

## Development of a Freeware for Analysis of Neuromagnetic Epileptic Discharges

Akira HASHIZUME<sup>1,3,\*</sup>, Kaoru KURISU<sup>1</sup>, Koji IIDA<sup>1</sup>,  
 Kazunori ARITA<sup>2</sup>, Tomohide AKIMITSU<sup>3</sup> and Nobukazu NAGASAKI<sup>4</sup>

1) Department of Neurosurgery, Hiroshima University, Hiroshima, Japan

2) Department of Neurosurgery, Kagoshima University, Kagoshima, Japan

3) Gamma Knife Center, Takanobashi Central Hospital, Hiroshima, Japan

4) Department of Oral Maxillofacial Radiology, Hiroshima University, Hiroshima, Japan

### ABSTRACT

We developed a freeware for the analysis of neuromagnetic epileptic discharges and named it "hns\_meg." It works as an executable standalone application, compatible with 32/64 bit Microsoft Windows Vista or Mac OSX 10.6. The program is designed for recordings from planar gradiometers and includes the following functions: listing of topographies of maximum gradient magnetic field ( $\partial B$ ) every 1 s throughout the measured time, two or three-dimensional topographical representations of  $\partial B$ , and time-frequency representations based on a maximum entropy method. Coupling the first function with an appropriate frequency filter is useful in efficiently finding spikes. The last two functions are attractive for users who want to try new analytical methods different from those in commercially available software packages.

**Key words:** *Epilepsy, MEG, Analysis*

Today, magnetoencephalography (MEG) is recognized as a useful examination in the evaluation of epilepsy<sup>10</sup>. Clustering areas of equivalent current dipoles (ECD), estimated at epileptic spikes, are assumed to be epileptogenic zones, and patients with ECD clustering have been reported to be candidates for epilepsy surgery<sup>5,12</sup>. Theoretically, a MEG user is supposed to scrutinize all the channels of both MEG and electroencephalography (EEG) throughout the measured time-span. However, the latest types of neuromagnetometers have hundreds of channels; consequently, full analysis of MEG recordings requires much time and effort. To shorten this analysis time, we have developed a new tool, the time-evolution list of a gradient magnetic field ( $\partial B$ ). In this paper, we defined  $\partial B$  not as vertical, but as planar  $\partial B$ , such as recordings from a planar gradiometer. That is, this tool is designed for raw data from a machine from Elekta-Neuromag, a leading company in the field of neuromagnetometers. The tool calculates maximum  $\partial B$  every 1 s on all MEG channels and makes a time-evolution list of  $\partial B$ . The list, processed through a 14–50 Hz band-pass filter, is helpful to find time domain including spikes,

which is the most time-consuming procedure in evaluating neuromagnetic recordings. This tool is also designed for users who feel that existing analytical tools for MEG recordings are too limited. In addition to the list function, the tool we describe in this paper has other functions, such as time-frequency representations (TFR), calculated by a maximum entropy method (MEM), and quasi-gradient magnetic-field topography (GMFT)<sup>3</sup>.

Frequency analysis of epileptic activity is a new frontier of study. Ochi et al showed the significance of frequency analysis in a study using multiple band filter analysis (MBFA)<sup>8</sup>. To facilitate frequency analysis in MEG, we added a frequency analysis function to the tool. We have also proposed GMFT to evaluate epileptic discharges as another viewpoint, different from conventional ECD analysis. GMFT can show magnetic-field gradients representing the location and distribution of epileptic discharges without the inverse problem of ECD, and sequential GMFTs can demonstrate the propagation of dynamic changes in the epileptic network. Original GMFT requires magnetic resonance images (MRI) and knowledge of digital image and communications in medi-

\*Address for correspondence: Akira Hashizume, M.D.

Department of Neurosurgery, Hiroshima University, 1-2-3 Kasumi, Minami-Ku, Hiroshima 734-8551, Japan  
 Phone:81-82-257-5227, FAX:81-82-257-5229 e-mail: wj8uc6@bma.biglobe.ne.jp

cine (DICOM) files is necessary. It is beyond the scope of this study to support all types of DICOM files, and we propose quasi GMFT instead. Quasi GMFT requires only a trigon mesh of the brain, and users can readily assess the essence of the GMFT technique.

We have included these functions in an executable standalone program and intend to release it as a freeware named `hns_meg`. It is compatible with Microsoft 32bit/64bit, Windows Vista, Mac OSX 10.6; the file names are `hns_meg.exe`, `hns_meg_x64.exe`, and `hns_meg_mac64.app`, respectively. The `hns_meg` has potential to shorten the analysis time of MEG recordings and to address the limitations of ECD analysis. The `hns_meg` has a graphical user interface, and this may be helpful to MEG users who want to apply new analytical methods and who are not, or do not have colleagues who are, expert programmers.

## METHODS

We wrote original codes in the computer programming language, MATLAB (MathWorks, Natick, Massachusetts, U.S.A.).

The tool has the following functions:

- 1) Loading Elekta-Neuromag's binary files, including raw data, measured with magnetoencephalography and/or electroencephalography with fewer than 64 electrodes.
- 2) Loading brain mesh files made by Elekta-Neuromag's unique segmentation software, SegLab.
- 3) Two types of band-pass filters: an elliptic filter and a least-squares linear-phase finite impulse response filter.
- 4) Customizing bipolar leads out of up to 64 EEG channels.
- 5) Convenient sensor selection to display targeted waveforms by clicking a bird's eye-view layout of sensors.
- 6) Isomagnetic contour map at an arbitrary time point. Referring to the contour maps of Elekta-Neuromag's software, Source Modelling<sup>7)</sup>, minimum norm estimations are employed. Magnetic fields at 304 virtual magnetometer coils located on the Dewar are calculated from currents of 208 nodes on a sphere with a 7 cm radius as well as Source Modelling.
- 7) Lists of maximum  $\partial B$  every 1 s throughout the measurements using only signals from planar gradiometers and not those from magnetometers. To be precise,  $\partial B = \sqrt{\partial B_0^2 + \partial B_\psi^2}$ , where  $\partial B_0$  is latitudinal  $\partial B$ , and  $\partial B_\psi$  is longitudinal  $\partial B$ .
- 8) Quasi GMFT on a two-dimensional sensor array or three-dimensional triangulated brain mesh. Two-dimensional quasi GMFT are drawn, based on Delaunay's triangulation function, built into MATLAB. In three-dimensional quasi GMFT, the sensors are moved in the normal direction of their planes until they meet the brain mesh. If

the sensor does not reach the mesh, it moves by 8 cm and then moves toward the center of the mesh. Signal strength at the mesh nodes is calculated according to the distance between the nodes and projected sensors, so that the strength at the mesh reflects that at the nearest sensor.

9) TFR based on MEM, a function built into MATLAB. Signals of paired orthogonal power spectra are root-squared every half-size of the sampling rates, with a step of one-quarter the size of the sampling rates. For example, if the sampling rate is 600 Hz, 300 points are processed with a 150-point step, where the frequency resolution is about 2 Hz.

10) TFR is shown three-dimensionally at the original sensor array position or at positions shrunk toward the individual brain mesh.

11) All code was written in MATLAB and C language, built with the MATLAB compiler 4.11, and packed with MATLAB Component Runtimes v711.

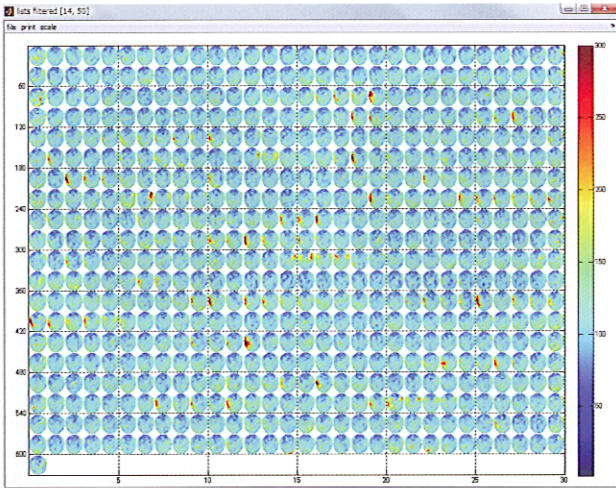
## ILLUSTRATIONS

In a 50-year-old female with drug-resistant epilepsy lasting 19 years, MRI disclosed atrophy of the left cerebral hemisphere. A conventional scalp EEG study disclosed spikes at F7 and T3. She consulted the Department of Neurosurgery, Hiroshima University Hospital, and underwent MEG for further evaluation for possible epilepsy surgery.

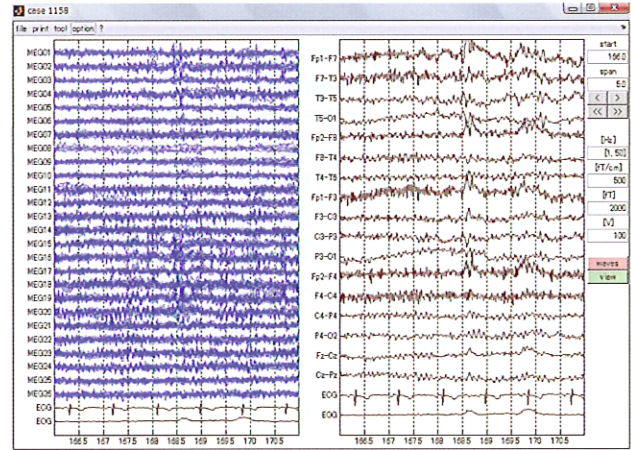
Figure 1 is a list of  $\partial B$  for 601 s. A 14–50 Hz band-pass filter was used. There are 601  $\partial B$  topographies, and each represents the maximum  $\partial B$  every 1 s. The top line indicates  $\partial B$  from 0 to 30 s, the second line indicates from 30 s to 60 s, and so on. Red areas within topographies indicate waveforms with high amplitudes, such as spikes or noise. In this case, red crescent spots were seen at 79 s, 108 s, 168 s, 182 s, and so on, in the left temporal areas, and large spikes were expected at these times and at the left temporal sensors. Thus, clinicians can narrow down time domains having spikes and shorten the analysis time.

Figure 2 shows the waveforms of all 204 gradiometer channels of MEG and all EEG channels from 166 to 171 s. Users can customize the bipolar lead pattern arbitrarily. The right panel is a user interface for selecting time domain, frequency domain, or amplitude height.

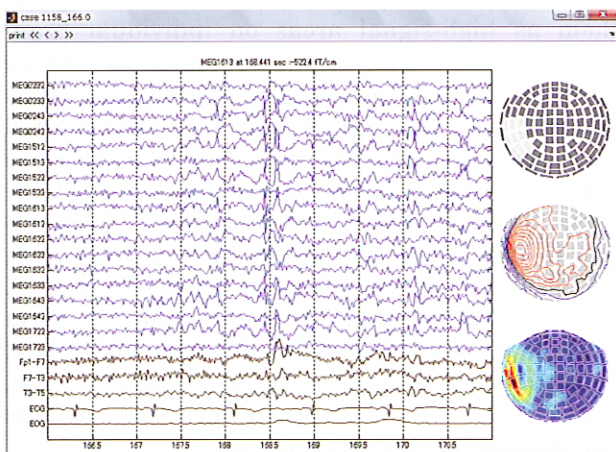
Figure 3 shows waveforms of selected MEG and EEG channels. Selected MEG sensors are highlighted in the sensor schematic in the upper right corner. Users can select channels by clicking the schematic. Both MEG and EEG show a spike peak at 168.441 s. An isomagnetic contour map and two-dimensional quasi GMFT at this time are shown in the middle and at the bottom of the right-hand panel, respectively. Contour lines are



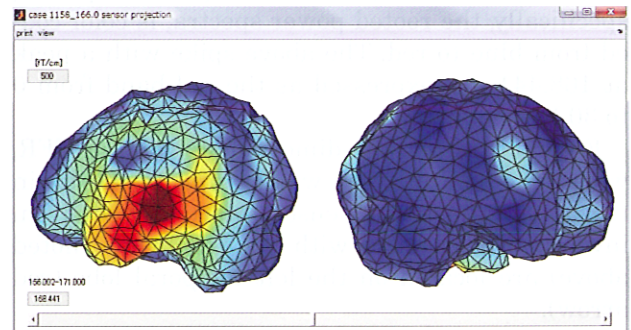
**Fig. 1.** A list of gradient magnetic fields ( $\partial B$ ) for 601 s. A 14–50 Hz band-pass filter was used. There are 601  $\partial B$  topographies and each topography represents a maximum  $\partial B$  every 1 s. The top line indicates  $\partial B$  from 0 to 30 s, the second line indicates from 30 to 60 s, and so on. Red areas within topographies indicate waveforms with high amplitudes, such as spikes or noise. In this case, red crescent spots are seen at 79 s, 108 s, 168 s, 182 s, and so on in the left temporal areas, and large spikes are expected at these times and at the left temporal sensors. Thus, clinicians can narrow down time domains having spikes and shorten the analysis time.



**Fig. 2.** Waveforms of all 204 gradiometer channels of magnetoencephalography (MEG) and 21 electroencephalography (EEG) channels, from 166 to 171 s. Users can customize the bipolar lead pattern arbitrarily. The right panel is a user interface for selecting time domain, frequency domain, or amplitude height.



**Fig. 3.** Waveforms of selected MEG and EEG channels. Selected MEG sensors are highlighted in the sensor schematic in the upper right corner. Users can select channels by clicking the schematic. Both MEG and EEG show a spike peak at 168.441 s. An isomagnetic contour map and two-dimensional quasi-gradient magnetic field topography (GMFT) at this time are shown on the right, in the middle and lower panels, respectively. Contour lines are drawn with 200 fT steps, and red and blue lines indicate efflux and influx, respectively.

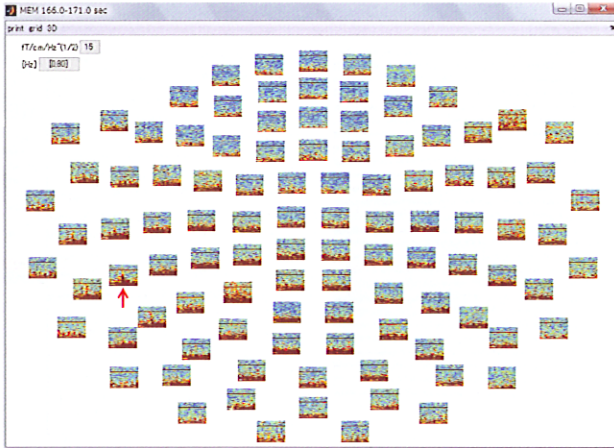


**Fig. 4.** Three-dimensional quasi GMFT at the same time point. The spike was interpreted as the red area in the patient's left temporal lobe. The user can watch the time evolution of the brain activities represented by the quasi GMFT by manipulating the lower toolbar.

drawn with 200 fT steps and red and blue lines indicate efflux and influx, respectively.

Figure 4 is three-dimensional quasi GMFT at the same time. The spike was interpreted as the red area in the patient's left temporal lobe. Users can watch the time evolution of the brain activities represented by the quasi GMFT by manipulating the lower toolbar.





**Fig. 5.** A bird's eye view of time-frequency representation (TFR) at the above time domain from 166 to 171 s, where the x-axis indicates time evolution, and the y-axis indicates frequency.

Strength of the magnitude spectra, namely, rooted power spectra, are color-coded from blue to red. The above spike with a peak at 168.441 s is expressed as the red band from 0 to 30 Hz (red arrow).

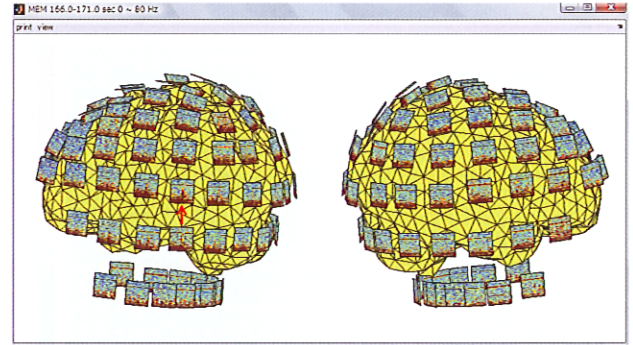
Figure 5 is a bird's eye view of TFR at the above time domain from 166 to 171 s, where the x-axis indicates time evolution, and the y-axis indicates frequency. The strength of the magnitude spectra, specifically, the rooted power spectra, is color-coded from blue to red. The above spike with a peak at 168.441 s is expressed as the red band from 0 to 30 Hz (red arrow).

Figure 6 is a three-dimensional view of TFR, where the sensor array was shrunk to the brain mesh and the lower sensors were moved 8 cm inwards. The sensors with the red bands (noted above) are located on the left temporal lobe (red arrow).

## DISCUSSION

Since 2000, MEGs have begun to be used in a few tens of hospitals in Japan; however, most clinicians have only used the default software that vendors supply. Many attractive signal analyses have been proposed in papers or at academic meetings. However, unfortunately, few sites have personnel with appropriate programming skills to try these new approaches. We believe that any such new proposed analysis must be verified at many institutes, and feedback from many reviewers is necessary in evaluating sophisticated new techniques to advance the standard level of analysis in MEG. Thus, we developed a program that includes some new tools, and we are prepared to release it as a stand-alone freeware, compatible with Microsoft Windows Vista or Mac OSX 10.6.

The list of  $\partial B$  is helpful in efficiently finding spikes. Of course, the list includes both real spikes



**Fig. 6.** A three-dimensional view of TFR, where the sensor array was shrunk to the brain mesh, and the lower sensors were moved 8 cm inward.

The sensors with the above red bands are located on the left temporal lobe (red arrow).

and noise as red spots, but it is unlikely that spikes with large amplitudes are false negatives. Current personal computers can provide results within a few minutes, including the procedure of transferring the files. We use this function to check whether measured MEG recordings include spiky activity and to decide whether we should continue the examination during routine MEG studies.

Quasi GMFT is based on the features of the planar gradiometer, which reflects underlying currents, i.e., brain electrical activity<sup>2</sup>). While ECDs interpret brain activities as electric moments localized at a few points, quasi GMFT interprets them as high-signal areas on individual brain meshes. To evaluate MEG recordings as voltage maps in electrocorticography<sup>1,9</sup>), this method is suitable. As with original GMFT, as we reported previously, this quasi GMFT does not reflect the activities of the cerebral base or deep brain structures. The appearance of this quasi GMFT is similar to that of the minimum current estimation (MCE), which is based on a minimum L1 norm<sup>6,11</sup>). However, the solution of the minimum L1 norm tends to be a sparse matrix, and even widespread epileptic discharges are interpreted as scattered, localized sources. Thus, we believe that MCE is not suitable for epilepsy analysis.

TFR is a tool for time-frequency analysis, and we named this function after the 4-D Toolbox released by Ole Jensen<sup>4</sup>). Whereas the 4-D Toolbox employs the Morlet wavelet, our tool uses MEM to squeeze the memory size of outputs and to prevent 'out of memory' errors. Our tool can display the TFR of each sensor, shrunk onto the individual brain mesh. This figure may enable straightforward understanding of the extent of the targeted frequency domain with regard to epileptic discharges, which can be quite cumbersome to evaluate by conventional ECD analysis.

The `hns_meg` is not intended to replace existing software packages provided by Elekta-Neuromag, but can be used together with those packages for further evaluation of neuromagnetic epileptic discharges.

Theoretically, this tool can be used for other types of neuromagnetometer without a planar gradiometer. Isomagnetic contour maps are drawn after calculation of the virtual magnetometer coils from the data of the planar gradiometer, and vice versa. Unfortunately, we do not currently have sufficient information on other types of neuromagnetometer, such as accurate sensor positions or file formats.

Finally, we note the disclaimer that this software must be used at the user's own risk.

## CONCLUSIONS

We developed a freeware, named `hns_meg`, for the analysis of neuromagnetic epileptic discharges, which can show the list of maximum  $\partial B$  every 1 s, as well as quasi GMFT and TFR.

## ACKNOWLEDGMENTS

We appreciate that Dr. Shigeki Kameyama, Nishi-Niigata Central Hospital, gave us the opportunity to test whether our tool could work at other Elekta-Neuromag sites.

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