MEG versus EEG Localization Test Using Implanted Sources in the Human Brain

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It is believed that the magnetoencephalogram (MEG) localizes an electrical source in the brain to within several millimeters and is therefore more accurate than electroencephalogram (EEG) localization, reported as 20 mm. To test this belief, the localization accuracy of the MEG and EEG were directly compared. The signal source was a dipole at a known location in the brain; this was made by passing a weak current pulse simulating a neural signal through depth electrodes already implanted in patients for seizure monitoring. First, MEGs and EEGs from this dipole were measured at 16 places on the head. Then, computations were performed on the MEG and EEG data separately to determine the apparent MEG and EEG source locations. Finally, these were compared with the actual source location to determine the MEG and EEG localization errors. Measurements were made of four dipoles in each of three patients. After MEGs with weak signals were discounted, the MEG average error of localization was found to be 8 mm, which was worse than expected. The average EEG error was 10 mm, which was better than expected. These results suggest that the MEG offers no significant advantage over the EEG in localizing a focal source. However, this does not diminish other uses of the MEG.

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There is increasing interest in the magnetoencephalogram (MEG) both as a clinical and as a research tool [1–4], and elaborate magnetic systems are beginning to appear in hospitals and research laboratories [5, 6]. The interest is due in part to the belief that the MEG can localize a source in the human brain to about 2 or 3 mm [7–14], hence, is more accurate than the electroencephalogram (EEG), reported to have an accuracy of 20 mm [15]. However, this belief is based only on indirect evidence, not on a direct MEG-EEG comparison; therefore, it could be in error. For example, it is based on MEG measurements only [9, 10, 13] or an MEG-EEG comparison due to a source of unconfirmed location in the brain [13]. Because of the importance of this belief, we performed a pilot study to compare MEG and EEG localization in a direct way. We compared them for the first time in the same human subject, due to a source of precisely known location in the brain. Our aim was to either validate the belief or see whether it is significantly in error. The results of this comparison are presented here.

The subjects in these measurements were epileptic patients being evaluated for surgical resection; they had previously received implantations of intracerebral electrodes to record their seizure activity [16]. On completion of those recordings, the same electrodes instead of recording signals were now used to produce a signal. A brief pulse of current, too weak to stimulate the brain but simulating a neural signal, was passed between two electrodes a short distance apart. This constituted a simple focal source (a dipole) where the location was accurately known from roentgenographs. First, the MEG and EEG signals due to this source were measured at the conventional number of 16 places over the head. Then, a computation (an inverse solution) was performed on the MEG and EEG data separately to determine the location of the MEG and EEG apparent sources; a significant part of this compu-

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tation was the use of a spherical model as an approximation to the actual head. Finally, the MEG and EEG apparent source locations were compared with the actual source location to determine the MEG and EEG errors of localization. Prior to the measurements in the patients, the entire procedure was tested in an artificial head to determine the basic system error. Measurements were then made in three patients, due to four dipoles at different locations in each patient. However, the MEG signals from seven of these 12 dipoles were too weak to be fully used here. Nevertheless, the MEG data from the other five dipoles were enough to yield valid conclusions, within the scope of this pilot project.

During these measurements, other data of only the EEG were recorded for a more comprehensive EEG localization study, without comparison to the MEG. This study is reported separately [17].

Methods

Measurement System

The measurement system can be grouped into source equipment, the EEG and MEG detection equipment, and the signal-processing hardware and software. Concerning the source equipment, the electrodes implanted in the brain are shown in Figure 1. These were platinum rings, 1 mm in diameter and 2 mm long, mounted as a group of six on a hollow plastic catheter, spaced 8 mm apart. The entire catheter was specially made to be nonmagnetic; thus, it contained no magnetic materials, and the internal wires to the electrodes were twisted to produce no magnetic field. Each dipole was due to alternate rings on the same catheter, hence was 16 mm long, and one of two dipoles at different depths along the catheter could be selected by a remote switch. Two of these nonmagnetic catheters, hence four dipoles, were used for our purpose in the patient. The 16-mm dipole was chosen here instead of the shorter 8-mm dipole to increase the MEG signal level; the signal from a dipole is proportional to the dipole length. We calculated the extra MEG and EEG localization errors in using this 16-mm length instead of a true zero-length dipole, and they are negligible here. Dipoles due to electrodes on two different catheters could not be used in this experiment because an extra, large magnetic signal would be created by the area or electrical loop between the catheters.

The dipole current pulse was a single 14-msec sine wave with rounded end points, repeated at the rate of 10/sec to allow signal averaging. The sine wave simulated a neural signal, and the rounding of the end points eliminated high-frequency components that produce capacity feed-through spikes in the EEG [18]. The current amplitude was always at the low value of 4.0 μA. Although larger currents through intracerebral electrodes have been reported by others [15], this low value was the maximum allowed by the Massachusetts Institute of Technology (MIT) to avoid patient injury, and contributed to our problem of weak MEG signal levels (see below). Further measures taken to avoid patient injury included balancing the sine-wave pulse to produce zero net charge through the brain, and using optical isolation on all

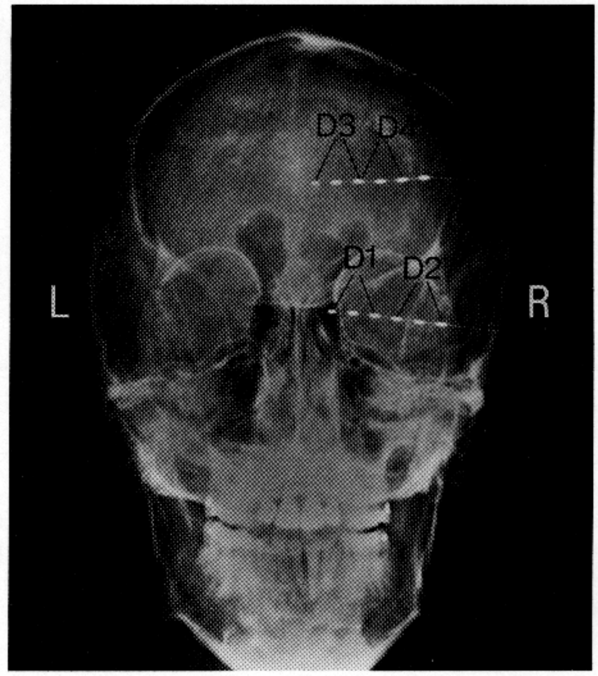

Fig 1. Anterior-posterior roentgenograph of Patient 3 showing a typical example of intracerebral electrodes in the brain just before our measurements were made. Six electrodes can be seen on each of the two catheters. D1, D2, D3, and D4 are the four dipoles, where each is due to the pair of electrodes indicated.

circuitry involving the brain to prevent unwanted current leakage.

The 16 EEGs were measured by conventional Grass electrodes pasted on the scalp, connected to Grass 5P11J amplifiers. The 16 MEGs are due to a single-channel system, moved from location to location for each MEG measurement. (Pros and cons of using a multichannel system are given in the Discussion section). This single channel is an in-line first-order asymmetric gradiometer. It consists of a 2.8-cm-diameter coil, parallel to and situated 8 mm from the scalp and which sensed the magnetic field; this was in series opposition to a more remote coil that essentially sensed any background field. The coil output was detected by an rf SQUID; the lower-noise dc SQUID was not necessary here. This arrangement measured the magnetic field component normal to the scalp, called B_z. (The single channel is part of a three-channel system in the same dewar, previously described [19], where the other two channels, which measure more complex field quantities, are not used in this report.) The MEG and EEG signals were similarly filtered in a bandwidth of 1 to 1,000 Hz, and were averaged in a DEC Microvax computer, which had a sampling rate of 5,208 Hz/channel. Later, to get rid of high-frequency SQUID noise in the MEG, each trace was low-pass digitally filtered, with the 3-dB point at 322 Hz. The MEG or EEG sine-wave signal amplitude on the trace was determined by sampling across six points at the opposite peaks, and taking the peak-to-peak difference.

To perform the inverse solutions, a multilayer spherical model was used, which has layers with different conductivities representing the brain, cerebrospinal fluid, skull, and scalp [20]. The spherical model was chosen instead of a more realistically shaped model both because the claims of 2 to 3-mm MEG localization are usually based on this model, and because more realistic models are not yet ready or convincing for MEG and EEG inverse solutions. In using our model, first the radius and sphere center for each patient, as well as the locations of the dipole and EEG electrodes, were obtained from roentgenographs; this is a simple and direct way to use the model, without "tailoring" or artificial manipulation, which would bias the localization errors. Then, the inverse solution was performed by using the moving-dipole method [21]. The solutions were obtained by iterative adjustments of the location, orientation, and amplitude of the dipole until the best fit between the measured data and that produced by the dipole is obtained. In calculating the MEG solutions, the small signal sensed by the rear coil of the gradiometer was considered. Also, the effects of changes in the radius and sphere center on the solutions were investigated and found to be small; that is, the changes in the localization errors were less than the radius and center changes.

Artificial Head Measurements

Before measuring the patients, we first tested our system by performing MEG and EEG localization in an artificial head previously described [18], which was a spherical, head-size, glass container filled with saline. The system was identical to that later used in the patients, including the same dipole source electrodes, except that the EEG surface electrodes were here silver wires glued to the inner glass surface. The purpose was to verify in this ideal arrangement that our system error was small enough to test the MEG-EEG claims in the patients. The system error can be understood in terms of its two component errors. The first consists of placement errors, which are the spatial displacements of EEG electrodes or the MEG coil from their intended location on the scalp; for the MEG, it also means an angular displacement of the coil from the intended orientation. The second is signal noise, which are extra random signals in the recorded waveform, for example, due to spontaneous brain signals. For any head, if a signal from a dipole is measured with no MEG or EEG placement errors and no signal noise, and if a model of the head is used in the inverse solution that is an exact match to the measured head, then the apparent dipole location must coincide exactly with the true location. Because, in our inverse solution, we used a spherical model that was exact for the artificial head, any localization error we obtained would be due only to placement errors and signal noise; this was our system error. In our plan, after verifying that this was low enough, we would then commence with the patient measurements.

The determination of the system error consisted of extensive and repeated MEG and EEG measurements for different dipole source depths and orientations. It was found that all MEG and EEG errors of localization ranged from 0 to a maximum of 3 mm; hence, we designated the system error to be 3 mm. This indicates that if we performed any single localization measurement again, we are reasonably certain the error would again be less than 3 mm. Although this value was not low enough (e.g., < 0.5 mm) to confirm the belief of 2 to 3-mm localization, it was nevertheless low enough to see whether the belief was significantly in error, and we proceeded with the patient measurements.

Patient Measurements

The patients, who were young adults under medical care at Beth Israel (BI) Hospital (Boston, MA), gave their informed consent for all procedures both at BI and at MIT, where the actual measurements were made. In the BI method of monitoring with intracerebral electrodes, 10 catheters were surgically implanted into the temporal and frontal lobes; eight were their standard catheters that were magnetic, and two were our nonmagnetic catheters previously described. After completion of the monitoring, the eight standard catheters were withdrawn because they would have produced magnetic interference, which left the two nonmagnetic catheters in the brain. There was no current path through any of the catheter skull holes, which would have distorted our results, because plastic screws had been used to close the holes. The general method of catheter implantation, however, resulted in an MEG problem. The standard surgical procedure is to insert the catheters laterally [16], so that our dipoles were oriented radial to the skull. This resulted in a suppressed MEG signal, already weak because of the low dipole current. This is because a radial dipole in a spherical conductor produces zero external magnetic field [22]; therefore, a radial dipole in an actual head produces an MEG signal that is suppressed compared with that of a tangential dipole at the same location [19]; there is no such suppression in the EEG. Hence, in a number of MEG signals, there was the problem of poor signal/noise (S/N). In Patient 1, however, one of the two catheters was inserted with an upward tangential tilt. The two dipoles on this catheter therefore gave especially large MEG signals and our best MEG data.

A grid was marked on the patient's shaved head, showing the places for the EEG electrodes and the MEG detector. These places were chosen for good information content averaged over the four dipoles to be used, and to avoid surgical sites. The measurements were made in the magnetically shielded room at MIT [19]. First, the EEG signals were measured. Each of the four dipoles was selected in turn by switching, and 560 pulses were averaged for each. Then, most EEG electrodes were removed to allow MEG access to those scalp areas, leaving several monitor electrodes still in place, and the MEG signals were measured. This was done by successively moving the MEG dewar to each of 16 places previously marked on the grid. At each place, the four dipoles were again selected in turn; however, now 280 pulses were averaged to save time.

Results

Examples of MEG and EEG traces are shown in Figure 2. As noted previously, the MEG and EEG placements were chosen for good information content, and it is seen that the MEG and EEG placements are different in each patient. The MEGs are grouped more anteriorly to take advantage of the MEG maximum in that area "across the dipole" [23]; the EEG maxima are "along the dipole," at a 90-degree angle to those of the MEG. Concerning the MEGs, the main feature of in-

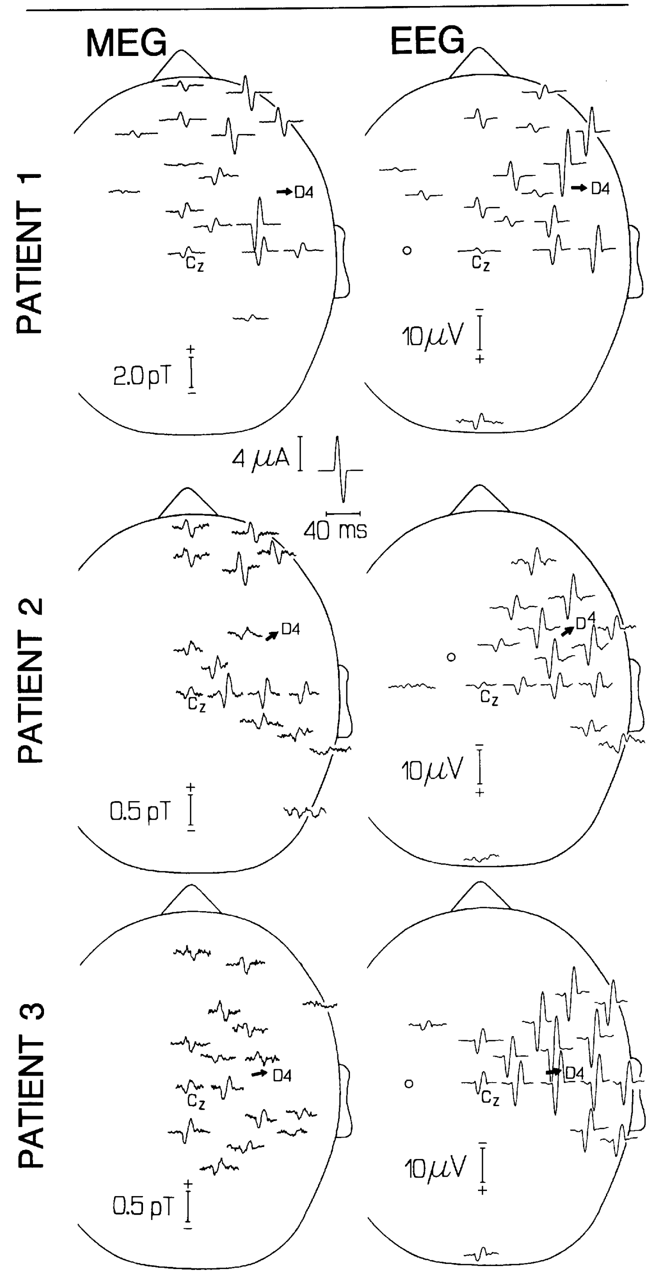

Fig 2. Examples of averaged MEG and EEG traces due to one dipole in each patient, and the single trace of the dipole current (upper center). The head is viewed from the top; C_z (10–20 EEG system) is at the apex. The dipole, which happens to be D4 in each case (out of D1, D2, D3, and D4), is shown as a short arrow, with direction during the first half of the sine wave. In the MEG maps, + denotes field out of the head. The area at the right of the dipole is blank because the protruding catheters prevented the dewar from being placed there. Although the MEG noise in all patients is similar, much more noise is seen in the traces of Patients 2 and 3 than in Patient 1 because of their more sensitive MEG scale. In the EEG maps, the reference is the circle at left center. In Patient 2, the slow waves in the EEG baselines is due to frequent spontaneous epileptic discharges; however, these produced almost no error because we measured the sine wave peak to peak, ignoring the baseline.

terest is their low signal levels in Patients 2 and 3 compared with the noise in these traces; this noise was mostly due to spontaneous brain signals. Although the apparently low ratio of S/N in these patients would perhaps be acceptable in some applications, it is suspect here because noise would degrade the localization accuracy we are seeking. We are therefore alerted to this problem and will estimate the extent of accuracy loss when analyzing the data. Concerning the EEGs, the reference placement is seen to be left central. We had originally recorded the EEGs with O_z (10–20 system) as reference but, because of muscle noise at O_z, the reference was later changed by computer manipulation to a more central electrode so that the O_z lead now produced one of the 16 traces. Although its placement is somewhat remote from the dipole, this should not bias the MEG-EEG localization comparison because it has adequate information content.

The localization results are shown in the Table. The approximate location and angle of the dipole was determined by visual examination of roentgenographs. The location, always on the patient's right, indicates its general depth and the regions of the brain covered in this study. The dipole angle was either approximately radial or tangential to the skull, to within 15 degrees, with no intermediate angles. This angle is important in the MEG S/N problem, which was handled in the following way: First, the MEG S/N was calculated for each dipole, yielding the column shown in the table. Each value in the column is the average of all 16 traces, where the signal is peak-to-peak and noise is the rms of the first third of the trace. Each MEG S/N value was then compared with the approximate dipole angle. As expected, a strong correlation was seen between the S/N and the angle, where the two large values (44 and 38) are from the tangential dipoles. The remainder of the S/N range (3–11) can be ascribed to small variations in the radial angle (within the 15°), and to differences in depth. We then could proceed to the next step, which was to see whether there was a correlation between the MEG S/N and the MEG error; if so, this would indicate that the weakness of the MEG signal did affect or degrade the MEG-EEG comparison, and the weak MEG data should be removed from consideration.

The MEG and EEG error is here defined as the distance between the apparent and actual source location for that dipole; for dipole D1 in Patient 2, the MEG was too weak to yield an inverse solution. A visual comparison of MEG error with S/N indeed shows that the error increases with decreasing S/N. More quantitatively, we calculated that the MEG error averaged over dipoles with S/N greater than 10, 8, 5, 4, 3, and 2 is, respectively, 8.0, 7.8, 8.7, 11.6, 14.4, and 15.3. A plot of these numbers shows the average to be about flat with decreasing S/N until 7 or so, at

Results of MEG and EEG Localization

Patient	Dipole	Approximate Location	Approximate Angle	MEG S/N	MEG Error (mm)	EEG Error (mm)
1	D1	Cingulate gyrus	Rad	11	13	15
	D2	Middle frontal gyrus	Rad	10	7	12
	D3	Parasagittal sup. frontal gyrus	Tang	44	7	1
	D4	Convex. sup. frontal gyrus	Tang	38	4	10
2	D1	Amygdala	Rad	3	No solution	17
	D2	Middle temporal gyrus	Rad	3	[24]	12
	D3	Supplementary motor area	Rad	6	[12]	10
	D4	Superior frontal gyrus	Rad	8	9	7
3	D1	Amygdala	Rad	5	[28]	7
	D2	Middle temporal gyrus	Rad	4	[40]	15
	D3	Supplementary motor area	Rad	5	[17]	9
	D4	Superior frontal gyrus	Rad	5	[7]	8
Average error, omitting data in brackets where the S/N < 8					8	10

Sup = superior; convex = convexity; rad = radial; tang = tangential; S/N = signal/noise.

which it begins to rise. Therefore, to be conservative, we can say that for S/N of less than 8 there is a worsening of the MEG error due to noise contamination. Hence, the MEG data from those six dipoles, shown in brackets, were removed from further consideration. The remaining MEG data from four dipoles in Patient 1 and one dipole in Patient 2 are therefore free of noise for our purposes, and it is these five dipoles that are averaged and directly give our MEG localization error. This average localization error is shown at the bottom to be 8 mm. This value, however, is stronger than only a five-dipole average because it is supported by the rejected dipoles, when the noise they contain is considered. That is, if the six values in brackets had been due to larger MEG signals, the previous plot shows that they would tend to approximately the 8-mm average; the rejected dipoles therefore indirectly contribute to the 8-mm average. In contrast to the MEG, the EEG S/N was always large (typically > 40) and hence is not listed, and the EEG average error of 10 mm is due to all dipoles. The EEG has no S/N problem because it is not suppressed by the radial dipole.

The five values in the MEG average and the 12 in the EEG average are not distributed randomly but depend on the dipole location and features of the particular patient's head. The meaning of these averages is, therefore, that they are the error to be expected when averaged over those source locations in those patients. The five and 12 dipoles, however, appear to be reasonably representative of many locations in young adult heads (more so for the 12 dipoles) and therefore are adequate for purposes of this pilot MEG-EEG comparison. Finally, the system error should be folded into the results, yielding MEG and EEG average errors that are most probably in the range of 6 to 10 mm and 8 to 12 mm, respectively. This is because the outside range limits would be 5 to 11 mm and 7 to 13 mm for MEG and EEG due to the 3-mm error; however, the probable error, assuming random system errors, is about two-thirds of this or 2 mm.

Discussion

The MEG average localization accuracy of 8 mm is somewhat worse than the 2 to 3 mm previously believed, whereas the EEG accuracy of 10 mm is better than the reported value of 20 mm. Concerning the MEG, there are no other studies reported of localization measurements by using intracerebral sources at known locations in the live human head; hence, there are no other results to which our 8 mm can properly be compared. In the only other reported localization measurement with a source of known location in the live human head [12,24], the source there was a current pulse through electrodes which were subdural, therefore very superficial. Our result also cannot be compared with other MEG localization measurements [9, 10, 13] where only artificial heads were used because of the differences in local electrical parameters between an artificial and actual head, which could affect MEG localization. In all those previous MEG studies, we note that EEGs were not measured and compared with the MEG.

Concerning the EEG, the previous report of 20-mm accuracy [15] was of a similar experiment with intracerebral electrodes but measuring only the EEG. Our improved accuracy appears to be due to the absence of spikes [18], which they had in abundance in their EEG signals due to their use of a rectangular pulse. It may also be due to the special care with which we maintained signal fidelity, such as by using a wide-frequency bandpass to not lose signal information. Our result of 10 mm is in good agreement with our larger EEG study in the same patients [17] in which more dipoles were used and an average EEG error of 11 mm was obtained. We conclude that when the 16-channel EEG is recorded with high fidelity, and a spherical model is used in the inverse solution, it is capable of twofold the accuracy, averaged over a variety of source locations, than had been supposed.

The cause of the 8 and 10-mm average localization errors can only be the use of the spherical model in the inverse solution, as an approximation to the actual head. This is because localization error, as previously noted, is due to a combination of placement errors, signal noise, and the use of an inexact model of the head in the inverse solution. Now, in the artificial head used here, where an exact model was used in the inverse solution, it was seen that placement errors and noise produced at most a 3-mm localization error; in the patients, the placement errors were slightly greater, resulting in an added localization error of perhaps 1 mm. Also, noise was not a factor here because we rejected the noisy MEG data; this leaves only the model as the cause. Thus, if an exact model of each patient's head would have been used, the MEG and EEG localization errors would here have been at most 4 mm. With an exact model and less system error, for example, with less placement error, it should be possible to attain the believed 2 mm for the EEG as well as the MEG. That is, there is no reason to believe that the improvement in the MEG accuracy would be any greater than for the EEG. No inverse solution, however, has yet been obtained in MEG or EEG by using a model more realistic than the spherical model.

Using an exact model of the head in the inverse computation would be a large undertaking. Not only would it be necessary to incorporate all the local shapes and conductivity inhomogeneities into the model, but the inverse calculation would be enormous, involving many iterations for each of the six dipole unknowns. To date, in the MEG, a model more realistic than the sphere has recently been used but only in the forward problem [25], in which the calculations are much simpler and not directly helpful in the inverse calculation. In the EEG, a model of realistic external head shape has been used in the inverse calculation [26] but was homogeneous and therefore lacked the all-important skull; the errors could therefore have been greater than with the spherical model.

There is also no reason to believe that MEG localization would have been any better if we had used a large multichannel MEG system instead of the single-channel system moved from place to place on the head. Certainly, we could have averaged longer and obtained better S/N, thereby salvaging the rejected seven dipoles; but this would not have reduced the average MEG error and would have only increased the range of applicability to more cases. It could also be argued that a multichannel system would have less placement error (which is questionable), but again that is not the problem; the MEG localization error is largely due to using an inexact model in the inverse solution, and that cannot be helped by using a multichannel system. In any case, the use of a multichannel system was not indicated for this particular experiment because of the two protruding catheters and eight protruding plugs of the removed catheters; these would have prevented the large dewar from being placed in optimal regions near the catheters, with resulting problems in interpreting the localization results. Although a seven-channel system was used in the other MEG measurement in the actual head [12] where less error was obtained, we again note that only subdural electrodes were used, and the errors would have been larger with deeper sources; their better accuracy cannot be significantly attributed to the use of the seven-channel system.

All these factors considered, we conclude that the MEG offers no great advantage over the EEG in localizing a dipole source. Because almost all focal sources in the brain can be approximated by a dipole when viewed from the surface of the head, this conclusion applies to almost all focal sources in the brain. For example, this applies to some components of evoked responses such as the early somatosensory responses. It also applies to those interictal epileptic spikes that are focal, where those most clinically interesting originate in the temporal lobe. Although the MEG localization accuracy from the two temporal dipoles in this experiment (D2 in Patients 2 and 3) was not used, the MEG accuracy from the frontal lobe, where most of the dipoles used were located, should apply to the temporal lobe. This is because there is no significant electrical difference between the frontal and temporal regions, although the temporal skull radius-of-curvature is larger. This should not strongly affect the temporal localization accuracy when using the spherical model, however, because the difference in curvature between the temporal skull and our sphere is no greater than the difference between the frontal skull radius and the sphere. Although these results do not apply to nonfocal (extended) sources in the brain, there is no evidence that the MEG would here localize any better than the EEG.

Thus, the belief or statement in the literature that the MEG localizes to within 2 to 3 mm in the human head now appears to be overstated. Furthermore, the belief the MEG localizes much more accurately than the EEG now also appears to be in error. We note, however, that these results do not diminish other uses of the MEG, such as distinguishing between radial and tangential sources, not readily done with the EEG, and where the MEG has already been successful [27]. In that regard, an additional result here is the proof of large suppression of the MEG due to the radial dipole in the actual human head (approximately a factor of six), which was proven previously only in the animal head [19]. This particular use of the MEG is thereby validated. Finally, this pilot study suggests that a larger study be performed to determine the MEG and EEG localization accuracy due to a wide variety of dipole locations in the head, especially including dipoles in the temporal lobe. A study of this type should use a pulse current greater than 4 μA, and should include patients with a variety of head sizes and shapes.

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