, but it requires a precise focus localization procedure. Magnetoencephalography (MEG) and electroencephalography (EEG) can be used for analysis of interictal activity. The aim of this prospective study was to compare clusters of source localization results with MEG and EEG using a three spherical shells (3SS) and a boundary element method (BEM) volume conductor model. The study was closed when 100 patients met the inclusion criteria. Simultaneous MEG and EEG were recorded during presurgical evaluation. Epileptiform signals were analyzed using an equivalent current dipole model. Centroids of source localizations from MEG, EEG, 3SS, and BEM in their respective combinations were compared. In a 3SS model, MEG source localizations were 5.6 mm inferior to those obtained by EEG, while in a BEM model MEG source localizations were 6.3 mm anterior and 4.8 mm superior. The mean scattering of source localizations between both volume conductor models was 19.5 mm for EEG and 9.6 mm for MEG. For MEG no systematic difference between BEM and 3SS source localizations was found. For EEG, source localizations with BEM were 5.9 mm posterior and 11.7 mm inferior to those determined using 3SS. No differences were found between the 46 temporal and the 54 extratemporal lobe epilepsy patients. The observed systematic differences of source localizations of epileptic spikes due to the applied source signal modality and volume conductor model should be considered in presurgical evaluation when only one source signal and volume conductor model is available. *Hum Brain Mapp* 28:315–322, 2007. © 2006 Wiley-Liss, Inc.

Key words: focal epilepsy; source localization; magnetoencephalography; volume conductor; equivalent current dipole

Contract grant sponsor: Deutsche Forschungsgemeinschaft; Contract grant number: STE 380/9-1, 1999.

The first two authors contributed equally to this work.

*Correspondence to: Dr. Gabriela Scheler, Department of Neurology, University of Erlangen-Nürnberg, Schwabachanlage 16 D-91054, Erlangen, Germany.

E-mail: gabriela.scheler@neuro.imed.uni-erlangen.de

Received for publication 5 October 2005; Accepted 2 March 2006

DOI: 10.1002/hbm.20277

Published online 24 August 2006 in Wiley InterScience (www.interscience.wiley.com).

INTRODUCTION

Epilepsy surgery aims principally to control seizures in patients with pharmacoresistant epilepsy. Depending on the epilepsy syndrome and the ability to clearly define and completely resect the epileptogenic zone, about 60% of the operated epilepsy patients remain seizure-free. Obviously, preservation of the functionally important cortex is a priority [Rosenow and Luders, 2001]. Thus, accuracy in localization of the irritative zone is crucial in presurgical evaluation.

Magnetoencephalography (MEG) and electroencephalography (EEG) can contribute to presurgical focus localization [Ebersole, 1996; Stefan, 1993; Stefan et al., 2003]. Source localizations from both MEG and EEG are faced with the "inverse problem," which has no unique solution. Additional constraints and an iterative optimizing algorithm provide the best estimate of the source localization. For the forward calculation, a volume conductor is needed. The head model determines the way in which a signal within the brain is transformed to the head surface; an accurate head model is crucial for source localization [Michel et al., 2004]. It includes the electromagnetic and anatomical properties of the head. The first and still widely used approximation is a homogenous and isotropic spherical head model. Boundary element methods (BEMs) can represent individual geometry of surfaces inside the head to some extent [He et al., 1987]. The theoretical differences and respective practical results between volume conductors have been reviewed [Cohen and Cuffin, 1991]. The goal is to estimate the individual features as closely as possible, since any deviation between the actual and the assumed volume conductor might influence the results [Parra et al., 2004]. Consistent with this, it was shown that MEG source localization errors of simulated dipoles are smaller for a three-layer compared with a one-layer BEM model, even when the triangle mesh density was reduced to achieve similar computation times in the three-layer model [Crouzeix et al., 1999].

Simulated EEG sources transformed to the surface with a BEM forward model were localized with a spherical shells volume conductor. Localization errors of 5–6 mm in the upper part and 15–25 mm in the lower part of the head were reported [Yvert et al., 1997]. Consistently, low errors (0.67 mm) for superficial dipoles and 25 mm for deep dipoles were described [Tomita et al., 1996].

In this study, EEG signals were recorded according to the international 10/20 system with an additional temporal-basal ring using 31 electrodes covering the whole head. MEG was recorded with two MEG sensors with 37 gradiometers positioned, respectively, over the region of interest and control areas. A dual sensor MEG provides flexibility for positioning in temporal regions, which is known to be a limit in whole-head MEG systems [Barkley, 2004] as well as for investigating children with smaller head volumes.

We analyzed the results of 1,846 source localizations from 100 patients during simultaneous MEG and EEG recordings, calculated with two different head models. Some patients were analyzed with more elaborate source models. To retain usability for current clinical procedures, however, we in-

cluded only calculations with the equivalent current dipole model in this study. The purpose of this study was to evaluate whether there are systematic differences in source localizations that depend on the signal modality (MEG/EEG) and the selected volume conductor model for a large clinical dataset.

SUBJECTS AND METHODS

We analyzed all patients who underwent presurgical evaluation including MEG and MRI at the Epilepsy Center Erlangen after January 1, 2001. The patients measured in the MEG are a subset of the patients evaluated for epilepsy surgery and were selected by the senior author. Especially for the earlier patients, MEG was performed in more complex cases; later, MEG was more routinely applied. Simultaneous MEG/EEG was not performed when the interictal spike frequency was only a few spikes a day in the EEG monitoring. The prospective study was closed when 100 patients met the inclusion criteria, that is, a focus classification as monofocal or multifocal and a minimum of five source localizations. An explanation for these criteria is given in the appropriate section of Subjects and Methods. From all the patients examined, interictal epileptic activity was found in 132 (66%) of 201 patients. All subsequent patients measured by MEG were included if they were not classified diffuse and had more than five spikes in the analysis. The average age $\pm$ SD at the MEG investigation was 31.5 ± 13.3 years (range, 7–63). All patients gave informed consent to scientific analysis of the acquired data. The local ethics committee approved the described procedures.

MEG was recorded on a dual unit 74-channel biomagnetometer system (Magnes II, 4-D Neuroimaging, San Diego, CA) inside a magnetically shielded chamber (Vakuum-schmelze, Hanau, Germany). The system consists of two sensors with 37 first-order gradiometers with a 5 cm baseline; the channels were separated on average by 2.8 cm. The position of the nasion and the preauricular points was digitized with a 3D digitizer (Polhemus, Colchester, VT) in order to create a common coordinate system for MEG and MRI.

Magnetic resonance imaging was recorded using a 1.5 T Siemens (Erlangen, Germany) Magnetom system until April 2001, and thereafter a 1.5 T Siemens Sonata. For magnetic source imaging, fiducials were applied at nasion and preauricular points. The head was scanned with an MPRAGE sequence in 144 coronal images with a size of 256×256 pixels (1.09 mm/pixel resolution in both directions) and a slice thickness including gap of 1.2 mm. An isotropic volume consisting of 1.1 mm symmetric cubes was generated from these images with CURRY v. 4.5 and 4.6 software (Compumedics Neuroscan, El Paso, TX).

Positioning of the MEG sensors was focused on previous clinical findings, but also covered control areas. Recording duration depended on the amount of epileptic discharge; if no or few epileptic discharges were seen in the online display, a total of 30 min was recorded for each position. The included patients had an average of 5.1 recording sessions,

lasting 18 min (± 6.4 SD) per session. The signal was band-pass-filtered (1–100 Hz) and digitized with a sampling rate of 520.8 Hz. EEG was recorded simultaneously, using 31 scalp electrodes, positioned according to the international 10/20 system including the temporal-basal ring. Flat silver-silver chloride electrodes were attached to a flexible, tight-fitting cap (Falk Minow, München, Germany) especially designed for the MEG environment. Electrode positions were digitized using the device mentioned above. The electrocardiogram was recorded to detect signal distortion in MEG during the QRS complex. MSI software (4-D Neuroimaging) was used for recording and data preprocessing in MEG and EEG.

The MEG/EEG source localization analysis was performed or reviewed by experts involved full-time in MEG/EEG analysis. Epileptic discharges were identified offline during visual inspection. Data were transferred to CURRY software v. 4.5 or 4.6 for source localization. CURRY provides a BEM volume conductor model consisting of triangular meshes for the liquor, skull, and skin surface. This volume conductor is built from individual MRI scans automatically or manually assisted in the case of large deformities. For both volume conductors the conductivity of the skull compartment was adjusted to one eightieth of the brain. The three spherical shell (3SS) volume conductor was automatically centered using the previously determined brain surface.

For MEG and EEG the signal-to-noise ratio was calculated and a singular value decomposition was used to omit spikes with more than one component of considerable size. The second half of the rising slope was selected for source localization. Source localization results were selected by standard criteria: a squared deviation between the forward model and the observed magnetic field of less than 20% and a confidence volume of less than 3 cm³. Coordinates of localizations were subjected to a cluster analysis, visualized in MR-slices, and stored in a database.

Given these source localizations, patients were categorized into monofocal, multifocal, and diffuse distribution groups. Source localizations were subjected to a hierarchical cluster analysis and 3D visualization. Epilepsy was considered multifocal if more than one distinct cluster of source localizations was found, diffuse if the source localizations were scattered over the neocortex and had no apparent clusters of source localizations. Both the hierarchical cluster analysis and the visualization yielded congruent results without any doubtful cases, which made a possible objective cutoff in the hierarchical cluster analysis unnecessary. According to the study design, only source localizations from a single focus can be compared. Therefore, all patients with diffuse localization distribution were omitted (17 of 132 patients); from patients with multifocal localization distribution the focus with most spikes was included. Patients were omitted if fewer than five spikes could be localized with the criteria mentioned above; this excluded an additional 15 patients. The study was closed when the targeted number of 100 patients met the inclusion criteria. From all

patients with interictal activity, 36% had a temporal lobe, 55% an extratemporal lobe epilepsy, and for 9% of the patients the epilepsy involved a temporal as well as an extratemporal lobe.

Assuming a normal distribution of the 3D scattering, the size of a sphere containing a certain quantile can be estimated from the mean deviation; 95% of the source localizations are within 1.815-fold of the mean deviation. Iteratively, all localizations outside this 95% confidence sphere were omitted. This procedure effectively eliminated outliers, which would also not be taken into account for the surgical resection. Centroids were determined for the remaining source localization results of all data groups. The distance of all source localizations to their respective center was calculated.

The area covered by the MEG sensor array in every recording position is smaller than the 10–20 EEG recording setup with a basal ring of electrodes, which covers the whole head. This could possibly result in high distances between MEG and EEG when a signal source was missed by either of the methods. To avoid distortion, MEG was compared to EEG only if source localization centroids were within a maximum distance of 3 cm. Epileptiform signals with sufficient signal quality for reliable source localization occurred only rarely within 10 ms in both MEG and EEG.

Statistical tests were performed by STATISTICA 6.0 (StatSoft, Tulsa, OK). Significance was accepted for $P < 0.05$. The brain as well as the algorithms are symmetrical on the left–right axis; the significance level for localization differences was therefore Bonferroni corrected for the double testing on the anterior–posterior and superior–inferior axis. Confidence intervals (CI) are provided if appropriate. Data are given as mean $\pm$ SD in the text, and are visualized as mean $\pm$ SEM in the figures if not mentioned otherwise. Student's *t*-test was used for parametric comparisons. Non-normally distributed data are given as medians and quantiles and were tested with Wilcoxon and Whitney-Mann *U*-test. All results were tested for significant differences between temporal and extratemporal located centroids of source localizations.

RESULTS

The analysis of the 100 patients yielded 1,353 MEG (3SS: 704, BEM: 649) and 493 EEG (3SS: 260, BEM: 233) source localizations. Only one source localization per epileptic spike for each model was used. The same criteria, regarding correlation and confidence volume, were demanded for all four calculations. Reliable source localizations from all groups of data, given two raw signals and two volume conductors, could not be determined in all patients. Of the 100 patients, 93 had MEG and 78 patients had EEG source localizations. This translates to 22% of the patients missed by EEG only, 7% missed by MEG only, and 71% detected by both methods.

Figure 1.

Scattering of source localizations of the patient with the most epileptic spikes. One symbol represents one epileptic spike projected onto the given sagittal plane. Every epileptic spike was localized with both volume conductor models, if standard quality criteria of source localization were fulfilled. Ellipses delineate area covering 80% of localizations on average. Note the distances between centroids of both volume conductors and the direction of the deviation. The small inset gives the position of these coordinates in the head.

Scattering of Source Localizations

The scattering, projected onto a 2D plane, is illustrated for the patient with the most source localizations (Fig. 1). The centroid of the cluster of source localizations and the distances of all source localizations to that centroid were calculated separately for all MEG and all EEG localizations of a patient. For MEG the median of these results was lower than for EEG (8.3 mm vs. 12.4 mm, $P = 0.008$, $n = 71$, Wilcoxon). Separate analysis of MEG and EEG for both volume conductors showed no differences in the median distance to the cluster center (MEG: 8.6 mm with 3SS, 9.4 with BEM, EEG: 8.8 with 3SS, 9.4 with BEM). This indicates systematic differences in the position of source localizations in EEG according to the choice of volume conductor. The cumulative percentage of localizations in a sphere with a given radius is illustrated in Figure 2A for the patient from the first figure. The percentage of patients that have half of the localizations within a sphere of the given diameter is shown in Figure 2B. The same results for different quantiles is provided in Figure 2C, here without differentiating the respective MEG/EEG 3SS/BEM combinations.

Depth of Localizations

The average depth from the head surface for MEG was 31.9 ± 12.8 mm (3SS) and 31.5 ± 12.9 mm (BEM), for EEG 34.8 ± 11.6 mm (3SS) and 32.3 ± 12.3 mm (BEM). EEG data localized with the 3SS volume conductor model were deeper in the head when compared to the average depth of all

source localizations (including EEG 3SS, $P = 0.006$, $n = 78$, t -test-dependent samples, Bonferroni-adjusted significance level $P < 0.012$, Fig. 3).

Relative Position of Source Localizations

All localizations were compared for left-right, anterior-posterior, and inferior-superior axes. Pooled source local-

Figure 2.

A: For the patient from Figure 1 the distances of source localizations to the centroid for the respective MEG/EEG 3SS/BEM combination are shown cumulatively. **B:** For all patients the medians are presented as a cumulative histogram. Note that there are no significant differences between the MEG/EEG 3SS/BEM combinations. The patient shown in Figure 1 has above-average variation in source localizations. **C:** The median, the 25%, 75%, and 90% quantiles of the distance of source localizations to the centroid. Distances were calculated not to a common centroid but independently to the centroid of the respective MEG/EEG 3SS/BEM combinations to avoid bias by systematic differences. The quantiles were calculated over these distances and visualized cumulatively. As an example, in 80% of the patients, 75% of source localizations were within a sphere with a radius of 18 mm. In diagrams A and B data have been summarized in 1-mm bins to limit the number of graphic symbols, which are placed in the middle of the bin.

Figure 3.

Histogram of the depth of the centroid for every patient, given separately for the source signal and the volume conductor. Using only the centroid for every patient avoids bias due to different numbers of source localizations. Depth was measured as the distance to the outermost surface of the 3SS volume conductor. Above the histogram the mean $\pm$ SEM is displayed. Note that centroids of EEG source localizations with a 3SS volume conductor are significantly deeper than the average of all centroids.

izations from both volume conductors from MEG were not different from those of EEG for these axes, the average distance being 17.8 ± 6.9 mm (Fig. 4A).

Source localizations from MEG and EEG were pooled to compare source localizations from both volume conductors. 3SS localizations were 1.7 ± 7.3 mm anterior ($P = 0.023$, $n = 100$, t -test, CI 0.2–3.1 mm) and 4.2 ± 7.3 mm superior ($P < 0.001$, $n = 100$, CI 2.8–5.7 mm) and the average distance between them was 11.0 ± 6.6 mm (Fig. 4B).

Volume Conductor Effects Depending on the Modality

The effect of different volume conductor models on source localization was analyzed for MEG (Fig. 5A) and EEG (Fig. 5B) separately. No differences were seen in MEG ($n = 95$, t -tests), while for EEG 3SS source localizations were 5.9 ± 11.0 mm anterior ($P < 0.001$, $n = 76$, t -test, CI 3.4–8.4 mm) and 11.7 ± 9.8 mm superior ($P < 0.001$, $n = 76$, t -test, CI 9.5–14.0 mm) when compared to BEM (Fig. 5B). The average distance between source localizations due to the volume

Figure 4.

Relative positions of MEG source localizations compared to the EEG and the BEM volume conductor model compared to 3SS. The position of the centroid of source localizations for every patient was determined on the left–right, anterior–posterior, and superior–inferior axes. **A:** Source localizations from both volume conductors taken together show no systematic difference between MEG and EEG. **B:** Source localizations from MEG and EEG taken together reveal that source localizations with a 3SS volume conductor model are on average superior to those with BEM. Data are shown as mean $\pm$ SEM.

conductor was 19.5 ± 8.1 mm for EEG, which is significantly larger than 9.6 ± 8.8 mm for MEG ($P < 0.001$, t -test with independent samples, Fig. 5C).

Figure 5.

Relative position of source localizations centroids due to chosen volume conductor for **(A)** MEG or **(B)** EEG. **C:** The average distance between centroids is smaller in MEG. The relative position of source localization centroids due to the source signal for **(D)** 3SS and **(E)** BEM. **F:** The distance between centroids of MEG and EEG is similar for both volume conductors. Data are shown as mean $\pm$ SEM.

Figure 6.

The common centroid of the four MEG/EEG 3SS/BEM combinations was calculated. The deviation of the respective centroids to the common centroid is visualized with standard error and standard deviation. The only significant difference between temporal and extratemporal clusters of source localizations was found on the anterior–posterior axis for EEG BEM. The means of the respective subgroups are shown.

MEG vs. EEG Depending on the Volume Conductor

Source localizations from MEG were compared with EEG for both volume conductor models separately. For the 3SS volume conductor model, source estimates from EEG were 5.6 ± 10.5 mm superior ($P < 0.001$, $n = 48$, t -test, CI 2.6–8.7 mm, Fig. 5D) when compared to MEG. With a BEM volume conductor, source estimations from EEG were 6.3 ± 12.9 mm posterior ($P = 0.001$, $n = 48$, t -test, CI 2.6–10.1 mm) and 4.8 ± 12.4 mm inferior ($P = 0.010$, $n = 48$, t -test, CI 1.8–8.5 mm, Fig. 5E) when compared to MEG. The average distance between MEG and EEG localizations was 19.6 ± 8.1 mm for 3SS and 20.3 ± 9.2 mm for BEM (Fig. 5F).

Relative Position to Common Centroid

We calculated the common centroid of the four centroids obtained from the respective MEG/EEG 3SS/BEM combinations. Common centroids were not calculated from the original source localizations to avoid bias due to the different number of source localizations in the four groups. Separate common centroids were used for MEG and EEG if these were more than 3 cm apart. Deviation from the common centroids are shown in Figure 6. Significant deviations from the common centroid were found for EEG 3SS (2.3 ± 5.9 mm posterior, 3.9 ± 6.4 mm superior, $P < 0.001$ each, $n = 78$, t -test against zero) and EEG BEM (3.9 ± 6.4 anterior, 5.3 ± 6.9 inferior, $P < 0.004$ each, $n = 78$, t -test against zero).

In EEG BEM, temporal located common centroids were 6.3 ± 6.8 anterior from the common centroid while extratemporal were only 1.7 ± 5.4 anterior ($P = 0.002$, t -test). No other differences between temporal and extratemporal located centroids were found.

DISCUSSION

In this study we systematically investigated the localization differences for 100 patients between MEG and EEG, both with the 3SS and a BEM head model using the equivalent current dipole model. EEG missed epileptic discharges in 22% of patients, while MEG missed epileptic discharges in 7% of the patients. The average recording time was about 90 min; therefore, longer than an average routine EEG. With MEG more epileptic spikes could be localized than with EEG (1,353 vs. 493 from both volume conductors each), which supports previous results [Lin et al., 2003]. It must be considered that the 10/20 system of EEG electrodes covered the whole head, whereas based on prior clinical results MEG sensors had a higher local channel density. However, the recording usually consisted of separate sessions with overlapping fields; thus, the area covered by the MEG sensors is larger than the sensor diameter.

It should be noted that scattering of source localizations has technical reasons; that is, the iterative source localization algorithm, accepted confidence volumes, and maximum difference between forward calculated and observed signals. The latter parameters are not uniformly set across laboratories. In our opinion, a well-chosen balance is necessary between cutoff parameters of the source localization algorithm and the percentage of extreme results that are not considered clinically. As well, there is the biological component; extension of the area generating epileptic spikes also contributes to the scattering of source localizations. These components cannot be distinguished by source localization methods. We hypothesized that the distribution of the scattering of source localizations would depend on the volume conductor, because the BEM volume conductor with its more curved surface might change the likelihood of nearby source localizations [Fuchs et al., 2001]. To our surprise, no differences were found between the median distance to the centroid of BEM and 3SS source localizations in both modalities. All EEG source localizations taken together were more scattered than all the MEG source localizations. However, this was not the case when the results were categorized by volume conductor model. This demonstrated that a smaller coverage of the brain by the MEG sensors or a higher local sensor density compared to the EEG does not result in less variance of the source localizations, but indicated a systematic effect of the volume conductor on EEG results and led to a closer investigation of the relative position of the centroids.

Any set of orthogonal axes could have been used for this purpose, the coordinates of the MRI stack that correspond to the left–right, anterior–posterior, and superior–inferior axis with little variation were chosen for practical reasons. It is

commonly accepted that MEG and EEG have different sensitivity concerning the source signal. EEG localization results in dipoles generated by implanted electrodes showed an upward bias of 9.3 mm for the 3SS model [Cuffin et al., 2001b]. This may correspond to the relative position of EEG source localizations when compared to MEG using the 3SS model. The same group reported a slightly lower upward bias for BEM results [Cuffin et al., 2001a], which is also supported by our results.

For EEG 3SS, localizations were systematically more anterior and superior than those for BEM. A systematic effect has been hypothesized but not quantified before; the largest deviations were also seen on the inferior–superior axis [Roth et al., 1993]. In MEG the chosen volume conductor had no systematic effect on source localization. The average distance between the centroids determined with different volume conductors was larger for EEG than those determined with MEG (19.5 vs. 9.6 mm). This is expected, because the estimated conductivities for the brain compartments have little effect on forward calculation in MEG, but a considerable effect for EEG. Electric impedance tomography or localization accuracy of implanted dipoles questioned the commonly used values for electrical conductivity; furthermore, the reported high interindividual variance might require such estimations to optimize EEG source localizations [Cuffin et al., 2001b; Gonçalves et al., 2003].

The depth of the source localization centroids was estimated as the distance from the outermost shell of the 3SS model. EEG calculated with a 3SS model resulted in deeper localizations, the 2.5 mm difference in depth between EEG 3SS and EEG BEM volume conductors is small compared to the 19.5 mm average distance between these centroids or compared to the systematic differences of the common centroid. The signal-to-noise ratio decreases slower with depth for EEG than for MEG [Fuchs et al., 1998] and this might also explain why more deeper EEG signals meet the chosen spike criteria. In a recent systematic investigation the signal/noise ratio was not homogeneously distributed; therefore, a selection bias could contribute to the observed systematic effects [de Jongh et al., 2005]. Epileptic foci with deeper centroids showed a higher variance of source localizations in MEG than epileptic foci with more superficial centroids. This is in agreement with simulation studies [Crouzeix et al., 1999; Tomita et al., 1996].

It should be noted that the number of temporal and extratemporal patients are about equal. In that respect, patient selection as well as the subjective decision to investigate the patient with MEG, both specific for the epilepsy center, might have had an effect on our results.

Our results do not allow for any conclusion about the localization accuracy. MEG or EEG with a certain volume conductor model might have a superior predictive value for a good outcome. This needs to be addressed in further studies. In a recent report a high coverage of a standardized result volume by the resection volume was positively corre-

lated with a good postoperative outcome [Fischer et al., 2005]. The most accurate source localization method should yield the highest correlation.

Until these results are available, other means might help to reduce localization bias due to the chosen method. In clinical practice there is often not enough time, money, or equipment available to acquire both MEG and EEG or calculate both forward models. Our study allows the incorporation of the reported systematic differences into the final result. This allows one to reduce the localization bias arising from the recorded source signal and the chosen volume conductor.

ACKNOWLEDGMENTS

The authors thank the Department of Neuroradiology and the Department of Neurosurgery for cooperation. G.S. was the principal investigator throughout the project duration and wrote the article; M.F. performed the data analysis and statistics and contributed to the article; C.H. devised the original study design. A.G., S.R., and A.P. were involved with clinical data acquisition, analysis, and contributed to the development of analysis routines; R.H. and M.K. developed essential parts of data interoperability between the systems used and maintained the MEG system. H.S. supervised all aspects of the study.

REFERENCES

- Barkley GL (2004): Controversies in neurophysiology. MEG is superior to EEG in localization of interictal epileptiform activity. *Prog Clin Neurophysiol* 115:1001–1009.
- Cohen D, Cuffin BN (1991): EEG versus MEG localization accuracy: theory and experiment. *Brain Topogr* 4:95–103.
- Crouzeix A, Yvert B, Bertrand O, Pernier J (1999): An evaluation of dipole reconstruction accuracy with spherical and realistic head models in MEG. *Clin Neurophysiol* 110:2176–2188.
- Cuffin BN, Schomer DL, Ives JR, Blume H (2001a): Experimental tests of EEG source localization accuracy in realistically shaped head models. *Clin Neurophysiol* 112:2288–2292.
- Cuffin BN, Schomer DL, Ives JR, Blume H (2001b): Experimental tests of EEG source localization accuracy in spherical head models. *Clin Neurophysiol* 112:46–51.
- de Jongh A, de Munck JC, Gonçalves SI, Ossenblok P (2005): Differences in MEG/EEG epileptic spike yields explained by regional differences in signal-to-noise ratios. *J Clin Neurophysiol* 22:153–158.
- Ebersole JS (1996): New applications of EEG/MEG in epilepsy evaluation. *Epilepsy Res Suppl* 11:227–237.
- Fischer MJM, Scheler G, Stefan H (2005): Utilization of magnetoencephalography results to obtain favourable outcomes in epilepsy surgery. *Brain* 128:153–157.
- Fuchs M, Wagner M, Wischmann HA, Kohler T, Theissen A, Drenckhahn R, Buchner H (1998): Improving source reconstructions by combining bioelectric and biomagnetic data. *Electroencephalogr Clin Neurophysiol* 107:93–111.
- Fuchs M, Wagner M, Kastner J (2001): Boundary element method volume conductor models for EEG source reconstruction. *Clin Neurophysiol* 112:1400–1407.

-
- Goncalves SI, de Munck JC, Verbunt JPA, Bijma F, Heethaar RM, da Silva FL (2003): In vivo measurement of the brain and skull resistivities using an EIT-based method and realistic models for the head. *IEEE Trans Biomed Eng* 50:754–767.
- He B, Musha T, Okamoto Y, Homma S, Nakajima Y, Sato T (1987): Electric dipole tracing in the brain by means of the boundary element method and its accuracy. *IEEE Trans Biomed Eng* 34:406–414.
- Lin YY, Shih YH, Hsieh JC, Yu HY, Yiu CH, Wong TT, Yeh TC, Kwan SY, Ho LT, Yen DJ, Wu ZA, Chang MS (2003): Magnetoencephalographic yield of interictal spikes in temporal lobe epilepsy — comparison with scalp EEG recordings. *Neuroimage* 19:1115–1126.
- Michel CM, Murray MM, Lantz G, Gonzalez S, Spinelli L, de Peralta RG (2004): EEG source imaging. *Clin Neurophysiol* 115:2195–2222.
- Parra J, Kalitzin SN, da Silva FHL (2004): Magnetoencephalography: an investigational tool or a routine clinical technique? *Epilepsy Behav* 5:277–285.
- Rosenow F, Luders H (2001): Presurgical evaluation of epilepsy. *Brain* 124:1683–1700.
- Roth BJ, Balish M, Gorbach A, Sato S (1993): How well does a three-sphere model predict positions of dipoles in a realistically shaped head? *Electroencephalogr Clin Neurophysiol* 87:175–184.
- Stefan H (1993): Clinical applications of MEG in epilepsy. *Brain Topogr* 5:425–427.
- Stefan H, Hummel C, Scheler G, Genow A, Druschky K, Tilz C, Kaltenhauser M, Hopfengartner R, Buchfelder M, Romstock J (2003): Magnetic brain source imaging of focal epileptic activity: a synopsis of 455 cases. *Brain* 126:2396–2405.
- Tomita S, Kajihara S, Kondo Y, Yoshida Y, Shibata K, Kado H (1996): Influence of head model in biomagnetic source localization. *Brain Topogr* 8:337–340.
- Yvert B, Bertrand O, Thevenet M, Echallier JF, Pernier J (1997): A systematic evaluation of the spherical model accuracy in EEG dipole localization. *Electroencephalogr Clin Neurophysiol* 102:452–459.