Article title: **Gradient magnetic-field topography for dynamic changes of epileptic discharges**

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Abstract

We developed gradient magnetic-field topography (GMFT) for magnetoencephalography (MEG). We plotted the Euclidean norms of gradient magnetic fields occurring at the centers of 102 sensors onto 49-point grids and projected these norms onto the MRI brain surface of a twelve-year-old boy who presented with neocortical epilepsy secondary to a left temporal tumor. The peak gradient magnetic field located posterior to the tumor and correlated to MEG dipoles. The gradient magnetic field propagated to the temporo-parietal region and corresponded with spike locations on electrocorticography. GMFT revealed the location and distribution of spikes while avoiding the inverse problem.

Scope: Disease-Related Neuroscience

Keywords: Magnetoencephalography; Gradient magnetic-field topography; Electrocorticography; Inverse problem; Dynamic changes; Neocortical epilepsy

[1]**Abbreviations:** DNT, dysembryoplastic neuroepithelial tumor; ECD, equivalent current dipole source estimation; ECoG, electrocorticography; GMFT, gradient magnetic-field tomography; IVEEG, intracranial video EEG; MEG, magnetoencephalography.

1. Introduction

Magnetoencephalography (MEG) is used to determine the location of epileptic foci in patients with or without visible lesions on MRI [Minassian et al., 1999; Otsubo et al., 2001]. A typical method for localizing magnetic sources of interictal epileptic discharges for epilepsy surgery is equivalent current dipole source (ECD) estimation. ECD requires certain assumptions to define conductor models of the “forward problem” and to formulate solutions of the “inverse problem” when calculating possible locations of sources. Investigators have applied various head models to solve the forward problems [Hämäläinen and Sarvas, 1989; Hämäläinen et al., 1993]. The inverse problem, however, is ill-posed, since in the absence of constraints a given magnetic-field pattern can be produced by an infinite number of intracranial sources. Thus, ECD employs an implicit assumption that a single ECD point represents the center of a population of activated neurons. Furthermore, ECD requires a high signal-to-noise ratio: high epileptic magnetic field compared to low background brain activity for a reasonable goodness of fit.

MEG sensors differ in alignment of pick-up coils: magnetometers, radial gradiometers, and planar gradiometers. Planar gradiometers contain paired coils and measure the difference between magnetic fields passing through each of the paired coils, thereby measuring a gradient of the magnetic field along the line between the centers of the coils. Planar gradiometers are useful for localizing brain activity since, when the measured gradient field is largest, the planar gradiometer is located immediately above a tangential source [Ahonen et al., 1993].

We developed gradient magnetic-field topography (GMFT) to visualize the gradient magnetic field on the brain surface at each time point during epileptic spikes, thereby avoiding the inverse problem. By coregistering GMFT on the MRI brain surface with locations of extraoperative subdural EEG electrodes, we compared the location, distribution, and propagation of epileptic spikes determined by MEG and electrocorticography (ECoG).

This paper introduces GMFT as a method to demonstrate the dynamic changes of epileptic spikes in three dimensions as compared with two-dimensional extraoperative subdural EEG in a patient with intractable neocortical epilepsy.

2. Case Report

Our patient was a twelve-year-old right-handed boy who had complex partial seizures since he was two years of age. MRI revealed a cystic tumor in the left temporal lobe. His intractable seizures consisted of head-turning to the right, confusion, and occasional aphasia with secondary generalization. His parents gave informed consent for all procedures.

MEG showed frequent polyspikes over the left temporal region (Fig. 1A, B). ECD localizations of interictal spikes were posterior to the lesion in the left posterior temporal region (Fig. 1C). GMFT of the prominent left temporal polyspikes showed the initial peak of activity posterior to the area delineated by the ECD localizations (Fig. 2A). Dynamic changes in GMFT revealed repetitive epileptic spike activities and an extended epileptic field over the left posterior temporal and parietal region (Fig. 1D, 2B, and the attached movie file).

Because of the patient’s right-handedness and left temporal lesion, we placed subdural electrodes over the left temporo-parietal lobes. Language representative cortex was superior to the lesion, in the posterior portion of the superior temporal gyrus. Intracranial video EEG (IVEEG) showed interictal spike discharges starting posterior to the lesion, then propagating anterior to the lesion over the middle temporal region (Fig. 2C, D). The initial and propagated areas of interictal discharge on GMFT correlated to those of IVEEG. The ictal onset zone localized posterior to the lesion over the posterior temporal region, identical to the area of initial interictal discharges, then propagated to the left hemisphere. GMFT at the initial spike peak was concordant to this ictal onset zone.

We resected the lesion and additional left posterior temporal cortex in the ictal onset zone posterior to the lesion. The histopathological diagnosis was dysembryoplastic neuroepithelial tumor (DNT). Except for one complex partial seizure two years after surgery, the patient has been seizure free on medication for three years.

3. Discussion

Standard ECD analysis delineates the spatial extent of an epileptogenic zone when reliable ECD localizations are accumulated to form a single cluster [Iida et al., 2005; Oishi et al., 2006]. One single cluster of MEG spike sources can indicate the primary epileptogenic zone for complete resection and seizure control. Multiple clusters indicate complex and extensive epileptogenic zones and necessitate intracranial EEG monitoring to evaluate the entire epileptogenic area. The spread of ECD localization is typically derived from estimated sources with forward and inverse solutions at multiple time points for each spike. We developed GMFT to understand the spatial extent of epileptic discharges, including multiple epileptic discharges, on the brain surface. Unlike ECD and spatial filters, GMFT did not require solving the inverse problem, preprocessing, and selecting the conductor model. GMFT is a direct source estimation revealing the gradient of the original magnetic field recorded by planar gradiometers. When multiple epileptic discharges occurred simultaneously or close together, GMFT was able to reveal the multiple sources. ECD localization at times projected a deep-seated source from widely extended epileptic discharges, but GMFT delineated the superficial extent of the cortical epileptic discharge.

Dynamic changes of complex epileptic discharges on the brain surface can reveal the characteristics of one single activity or even multiple activities in the epilepsy network [Chen, et al, 2002; Otsubo et al., 2001]. Epileptogenic discharges show various types of spikes, polyspikes, repetitive spikes, sharp waves and slow waves [Palmini et al., 1995]. Single moving dipole analysis, however, cannot demonstrate the dynamic changes of spike propagations. Cortically constrained, minimum norm-based spatial filtered dynamic statistical parametric maps, demonstrated the statistically significant power of epileptic discharges compared to that of background activity and revealed the dynamics of interictal discharges on inflated cortical surface images [Shiraishi et al., 2005]. GMFT directly projects the gradient of magnetic field, the steepest of which represents the largest source of epileptic discharges, on the brain surface. We confirmed the GMFT distribution of interictal epileptic discharges by voltage topographic mapping using subdural EEG electrodes. Changes in the GMFT gradients reflected sequential changes in epileptic sources, thus enabling us to visualize the dynamic magnetic-field changes.

GMFT patterns can predict the location, distribution, and propagation of interictal epileptic discharges for planning intraoperative ECoG and have the potential to ensure that the extraoperative ECoG grid covers the interictal zone and will likely cover the ictal onset and epileptogenic zones in a subset of neocortical epilepsy.

Limitations of the GMFT method are the following: 1) GMFT loses the directions of ECDs. GMFT shows only the topography of gradient differences of the magnetic field in each coil. The orientation of ECDs supported the locations of ECDs in spikes along the central and interhemispheric sulci [Salayev et al., 2006]. 2) No coil covered the cerebral bases, such as the frontal, temporal, and occipital bases, so GMFT was unable to project topography over the cerebral bases. 3) GMFT projected both superficial and deep-seated sources onto brain surfaces. Actual small deep-seated sources might show up as a small field-of cortex on the top of the source or be obscured by background noise. 4) The spatial resolution of GMFT was dependent on the density of sensors in the MEG system. More densely populated sensor arrays would provide higher spatial resolution.

4. Conclusions

We developed GMFT that projected the gradient magnetic fields of interictal epileptic discharges onto the volume-rendered brain surface from a patient's MRIs. GMFT showed magnetic-field gradients representing the location and distribution of epileptic discharges without the inverse problem of ECD. Sequential GMFTs demonstrated the propagation of dynamic changes in the epileptic network. This preoperative analysis of interictal epileptic discharges may improve how neurosurgeons construct ECoG grids that cover the entire epileptic network.

5. Experimental Procedure

We used a whole-head neuromagnetometer, (Neuromag System, Elekta-Neuromag, OY, Finland), consisting of 102 identical sensors, each containing two planar gradiometers positioned at right angles to each other and one magnetometer. Time-varying signals from the two planar gradiometers reflect changing gradients of the magnetic field in two orthogonal directions at each sensor location (Fig. 1A). The sensor element with the highest total gradient field would indicate a current dipole beneath the sensor.

We recorded MEG data at 600.615 Hz. We simultaneously recorded EEG using 19 scalp electrodes. We analyzed MEG and EEG data with a **10-50** Hz band-pass filter. We visually selected interictal epileptiform discharges.

Using data from all MEG sensors and assuming a homogeneous spherical conductor, we conventionally analyzed single ECD localizations at spike peaks. We coregistered ECD localizations with dipole strengths of 100-500 nA or confidence volumes of less than 0.1 cubic mm onto the patient’s MRIs (Fig. 1C).

We used a 1.5 Tesla MRI scanner (SIGNA or SIGNA HORIZON, GE HealthCare, Waukesha, USA) to obtain brain-volume data from three-dimensional spoiled gradient recalled acquisitions in the steady state (3D-SPGR). From the MRI data, we manually segmented brain voxels and calculated volume rendered brain images from the segmented voxels [Hashizume et al., 2002].

To generate GMFT, we calculated the root square of both planar gradiometer signal values at each sensor location (Fig. 1B). We created a 7 x 7 rectangular grid with 1.5 mm distance for each sensor. We projected each of the 49 grid points vertically onto the volume rendering of the brain surface on MRI. We excluded points with more than 10 cm between grid points and brain surface. We calculated field-gradient values for each of the grid points at each time point. We then copied gradient signal values to the projected 49 points of the rectangular grids from the 102 sensors and smoothed the GMFT on the brain surface using a nearest-neighbor interpolation (Fig. 1D).

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Figure legends

Figure 1

Figure 1A shows two time series, one from each planar gradiometer, for each of 102 sensors. Figure 1B overlays the root-square signal values for all 102 sensors. Figure 1C shows the equivalent current dipole locations of interictal spikes occurring posterior to the lesion, in the left posterior temporal region. Figure 1D shows sequential changes of GMFT for the polyspikes of Figure 1B using maximum sensor values at 16.7 ms intervals. GMFT depicts the reverberating epileptic spikes and extends the epileptic field over the left posterior temporal and parietal regions (Figure 1D and the attached file, movie.mpg).

Figure 2

Figure 2A and B show GMFT of the prominent left temporal polyspikes. The initial peak (A) locates the focal GMFT posterior to the lesion. The consecutive peak of polyspikes locates regional GMFT over the posterior temporal and parietal regions 16.7 ms later. Figure 2C and D show voltage topographies of polyspikes recorded on extraoperative subdural EEG. The initial peak (C) shows dipole voltage topography of discharges (blue, positive; red, negative), posterior to the lesion over the posterior temporal region. The consecutive spike (D) shows negative discharges extending over the middle to posterior portion of the left temporal region 100 ms later.

Movie legends

A movie of gradient magnetic-field topography (GMFT) makes dynamic changes of magnetic-field activities visible on the 3-D MRI of the brain surface (lower) along with epileptic discharges of MEG (upper).

Figure 1

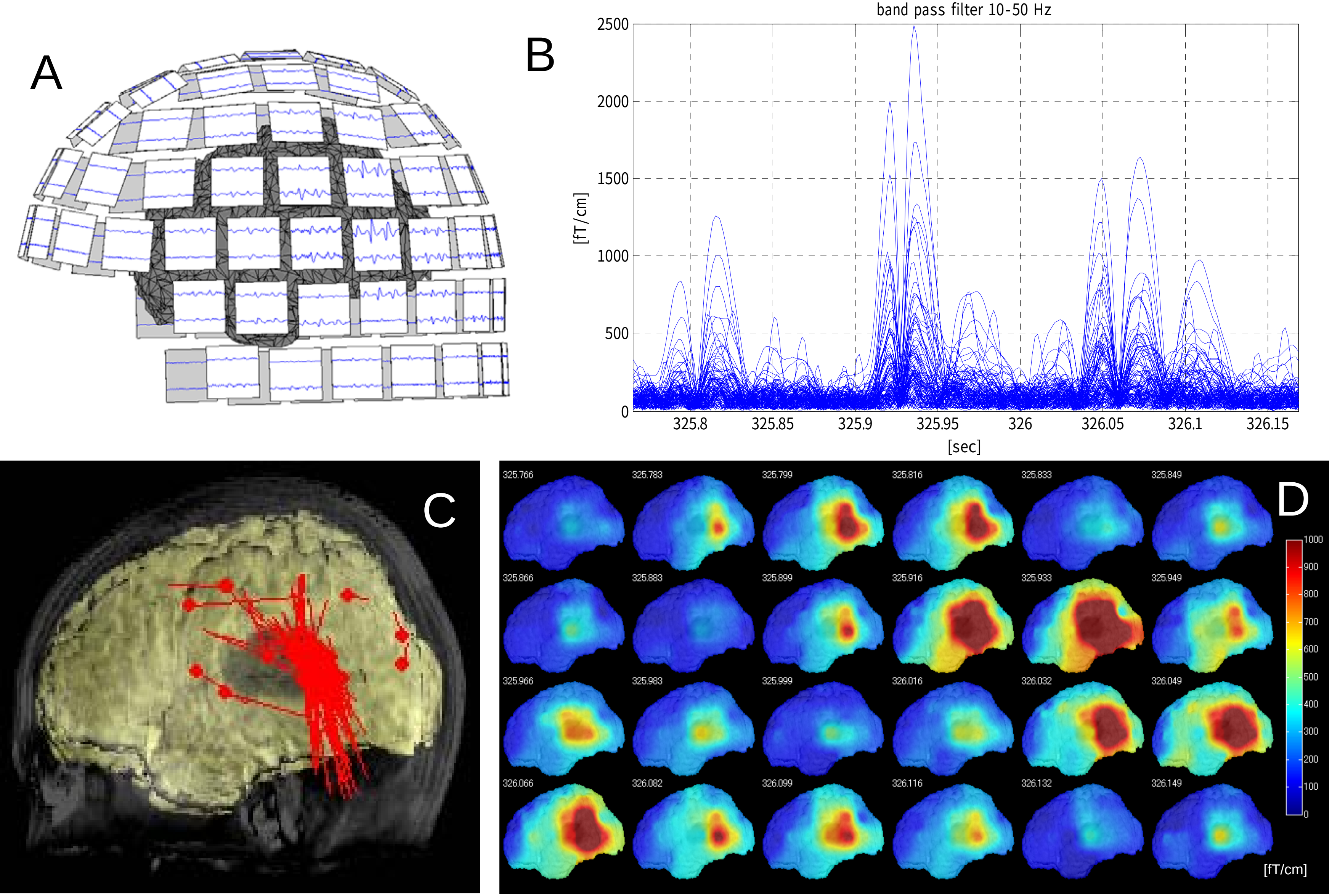
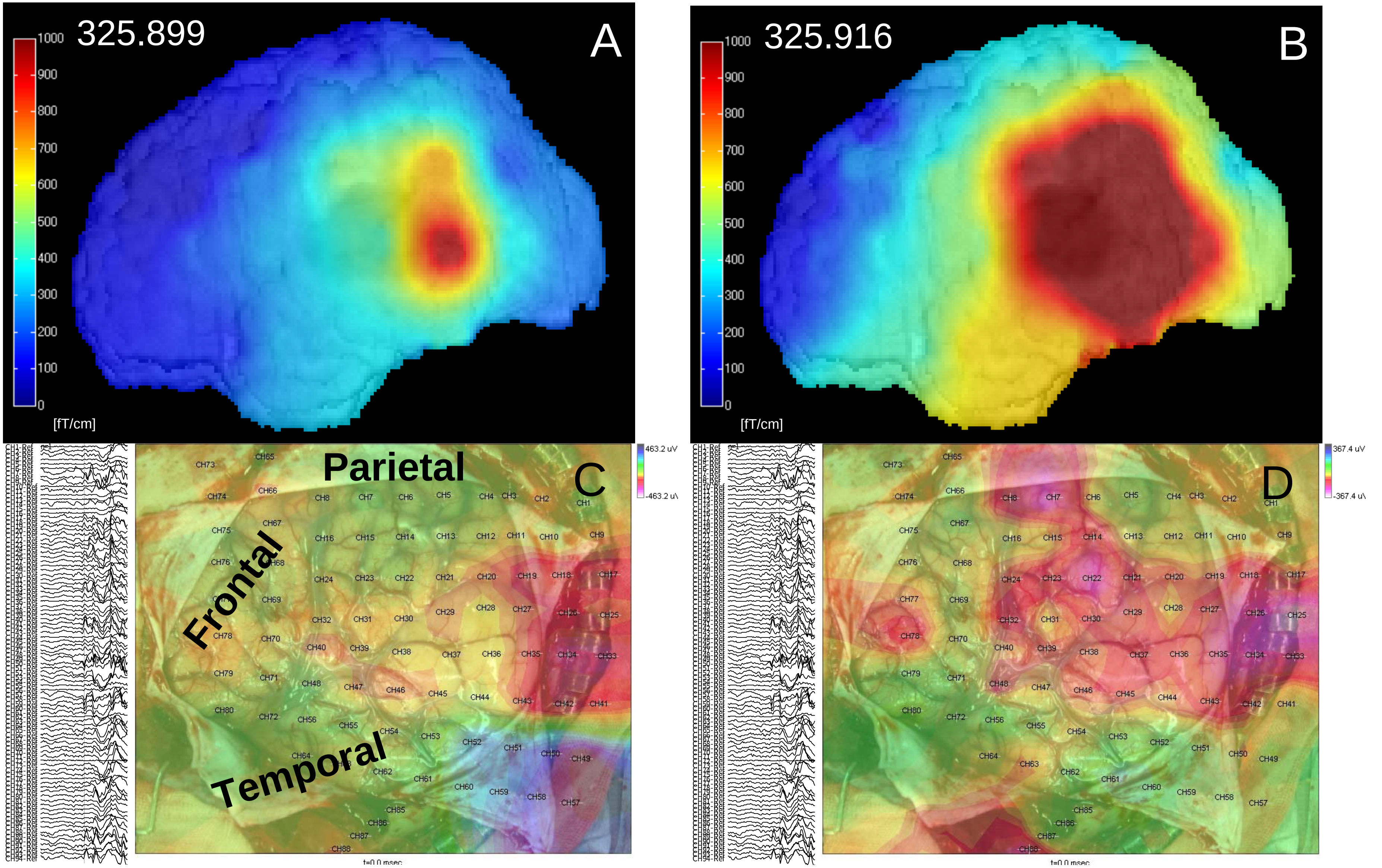


Figure 2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A
325.916
B
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Parietal
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463.2 uV
-463.2 uV
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