A boundary element method-based cortical potential imaging technique has been developed to directly link the scalp potentials with the cortical potentials with the aid of magnetic resonance images of the subjects. First, computer simulations were conducted to evaluate the new approach in a concentric three-sphere inhomogeneous head model. Second, the corresponding cortical potentials were estimated from the patients’ preoperative scalp somatosensory evoked potentials (SEPs) based on the boundary element models constructed from subjects’ magnetic resonance images and compared to the postoperative direct cortical potential recordings in the same patients. Simulation results demonstrated that the cortical potentials can be estimated from the scalp potentials using different scalp electrode configurations and are robust against measurement noise. The cortical imaging analysis of the preoperative scalp SEPs recorded from patients using the present approach showed high consistency in spatial pattern with the postoperative direct cortical potential recordings. Quantitative comparison between the estimated and the directly recorded subdural grid potentials resulted in reasonably high correlation coefficients in cases studied. Amplitude difference between the estimated and the recorded potentials was also observed as indexed by the relative error, and the possible underlying reasons are discussed. The present numerical and experimental results validate the boundary element method-based cortical potential imaging approach and demonstrate the feasibility of the new approach in noninvasive high-resolution imaging of brain electric activities from scalp potential measurement and magnetic resonance images.

Key Words: high-resolution EEG; cortical potential imaging; SEP; boundary element method; realistic geometry head model; central sulcus.

INTRODUCTION

Brain activation is a spatio-temporally distributed process. While conventional EEG has an unsurpassed millisecond scale of temporal resolution, its spatial resolution (or imaging accuracy) is limited due to the blurring effect of the head volume conductor, especially because of the low-conductivity skull layer (Nunez, 1981). Tremendous effort has been made to improve the spatial resolution of EEG. Of particular interest is the recent development of the cortical potential imaging technique, in which an explicit biophysical model of the passive conducting properties of a head is used to deconvolve a measured scalp potential distribution into a distribution of electrical potential over the cortical surface. Because the cortical potential distribution can be experimentally measured (Gevins et al., 1994; Towle et al., 1995) and compared to the inverse imaging results, the cortical potential imaging approach is of physiologic importance. Not affected by the insulating skull layer, the estimated cortical potentials offer more spatial details in assessing the underlying brain activity compared to the blurred scalp potentials.

An early attempt to reconstruct the cortical potentials used an intermediate hemisphere equivalent dipole layer to generate an inward harmonic potential function in a homogeneous sphere head volume conductor model (Sidman et al., 1990). The inverse procedure estimated the equivalent dipole distribution from the scalp EEG, and then the cortical potentials were reconstructed by solving the forward problem, from the estimated equivalent dipole layer to the cortical potentials. Recently, several approaches have been reported to further the effort along this line. He and co-workers used a concentric three-sphere head model to include the significant conductivity inhomogeneity, the skull, in the head volume conductor and a closed-spherical dipole layer with higher density to improve the numerical accuracy (He et al., 1996; Wang and He, 1998; He,
Babiloni et al. (1997) further extended the approach to include both the skull inhomogeneity and the realistic geometry of the head by means of the boundary element method (BEM), based on the isolated problem approach (Hamalainen and Sarvas, 1989).

Gevins and co-workers (1994) developed the “Dublurring” approach to estimate directly the cortical potentials from the scalp EEG recordings using a finite element method (FEM). An initial empirical validation of their approach was conducted by comparing estimated cortical potentials with those measured with subdural grid recordings from two neurosurgical patients. Promising results were reported in their experimental studies and dramatic improvement of spatial resolution was achieved in the cases shown. However, a mathematical comparison between the grid and the estimated cortical potentials in the two patients were not available.

An alternative approach has been explored by Srebro et al. (1993) who directly linked the evoked potential field on the scalp with the cortical potential field by means of the BEM in a homogeneous head model. Although their physical and human visual evoked potential experiments demonstrated the more localized nature of the estimated cortical potentials compared to their scalp field counterparts, the effect of significant conductivity inhomogeneity—the skull—was not considered in their head model.

### TABLE 1

<table>
<thead>
<tr>
<th>Electrode number</th>
<th>Config. 1</th>
<th>Config. 2</th>
<th>Config. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CC</td>
<td>RE</td>
<td>CC</td>
</tr>
<tr>
<td>32</td>
<td>0.913</td>
<td>0.372</td>
<td>0.897</td>
</tr>
<tr>
<td>64</td>
<td>0.929</td>
<td>0.347</td>
<td>0.912</td>
</tr>
<tr>
<td>128</td>
<td>0.947</td>
<td>0.308</td>
<td>0.930</td>
</tr>
<tr>
<td>310</td>
<td>0.957</td>
<td>0.294</td>
<td>0.940</td>
</tr>
<tr>
<td>640</td>
<td>0.958</td>
<td>0.253</td>
<td>0.953</td>
</tr>
<tr>
<td>1280</td>
<td>0.959</td>
<td>0.268</td>
<td>0.953</td>
</tr>
</tbody>
</table>

Note. 10% potential noise and 2% geometry noise were considered, and the average results over 10 trials of noise generation are presented. Config. 1, one tangential dipole with eccentricity of 0.65, and \(\pi/6\) with respect to z axis. Config. 2, two tangential dipoles with eccentricity of 0.65, each of which is \(\pi/7\) with respect to z axis. Config. 3, one dipole at (0.15, 0, 0.65) pointing to \(+x\) direction and two dipoles located at (0, ±0.4, 0.5) pointing to \(+z\) direction.

### TABLE 2

<table>
<thead>
<tr>
<th>Noise level</th>
<th>Config. 1</th>
<th>Config. 2</th>
<th>Config. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CC</td>
<td>RE</td>
<td>CC</td>
</tr>
<tr>
<td>10% PN</td>
<td>0.957</td>
<td>0.304</td>
<td>0.951</td>
</tr>
<tr>
<td>15% PN</td>
<td>0.941</td>
<td>0.320</td>
<td>0.934</td>
</tr>
<tr>
<td>20% PN</td>
<td>0.924</td>
<td>0.330</td>
<td>0.913</td>
</tr>
<tr>
<td>25% PN</td>
<td>0.913</td>
<td>0.374</td>
<td>0.894</td>
</tr>
<tr>
<td>5% GN</td>
<td>0.963</td>
<td>0.277</td>
<td>0.951</td>
</tr>
<tr>
<td>2% GN + 10% PN</td>
<td>0.947</td>
<td>0.308</td>
<td>0.930</td>
</tr>
<tr>
<td>5% GN + 10% PN</td>
<td>0.939</td>
<td>0.319</td>
<td>0.916</td>
</tr>
</tbody>
</table>

Note. For each noise level, 10 trials of noise were generated and the averaged results are presented.

### TABLE 3

<table>
<thead>
<tr>
<th>Noise level</th>
<th>Config. 1</th>
<th>Config. 2</th>
<th>Config. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CC</td>
<td>RE</td>
<td>CC</td>
</tr>
<tr>
<td>10% PN</td>
<td>0.923</td>
<td>0.327</td>
<td>0.905</td>
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<tr>
<td>15% PN</td>
<td>0.890</td>
<td>0.362</td>
<td>0.885</td>
</tr>
<tr>
<td>20% PN</td>
<td>0.858</td>
<td>0.421</td>
<td>0.836</td>
</tr>
<tr>
<td>25% PN</td>
<td>0.849</td>
<td>0.431</td>
<td>0.820</td>
</tr>
<tr>
<td>5% GN</td>
<td>0.918</td>
<td>0.319</td>
<td>0.906</td>
</tr>
<tr>
<td>2% GN + 10% PN</td>
<td>0.913</td>
<td>0.372</td>
<td>0.897</td>
</tr>
<tr>
<td>5% GN + 10% PN</td>
<td>0.900</td>
<td>0.362</td>
<td>0.881</td>
</tr>
</tbody>
</table>

Note. For each noise level, 10 trials of noise were generated and the averaged results are presented.
Recently a new cortical potential imaging algorithm has been reported (He et al., 1999), in which both the realistic geometry and the inhomogeneity of the head can be taken into consideration using the BEM. This BEM-based algorithm offers unique features of connecting directly and efficiently the cortical potentials to the scalp potentials via a transfer matrix with inclusion of the low-conductivity skull layer. In the present study, the BEM-based direct cortical potential imaging approach is systematically evaluated in computer simulations and validated in somatosensory evoked potential (SEP) experiments in three patients by quantitative comparison of the estimated cortical potentials with the direct potential recordings from a subdural grid over the somatosensory cortex. We demonstrate that the BEM-based cortical potential imaging approach provides an accurate and robust means of linking the scalp potentials with the cortical potentials. Such a noninvasive brain mapping technique may greatly increase our abilities to accurately localize rapidly changing patterns of brain activation and to aid presurgical evaluation in medically refractory epilepsy.

MATERIALS AND METHODS

BEM-Based Cortical Potential Imaging Technique

Assume that the head is approximated by a three-shell volume conductor as shown in Fig. 1, with the three shells representing the scalp ($S_1$), the skull ($S_2$),
FIG. 4. At eight time instants around 20 ms after the onset of right median nerve stimuli for patient 1 (both EEG and ECoG were sampled at 5689 samples/s). (a) The recorded scalp potential maps; (b) the direct recorded subdural grid potentials; (c) the estimated subdural grid potentials. All the maps are normalized and the colorbars are shown on the right. The CC and RE values between the estimated and the recorded subdural grid potentials for each time instant are listed at the bottom.
and the brain ($S_3$), and each shell is homogeneous but has different electrical conductivity. Since brain electrical sources exist only inside the brain, Green's 2nd identity can be applied to volumes $V_1$ and $V_2$ separately. After mathematical manipulations, the cortical potential $U_3$ can be directly related to the scalp potential $U_1$ by (He et al., 1999)

$$U_1 = T_{13}U_3,$$  \hspace{1cm} (1)

where $T_{13}$ is the transfer matrix from the cortical potential to the scalp potentials. In practice, the vector of the measured scalp potentials $\Phi$ is a subset of the potential vector $U_3$. Therefore, $\Phi$ can be connected with the cortical potentials by

$$\Phi = AU_3,$$  \hspace{1cm} (2)

where $A$ is the submatrix of $T_{13}$. To account for the low-conductivity skull layer, an adaptive approach has been developed to achieve high numerical accuracy in the transfer matrix $A$ (He et al., 1999).

The inverse problem of cortical potential imaging is to seek the unknown $U_3$ from the measured $\Phi$. To overcome the ill-posed nature of the inverse problem, zero-order Tikhonov regularization can be applied (Tikhonov and Arsenin, 1977),

$$U_3 = (A^T A + \lambda I)^{-1} A^T \Phi,$$  \hspace{1cm} (3)

where $\lambda$ is the regularization parameter, which is used to suppress the effect of noise. The determination of the regularization parameter can be achieved by the L-curve approach, in which the optimal $\lambda$ is chosen at the corner point of the L-curve obtained by plotting the norm of the solution versus the norm of the corresponding residual (Hansen, 1990).

Simulation Protocols

In computer simulations, the head volume conductor was approximated using an inhomogeneous three-concentric-sphere model (Rush and Driscoll, 1969), in which the radii of the brain, the skull, and the scalp spheres were taken as 0.87, 0.92, and 1.0, respectively. The normalized conductivity of the scalp and the brain was taken as 1.0 and that of the skull as 1/80. Each surface of the three spheres was discretized uniformly into 1280 triangle elements. The transfer matrix $T_{13}$ was calculated as described by He et al. (1999), and its different submatrices corresponding to different numbers of scalp electrodes were obtained. A single or multiple dipole(s) with different orientations was used to represent a single or multiple well-localized areas of brain electric activity. The scalp potentials and the cortical potentials corresponding to a given source configuration can be calculated analytically (Wang and He, 1998). Gaussian white noise (GWN) with varying noise level was added to the forward calculated scalp potentials to simulate noise-contaminated EEG measurements. The noise level is defined as the ratio between the standard deviation of noise distribution and that of the simulated scalp potential distribution. GWN with varying noise level was also added to the geometry coordinates of the scalp electrodes, to simulate the scalp electrode placement uncertainty. The zero-order Tikhonov regularization was used to inversely estimate the cortical potentials from the noise-contaminated scalp potentials, and the L-curve method was applied to determine the regularization parameter. The accuracy of the inverse solution was evaluated by the correlation coefficient (CC) and relative error (RE) between the estimated and the analytic cortical potential distributions, which are defined as

$$CC = \frac{U_{3,a} \cdot U_{3,e}}{|U_{3,a}| \cdot |U_{3,e}|}$$ and $$RE = \frac{|U_{3,a} - U_{3,e}|}{|U_{3,a}|},$$

where $U_{3,a}$ and $U_{3,e}$ are the analytic and estimated cortical potentials, respectively.

SEP Studies of Patients

The present BEM-based cortical potential imaging technique was directly validated using the subdural SEP data recorded from three neurosurgical patients.

Subjects. Three neurosurgical patients being evaluated for cortical resection due to medically refractory epilepsy participated in the present study. Informed written consent was obtained according to a protocol approved by the Institutional Review Board of The University of Chicago.

SEP recording. Both scalp and subdural SEP recordings were taken in the relaxed awake state. To facilitate the comparison between the estimated and the directly recorded cortical potentials, the scalp SEP was made several days before grid implantation. Median nerve SEPs were elicited by 0.2-ms-duration electrical pulses delivered to the wrist at 5.7 Hz at motor threshold. Five replications of 500 stimuli were averaged. Using a commercial signal acquisition system (Neurosoft Inc., VA), 32-channel scalp EEG referenced to $C_z$ was amplified with gain of 5000 and band-pass filtered from 1 Hz to 1 kHz. The cortical SEPs were recorded from a $4 \times 8$ rectangular electrode grid with interelectrode distance of 1 cm, placed directly on the surface of the brain as part of their diagnostic evalua-
tion for surgery. The 32 channels electrocorticogram (ECoG) referenced to the contralateral mastoid was also band-pass filtered from 1 Hz to 1 kHz, but a gain of 1000 was used.

MRI and boundary element modeling. Three-dimensional (3-D) MR images were obtained from each subject with a Siemens 1.5 Tesla scanner using T1-weighted images composed of 60 continuous sagittal slices with 2.8-mm slice thickness.

A software package was developed to construct the BEM head models from the MR images. In brief, the MR images were edge-detected and contoured for the scalp, the skull, and the cortical surfaces. Nodal points representing the contours of the three layers were extracted and downsampled. For each layer, the surface between two adjacent slices was constructed by connecting the corresponding nodal points to generate the triangle mesh. The normalized conductivity of the scalp and the brain was taken as 1.0 and that of the skull as 1/80.

Registration of scalp electrodes. Scalp electrodes were located in the MRIs by a combination of two methods: surface fitting and fiducial point registration. On each occasion that the scalp recordings were obtained, 33 electrode locations and 11 fiducial points (nose tip, nasion, preauricular fossae, external auditory meati, external canthi, mastoids, and left cheek) were digitized three times using radiofrequency localizer (Polhemus Fastrak, VT), the stylus of which was placed at each electrode location marked on the scalp. One hundred and fifty points on the scalp were also digitized along with the electrode locations and fiducial points to provide a patient-specific coordinate reference for registering the electrode locations with the MRI images. A surface-matching algorithm was used to fit the digitized scalp to the MRI segmented scalp (Pelizzari et al., 1989; Towle et al., 1993). The discrepancy between the first 7 digitized fiducial points listed above and their corresponding locations as identified on the MRI slices provided an index of registration accuracy.

Registration of subdural electrodes. The subdural recordings were registered to the MR images using two procedures. The relationship of the electrode arrays and radio-opaque markers placed on the contralateral scalp was determined from a 3-D reconstruction of skull films (Metz and Fencil, 1989). They were then located on a hybrid skin/brain segmented surface for each patient using the surface-fitting algorithm (Towle et al., 1995). The fitting process was finalized by ensuring that the distances to the anterior and posterior poles and the inferior surface of the brain were proportional in the lateral skull film and the MRI. A second registration procedure involved identifying the electrode locations in intraoperative photographs of the craniotomy and manually transferring their locations to the 3-D-rendered cortical images so that the location of the grid relative to the craniotomy and gyral patterns appeared identical in the two images. This required the extrapolation of electrode locations, which were not visible in the photographs. Neither technique appeared clearly superior to the other, so the results of the two strategies were averaged, yielding an error term for the grid registration process.

RESULTS

Algorithm Evaluation by Numerical Simulations

Effects of number of surface electrodes. Table 1 shows an example of the simulation results for the effects of number of electrodes in the three-concentric-sphere head model. The 1280 × 1280 transfer matrix $T_{13}$ was constructed using the present BEM approach. Different electrode configurations—32, 64, 128, 310, and 640 electrodes located uniformly over the upper hemisphere—were employed in the simulation, and the all-sphere 1280-electrode system was shown to serve as a reference. One dipole, two dipoles, or three dipoles were used to simulate three different configurations of well-localized brain electric activities (see Table 1 Note for detailed description of the dipole configurations). Then 10% GWN was added to the forward calculated scalp potentials to simulate potential noise (PN), and 2% GWN was added to the electrode positions to simulate geometry noise (GN). The cortical potentials were then inversely estimated from the noise-contaminated scalp potentials by solving Eq. (3) for a regularization parameter determined by the L-curve method (Hansen, 1990). For each noise level, 10 trials of GWN were generated and simulation was conducted. The CC and RE between the estimated and analytic cortical potentials are averaged and shown in Table 1.

Table 1 indicates that the higher the density of the surface electrodes, the higher the CC (and the lower the RE) of the inverse estimation. For the cases studied, CC was 0.91 or larger (RE was 0.37 or smaller) when 128 or more electrodes were used, and CC of greater than 0.87 (RE less than 0.43) was achieved when 32 electrodes were used. Also note that CC drops (and RE increases) as the number of dipoles increases, given a fixed electrode configuration. This is expected since higher spatial sampling is needed to resolve higher source complexity. Table 1 suggests that reasonable inverse estimation can be obtained with 32 electrodes for a limited number of localized sources, while 128 or more electrodes are desirable for more complex source configurations.

Effects of noise. Table 2 shows the simulation results for the effects of noise (average for 10 trials of noise generation), when 128 electrodes were used.
FIG. 5. At eight time instants around 30 ms after the onset of right median nerve stimuli for patient 1 (both EEG and ECoG were sampled at 5689 samples/s). (a) The recorded scalp potential maps; (b) the direct recorded subdural grid potentials; (c) the estimated subdural grid potentials. All the maps are normalized and the colorbars are shown on the right. The CC and RE values between the estimated and the recorded subdural grid potentials for each time instant are listed at the bottom.
Three different source configurations the same as noted in Table 1 were used to simulate well-localized brain electric activities. Seven different cases of the potential noise and geometry noise were considered to simulate the noisy conditions in practical measurement: (1) 10% PN, (2) 15% PN, (3) 20% PN, (4) 25% PN, (5) 5% GN, (6) 2% GN plus 10% PN, and (7) 5% GN plus 10% PN. Similarly, Table 3 shows the simulation results for the effects of noise, when 32 electrodes were used. The source configurations and the noise conditions are the same as those in Table 2.

Tables 2 and 3 indicate that the higher the noise level, the lower the CC (and the higher the RE). However, CC is greater than 0.80 (RE is less than 0.47) for the 32 electrodes, and CC is greater than 0.88 (RE is less than 0.43) for the 128 electrodes, in all the cases studied. Consistent as above, better performance is achieved when the number of dipole sources is decreased or when a higher density of surface electrodes is used. Tables 2 and 3 suggest that the present inverse procedure is quite robust against measurement noise, including both potential noise and electrode placement uncertainty.

As examples, corresponding to three source configurations (same as those in Tables 1–3). Figs. 2a–c, respectively, show the top view of the 10% potential noise-contaminated scalp potential maps (top), analytic cortical potential maps (middle), and inversely estimated cortical potential maps (bottom), when 128 scalp electrodes were used. Figure 2 clearly indicates that the estimated cortical potential maps can effectively reduce the blurring effect observed in the scalp potential maps and recover the underlying brain electric activities with much improved spatial resolution. Also note the similarities between the spatial patterns of the estimated and the analytic cortical potential maps, as indicated by the high CC obtained (greater than 0.91 for the cases studied).

Algorithm Validation in Human Experiments

The present BEM-based cortical potential imaging technique was validated using scalp and subdural SEP recordings in three neurosurgical patients. The estimated cortical potentials were quantitatively compared to the direct subdural recordings. The realistic geometry boundary element head models of the patients were constructed from their MR images, and the number of nodes and triangles in three layers (scalp, skull, and epicortical surfaces) are summarized in Table 4. As an example, Fig. 3 illustrates the three-layer...
boundary element head models of patient 1, constructed from his MR images.

Thirty-two channel scalp SEP waveforms in response to right median nerve stimuli were recorded from patient 1 before the open-skull surgery. Polarity inversion of SEPs is observed over the left hemisphere. The Cartesian coordinates of the electrodes were determined using a radio frequency localizer (Polhemus Fastrak, VT) and then registered with the MR images of the subject using the method as detailed above. Also elicited by the right median nerve stimuli, the cortical SEP waveforms were recorded from a 4×8 subdural electrode array implanted in the same patient during surgery. The electrode array was registered with the MR images using the procedures as described above. Similarly, an inversion of SEPs is observed in the grid recordings, suggesting the overlapping of central sulcus beneath the electrode array.

Figure 4a shows the recorded scalp potential maps for patient 1, at eight time instants around 20 ms after the onset of right median nerve stimuli. The maps show clearly the dipolar N/P20 pattern of frontal positivity/parietal negativity over the left scalp. Note that the scalp potential maps are blurred due to the head volume conduction and interpolation between the widely spaced scalp electrodes. By solving the inverse problem, the cortical potentials at the 32 subdural grid electrodes were estimated from 32-channel scalp potentials, and Fig. 4c shows the reconstructed cortical potential maps over the subdural grid at eight time instants around N/P20. By examining the maps in a time sequence, the strengths of positive/negative activities reveal an evolving pattern that peaks at around 20 ms after the onset of stimuli. The direct subdural grid recordings are displayed in Fig. 4b. Both the estimated and the directly recorded grid potentials show localized positive/negative peaks at the posterior edge of the electrode array and reveal similar dipolar grid potential patterns. Note that polarity inversion was clearly demarcated in both the estimated and the recorded grid potential maps. As a quantitative measure, the CC and RE values between the estimated and the recorded grid potentials were calculated for each of the eight time instants and are listed at the bottom of Fig. 4. Averaged over the eight pairs of maps, a mean CC of 0.73 with standard deviation of 0.02 was achieved, which explains the similarities in spatial pattern in the estimated and the measured grid potential maps. On the other hand, relatively high RE values with mean of 0.80 and standard deviation of 0.01 were obtained, indicating the difference of the amplitude in the estimated and measured cortical potentials, especially near the posterior edge of the grid, where the estimated distribution is smoother than the recorded distribution.

Similarly, Fig. 5 shows (a) the measured scalp potential maps, (b) the direct recorded grid potentials, and (c) the estimated grid potentials for subject 1, at eight time instants around 30 ms after the onset of right median nerve stimuli. Different from N/P20, the scalp potential maps show a reversal dipolar pattern of N/P30, with frontal negativity and parietal positivity over the left scalp. As expected, the blurring effect of the scalp potential maps was greatly reduced in the inversely estimated cortical potential maps, which show much more localized areas of positivity and negativity at the posterior edge of the electrode grid. Consistently, the estimated and recorded grid potentials have similar distribution patterns and have a mean CC of 0.84 with a standard deviation of 0.01 averaged over eight time instants as listed. Lower RE values as compared to those of N/P20 were obtained, with a mean of 0.61 and a standard deviation of 0.01. Again, the central sulcus was clearly demarcated in both the estimated and the recorded grid potential maps, by the separation of negative and positive potential extrema.

Similar data analysis was performed on patients 2 and 3, both of whom were given left median nerve stimuli before and during the surgery, to obtain scalp and cortical SEP recordings. Figures 6 and 7 show the results at four time instants around 30 ms after the onset of right median nerve stimuli, for patients 2 and 3, respectively. Consistently, the estimated grid potential maps closely approximate the direct recorded grid potential maps, with CC = 0.75 ± 0.01 and RE = 0.68 ± 0.01 for patient 2 and CC = 0.75 ± 0.02 and RE = 0.77 ± 0.03 for patient 3, in the cases studied. The clear separation of the positive and negative areas of activities in the grid potential maps also suggests the underlying structure of the central sulcus.

**DISCUSSION**

A number of investigators have attempted to image the distributed brain electric activities from noninvasive EEG/MEG measurement by solving the EEG/MEG inverse problem, without ad hoc assumption on the number of neuronal electrical sources. One approach is to seek the so-called linear inverse solutions within the 3-D volume of the brain, in which a 2-D or 3-D distribution of current dipoles is used to represent brain electric sources (Wang et al., 1992; Pascual-Marqui et al., 1994; Sekihara and Scholz, 1995; Phillips et al., 1997; Van Veen et al., 1997; Grave de Peralta-Menendez et al., 1997; Fuchs et al., 1999; Babiloni et al., 2000; He et al., 2002). Another approach is to constrain the solution space to the cortical surface, termed cortical imaging, which aims at reducing the blurring effect observed in the scalp potential distribution (Sidman et al., 1990; Dale and Sereno, 1993; Srebro et al., 1993; Gevins et al., 1994; Nunez et al., 1994; He et al., 1995).
Among cortical imaging methods, both cortical potentials (Sidman et al., 1990; Srebro et al., 1993; Gevins et al., 1994; Nunez et al., 1994; He et al., 1996, 1999, 2001; Babiloni et al., 1997; Edlinger et al., 1998; Wang and He, 1998; Lian and He, 2001) and cortical currents (Dale and Sereno, 1993; Philips et al., 1997; Babiloni et al., 2000) have been used to represent the underlying brain electrical activity. The cortical current model can be theoretically considered an equivalent single-layer source representing the actual source distribution inside the brain. It has also physiological importance in that the estimated cortical current distribution may reflect the neuronal current sources in the cortical region, if the scalp potentials are primarily originated from the cortical sources. On the other hand, the cortical potential can also be regarded as an equivalent source representing the underlying brain electrical activity, being proportional to an equivalent double-layer source. The cortical potentials can be measured in an experimental and clinical setting, allowing direct validation of the cortical potential imaging methodology. Since there is essentially no bioelectric source between the epicortical and the scalp surfaces, the cortical potential approach may also be viewed as a downward continuation (Edlinger et al., 1998) of the potential field.

The present approach represents, to our knowledge, the first available means of directly estimating the epicortical potentials from the scalp potentials in a realistically shaped inhomogeneous head model by means of the boundary element method. The present method has the capability of reconstructing the distribution of electrical potentials over the cortical surface, thus offering an ability alternative to that of the dipole localization approaches, in which assumption on the number of source dipoles needs to be made (Scherg and Von Cramon, 1985; He et al., 1987; Mosher et al., 1992; Cuffin, 1995). The present cortical potential imaging approach does not attempt to explicitly estimate neural sources underlying the epicortical surface, as other linear inverse solutions do (Dale and Sereno, 1993; Pascual-Marqués et al., 1994; Babiloni et al., 2000). What we attempt to achieve is to noninvasively estimate cortical potentials, which are otherwise recorded using subdural grid electrodes in a clinical setting for neurosurgical patients, from noninvasive scalp potentials and the subjects’ MR images.

The present approach differs from the indirect BEM-based cortical potential imaging technique (Babiloni et al., 1997) in that there is no need to construct the intermediate dipole layer. The inclusion of the low-conductivity inhomogeneity in the head model dramatically improves the accuracy of the transfer matrix over that of the previous direct BEM-based cortical potential imaging approach (Srebro et al., 1993). Compared to the FEM-based cortical potential imaging method (Gevins et al., 1994), the use of the BEM offers the unique feature of reducing the computational load while concurrently accounting for the realistic geometry and inhomogeneity of the head model. The experimental validation of the cortical potential imaging approach by comparing estimated cortical potentials with those measured with subdural grid recordings was first reported by Gevins et al., (1994), in which no formal quantitative comparison was made. With the availability of the technique for registering electrodes relative to cortical anatomy (Towle et al., 1993, 1995), the present study reports, for the first time, the quantitative comparison of the cortical potential imaging inverse solution with the direct subdural grid recordings in humans. The reasonably high CC values between the estimated and the direct recorded subdural grid potentials demonstrate the validity of the present BEM-based cortical potential imaging approach in reconstructing spatial distributions of cortical potentials and suggest its potential for clinical applications.

In the present study, the cortical potentials were estimated from preoperative scalp SEPs over the subdural surface and compared with the postoperative subdural potential recordings. Therefore, the present cortical potential imaging was performed over the subdural surface and should be interpreted as “subdural” potential imaging. The use of subdural potential is for the purpose of quantitatively comparing the estimated subdural potentials with the direct subdural recordings. Thus, in the present study, the epicortical surface is simply approximated by the subdural surface, without considering the realistic cortical surface structure with its high degree of folding (Dale and Sereno, 1993; Dale et al., 1999).

Intraoperative localization of sensorimotor cortex is of increasing importance as neurosurgical techniques allow safe and accurate removal of lesions around the central sulcus. Although electrical stimulation of cerebral cortex or direct cortical recordings of SEPs have been shown to be helpful for localizing sensorimotor cortex based on phase reversal of SEPs (Wood et al., 1988; Cakmur et al., 1997), functional localization of central sulcus from noninvasive scalp SEPs would provide a beneficial tool for presurgical planning. Recently, a dipole tracing method has been reported for preoperative functional localization of the primary somatosensory cortex from scalp SEPs recorded from patients, and less than 10 mm localization error was reported in the cases studied (Mine et al., 1998). Functional MRI techniques have also been used to identify and localize the primary somatosensory cortex (Rao et al., 1995). The present cortical potential imaging technique provides another noninvasive means of identifying the central sulcus presurgically. In Figs. 4–7, the
polarity reversal of the estimated subdural grid potential distribution, which is highly consistent with the direct subdural grid recordings, clearly suggests the underlying structure of central sulcus and is confirmed by the visual inspection during surgery.

The present simulation studies in a three-sphere inhomogeneous head model demonstrate that the present inverse procedure is robust against measurement noise (Table 2 and 3), and the cortical imaging results have much enhanced spatial resolution compared to the scalp potential observations (Fig. 2). High-density surface electrodes are preferred to resolve multiple simultaneously active brain electric sources, while reasonable inverse estimation can still be obtained with 32 electrodes for simple source configurations (Table 1), as the examples of the present human SEP experiments demonstrate.

We have chosen the CC and RE as two quantitative measures to evaluate the similarity and difference between the estimated and the recorded subdural grid potentials in the present study. The CC index provides an indication of the similarity between the topographies of the potential distributions, while the RE index indicates the difference in the absolute values of the potentials. Many factors may affect these indexes in human experiments: for example, different experimental conditions for the presurgical scalp SEP vs cortical SEP during the open-skull surgery, unavoidable grid-MRI registration error, numerical calculation error, etc. In addition, regularization improves the stability of the inverse problem but usually leads to less sharper spatial features than the "true" cortical potentials as a trade-off. In addition to the L-curve approach (Hansen, 1990), different methods can be applied to determine the regularization parameter (Wahba, 1977; Morozov, 1984; Colli Franzone et al., 1985; Johnston and Gulrajani, 1997; Lian and He, 2001), thus possibly leading to slightly different inverse solutions, which is beyond the scope of the present study. Despite these factors, reasonably high correlation coefficients (greater than 0.70) were obtained in the reported experimental cases, as observed in the similarities between the estimated and the measured subdural grid potential maps in Figs. 4–7, notably that relatively higher RE values (range from 0.59 to 0.82) were obtained for the experimental results than for the simulation results (range from 0.25 to 0.46). In addition to the factors mentioned above, the altered volume-conductor properties may also contribute to the difference between the amplitudes of the estimated and measured cortical potentials—during the open-skull surgery when the grid electrodes were exposed to the air, the directly recorded cortical potential should produce higher potential values than those in the presurgical closed-skull

**FIG. 7.** At four time instants around 30 ms after the onset of left median nerve stimuli for patient 3 (both EEG and ECoG were sampled at 5000 samples/s). (a) The recorded scalp potential maps; (b) the direct recorded subdural grid potential maps; (c) the estimated subdural grid potentials. All the maps are normalized and the colorbars are shown on the right. The CC and RE values between the estimated and the recorded subdural grid potentials for each time instant are listed at the bottom.

<table>
<thead>
<tr>
<th></th>
<th>29.2 ms</th>
<th>29.6 ms</th>
<th>30.0 ms</th>
<th>30.4 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>0.7408</td>
<td>0.7644</td>
<td>0.7720</td>
<td>0.7319</td>
</tr>
<tr>
<td>RE</td>
<td>0.7741</td>
<td>0.7570</td>
<td>0.7432</td>
<td>0.8017</td>
</tr>
</tbody>
</table>
condition (Shahidi et al., 1994). For the applications of source localization from subdural recording, even though the absolute values of the estimated potentials differ from the “true” potentials, this will affect only the relative strength of the estimated current sources. Nonetheless, as long as the estimated and recorded potentials have similar spatial distribution (high CC), the accuracy of the source localization will not be much affected.

In summary, the present BEM-based cortical potential imaging approach provides an accurate and robust means to directly and noninvasively link the scalp potentials with the cortical potentials and takes both the head geometry and the skull conductivity inhomogeneity into consideration. Quantitative comparison of the estimated and recorded subdural potentials shows promising results, suggesting the validity of the present BEM-based cortical potential imaging approach and potential clinical applications. The present BEM-based cortical potential imaging approach not only may provide a useful means of noninvasive localization of the central sulcus to aid surgical planning, but also has potential applications in other clinical and cognitive studies, e.g., to facilitate localization of the foci of epileptic discharges or the identification of eloquent cortical regions.

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