Somatosensory Source Localization for the Magnetoencephalography (MEG) Inverse Problem in Patients with Brain Tumor

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***Abstract* — The source of the somatosensory evoked field (SEF), is one of the standard paradigm used for pre surgical mapping of brain tumor. The surgical management of the tumors requires a detailed mapping of cortical regions involved in sensory functions to avoid further deterioration of function. We investigated the early component of somatosensory evoked field (SEF) between 20 – 25 ms for the somatosensory response between normal and brain tumor patients and deflections in peak latency of N20M may be occurred due to present of tumor. The N20M somatosensory evoked field (SEF) corresponding electrical median nerve stimulation was measured using whole head 306 ELEKTA Neuromag® MEG system. The MEG was accurately localize the origin of intraneuronal electric currents that contribute to extra cranial magnetic fields by fitting to an equivalent current dipole model (ECD). In the present study, the equivalent current dipole model is used to determine the source location of somatosensory cortex (SI) displacement due to the tumor in the central sulcus. The ECD inverse problem method had shown that the N20M SEF for unaffected hemisphere and normal subjects were located in the primary somatosensory cortex (SI) and for the affected hemisphere, the ECD source had deflected in few millimeters far from S1 cortex. We have confirmed that, the enlarged of ECD strength also occurred due to the tumor and the difference of N20M in brain tumor either in AH or UH indicated the neural pathways to the response to N20M in normal subjects might be independent.**

Keywords- ***Magnetoencephalography(MEG), median nerve, equivalent current dipole(ECD),displacement,N20M, Somatosensory***

I. Introduction

Accurate brain mapping protocols are essential for localization of the central sulcus to ensure successful surgical excision of tumors involving the postcentral gyri. This is because when the tumor grows up it surrounds the eloquent area such as the somatosensory cortex as it is always a challenge for neurosurgeons in making the decision before the surgery. In brain tumor cases, when the tumor's growing displaces gyri and sulci[1], the knowledge about brain region's functional significance becomes crucial as well as the corresponding topology of fiber tracts. The previous studies have revealed that tumors or vascular malformations may distorts brain anatomical landmarks and making it impossible to identify and they suggested that functional landmarks depicting eloquent brain areas are valuable planning adjunct before brain tumor surgery [2, 3]. However the neuroimaging techniques for mapping the important of brain areas have made enormous advances. In advance to positron emission tomography (PET) and functional magnetic imaging (fMRI), Magnetoencephalography (MEG) proved to be more valuable neuroimaging tool for the localization of intracranial neuroelectrical sources[4-6]. MEG provides one modality for functional mapping with excellent temporal and good spatial accuracy. In contrast with MEG, EEG measured both oriented tangential and radial to the scalp but it generate noisy signals. To resolve the EEG ambiguity, MEG was employed since radially oriented currents that contribute very little to the measured magnetic fields. For the first step, in the every of source analysis approach, the forward problem need to be solved to determine the signal propagation which are involves in calculating the electrical potentials or magnetic fields generated by known current sources for a given head model. In this study, the forward MEG problem can be solved by analytically using spherical model and numerically using a boundary-element method (BEM). However, in the second step of signal processing, the inverse problem method applied to estimate the current sources inside the brain that best fit the measured data. In our work, we used the equivalent current dipole (ECD) that will be modeled to find the accurate location of the SEF in the brain tumor patients also to evaluate the relation of the ECD strength due to the tumor location which applied on the certain constraints to obtain a unique solution. In the dipole model approaches, each of the active brain regions being modeled with at least one-point like dipole with its position and orientation being fixed.. This approach is best suited for cases where it can be assumed that neuronal activity is localized into a small number of distinct of the brain[7].

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II. METHODS

A. Subjects

From the retrospective brain tumor patient's data available in the Laboratory for Magneto encephalography and Event Related Potential (Neurosciences), Hospital Universiti Sains Malaysia Kubang Kerian, Kelantan, Malaysia 5 patients (three females and two males; mean age 37 years, range 20- 50 years) with brain tumor near or in the somatosensory cortex were studied, denoted as P1-P5. The degree of malignancy and locus of the tumor differed among patients (see Table 1). Patients with tumor far from somatosensory cortex and patients with the age greater than 50 years old are excluded from this study. In addition,5 normal (four males and one female) retrospective subjects were included, denoted as N1- N5. Before entering the magnetic shielded room (MSR), every subject need to be screened and removed first to make sure that no implanted medical devices or metallic foreign bodies like braces, dental filling or any ferromagnetic component that can induce artifacts during data recording.

Table 1: Patient profiles

Patient	Malignancy	Locus	Age	Gender
P1	HGG	Parietal,L	20	F
P2	HGG	Parietal,R	44	M
P3	HGG	Parietal,L	20	F
P4	HGG	Parietal, L	50	M
P5	HGG	Parietal, R	50	F

HGG: High Grade Glioma; R:right; L: left, F: female; M: male

B. Recording Somatosensory Evoked Magnetic Fields

The magnetic fields were measured with a whole head 306 channels Neuromag® Vectorview System (Elekta Neuromag Oy, Helsinki, Finland) which is contained in a magnetic shielded room (MSR) constructed from layers of aluminum and μ-metal, an alloy of extremely high magnetic permeability that is designed to occlude extraneous electrical and magnetic fields. MEG operates with superconducting interference device (SQUID**)** immersed in cool liquid helium which is a very low noise detector of magnetic fields that converts the magnetic flux threading a pickup coil into voltage allowing detection of weak neuromagnetic signals. However, the Philips′ Achieva 3.0T X-series MRI anatomical images were acquired for MEG-MRI overlay data processing method. The somatosensory stimulation was performed electrically using electrodes placed on the skin over the course of the median nerve at the wrist. The sensory paradigm was delivered using internally driven Neuromag software (Elekta Neuromag Oy). Constant current pulses with duration of 0.2 ms were used. The average stimulation rate was 1 Hz. The amount of current was determined for each patient individually by one MEG technician who gradually increased the current intensity while another technician monitored the elicited response until a small thumb twitch was observed. The electrical stimulus was delivered alternately from the left and right until both thumbs twitch each other. The mean stimulus intensity was 6.5 mA (range, 4.0 – 9.0 mA) and a minimum of 200 epochs were recorded for all stimulations. During MEG recordings, patients were asked to remain motionless and avoid from blinking or eye movements for 5 to 10 minutes.The MEG, band-pass filtered between 0.01 and 200Hz and the signals were sampled at 1000Hz.

C. Ethical Consideration

The study was approved by the Medical Ethics Committee of the School of Medical Sciences, Universiti Sains Malaysia Kubang Kerian before acquiring the retrospective data. The Ethical Approval Number was JEPeM-USM Code: USMKK/PPP/JEPeM [275.3 (7)]

III. DATA ANALYSIS

A. Head Model

For an accurate source localization of the SEF source, one need to consider is an appropriate head and source model. To localize the sources of the magnetic fields it is crucial to develop head models that incorporate the correct geometry and distribution of the electrical conductivity in the actual heads. As the primary current (major) and volume current (least) is responsible for the recorded magnetic field, a priori knowledge of the conductivity characteristic is indispensable for generating a solution to the forward problem[8]. Since this study addresses the source of the MEG in the somatosensory cortex which is located in the upper part of the brain, we will consider to use the spherical models as analytical model and BEM models as numerical model for accurately describe the individual head geometry with MRI anatomical information. The spherical model used from Elekta Neuromag Software Package and the BME model is used from the Statistical Parametric Mapping (SPM8) toolbox[9].

B. Source Analysis

The aim of the neuromagnetic inverse problem is to estimate the source current density underlying the MEG signal measured outside the head. One of the inverse problem approach is applied the discrete source analysis; Equivalent Current Dipole (ECD). The ECD is the most appropriate when we assume that measured field at a discrete time point is generated by a single source that had been used in localizations of the eloquent brain area after evoked stimulus and interictal spikes[8]. In this study, the ECD was calculated using the average waveform obtained by 200 epochs. The general equation for the computation of current dipole model has shown in the following equation[10].

$$\overrightarrow{Br^{\rightarrow}} = \frac{\mu_{\circ}}{4\pi} \frac{\overrightarrow{Q} \times (r^{\rightarrow} - r_{\circ}^{\rightarrow})}{\left|r^{\rightarrow} - r_{\circ}^{\rightarrow}\right|^{3}}$$

$\overrightarrow{Br^{\rightarrow}}$ = the field at a point $r^{\rightarrow}$ in space, $r_{\circ}^{\rightarrow}$ = vector from the center of the sphere to the dipole, then $Q^{\rightarrow}$ = the current dipole moment, and the permeability of the free space was expressed as $\mu_{\circ}$. The ECD source analysis was based on the single ECD model in a spherical model fitted to the digitized head shape of each subject. The

location of the (X, Y, Z positions), its orientation and amplitude of the best-fitting single ECD were estimated for each SEF N20m time point.

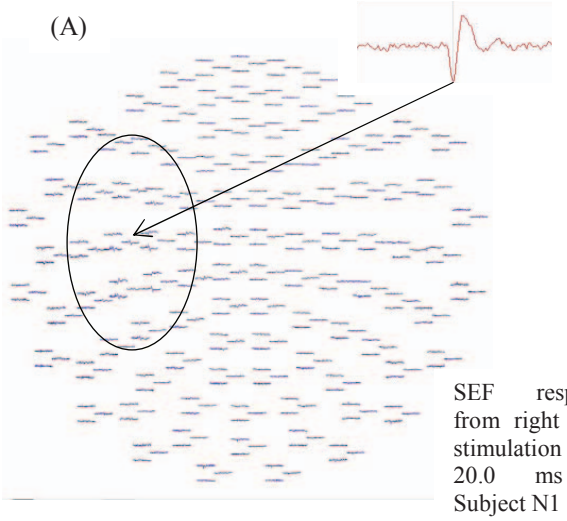
IV. Result

In this section we represented results observed from 5 brain tumor patients and 5 normal subjects. The waveforms of the somatosensory evoked field were measured from 306 channels ELEKTA Neuromag, MEG system with stimulated both left and right hand alternately to find the exact median nerve respectively. For all 5 normal subjects, the dipole locations were based on the main peak which occurred between 20-23ms after the stimulus onset for the thumb. Figure 3 shows the SEFs to the right and left median nerve stimulation for normal subjects, N1. Each of the peaks showed a magnetic field distribution with a tangential ECD at the primary somatosensory cortex. In the anatomic MRIs, the ECD sources were localized within the area of postcentral sulcus. Figure 3 visualizes the source localizations with respect to the individual anatomy of the Normal Subject 1, N1. The source localization of the normal subjects was summarized in Table 1.

TABLE 1: PEAK LATENCIES (MS),SEF SOURCE LOCALIZATION IN N20M SELECTED IN EACH SUBJECT AND ECD STRENGTH OF NORMAL SUBJECTS

Subject ID	Peak Latencies (ms)		N20M SEF Localization		ECD Strength, Q (nAm)	
	LH (ms)	RH (ms)	Right Hand	Left Hand	RH	LH
N1	20 .0	20.0	PCG	PCG	13.1	10.1
N2	23.0	22.9	PCG	PCG	13.1	11.0
N3	22.0	22.0	PCG	PCG	6.7	7.5
N4	22.9	22.9	PCG	PCG	10.3	10.5
N5	23.0	23.0	PCG	PCG	8.0	8.6

PCG: Postcentral Gyrus; RH: Right Hemispehere; LH: Left Hemisphere; ECD strength; nAm(nanoamperemeter); LH: Left Hand Stimulation;RH: Right Hand Stimulation



SEF response from right hand stimulation at 20.0 ms in Subject N1

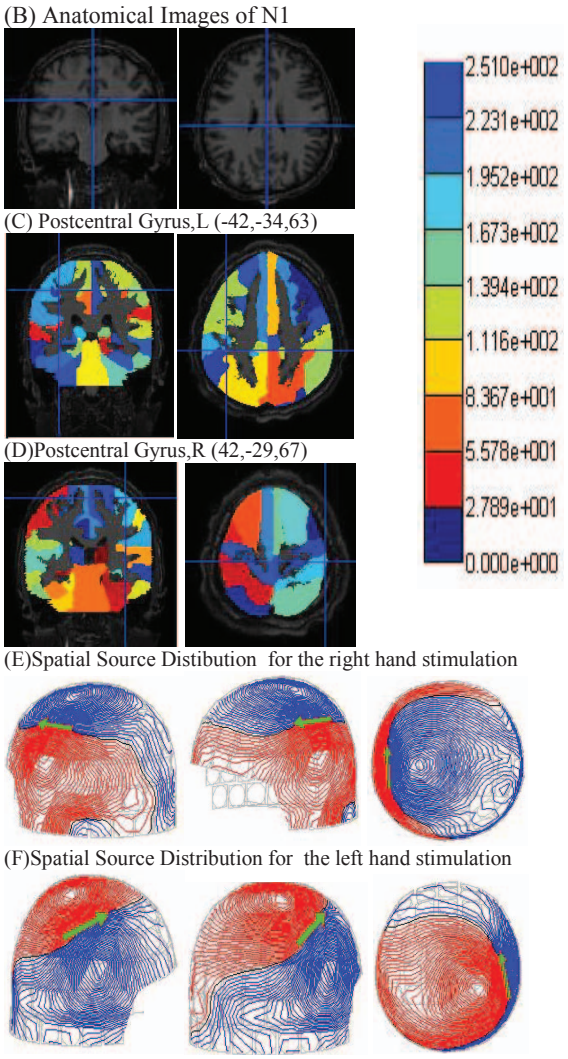


Figure 3: (A) Full scalp distribution from left hand response of somatosensory recorded from 306 channels ELEKTA Neuromag, MEG; with the response of N20M,SEF in Subject N1 at 20.0ms (B)T1 MRI images in coronal and axial view (C) Source localization of SEF localized on the PCG,L (D) Source Localization of SEF on the PCG,R. The cross-hair intersection denotes the voxel of maximum activation overlay with IBASPM 71 region atlas. ;(E)Spatial source distribution of a time varying dipole model with the strength of ECD was 13.1nAm for RH and (F) 10.1 nAm for LH.

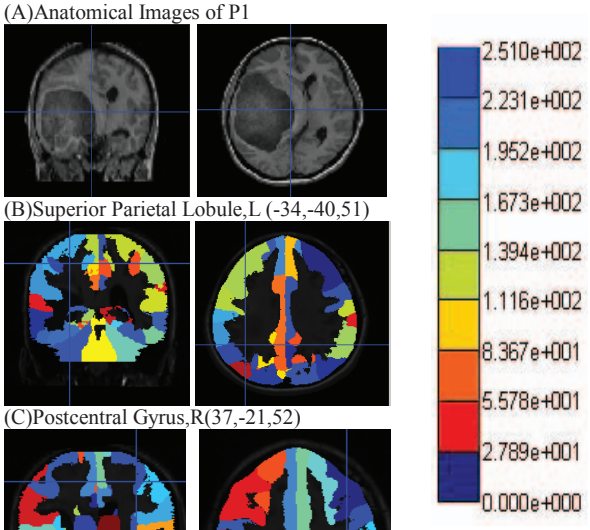
Table 2 summarized the reliable somatosensory evoked field (SEF) for the N20M component of 5 brain tumor patients. The source localization and may be differ from brain tumor patients due to tumor location respectively. However, the corresponding of SEF latency (ms) , ECD strength (Q) of affected (AH) and unaffected (UH) hemispheres, nAm (nanoamperemeter) is also listed in Table 2. All patients had a first component of SEF with peak latency between 23 – 25 ms. All patients had localized the source in few millimeter far from somatosensory cortex (shown in Figure 4). We would summarize that there are enlarged in ECD strength in the AH compared with UH in brain tumor patients. There is relationship was found between locus of tumor and the somatosensory source localization.

TABLE 2: SOMATOSENSORY EVOKED FIELD CHARACTERISTIC

Patient ID	Locus of Tumor	Peak Latencies (ms)		ECD Strength, Q (nAm)		N20M SEF Localization	
		AH	UH	AH	UH	AH	UH
P1	Parietal , L	23.7	21.5	43.7	23.0	SPL, L	PCG , R
P2	Parietal , R	23.4	22.0	20.7	12.8	IFG, R	PCG , L
P3	Parietal , L	22.5	22.0	34.4	23.4	AG, R	PCG , L
P4	Parietal , L	25.1	23.6	31.3	20.6	SPL, L	PCG ,R
P5	Parietal , R	24.2	23.1	19.3	8.7	SPL, R	PCG , R

AH: affected hemisphere; UH: unaffected hemisphere; Q, equivalent current dipole strength; nanoamperemeter; R: right, L: left, SP: Superior Parietal Lobule ,AG: Angular Gyrus,PCG:Postcentral Gyrus, IFG:Inferior Frontal Gyrus.

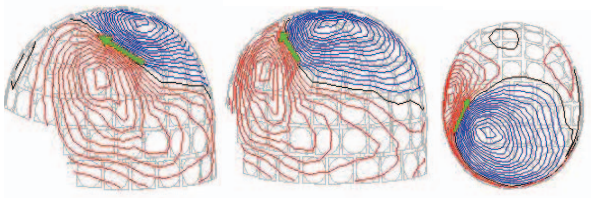
(A)Anatomical Images of P1



(B)Superior Parietal Lobule,L (-34,-40,51)

(C)Postcentral Gyrus,R(37,-21,52)

(D)Spatial Source Distibution for the right hand stimulation



(E)Spatial Source Distribution for the left hand stimulation

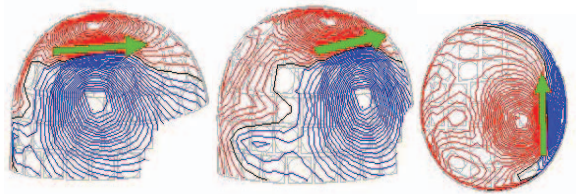


Figure 3: Mapping of the N20M somatosensory evoked field for P1 with tumor in the left parietal hemisphere as shown in anatomical images (A)T1 MRI images in coronal and axial view.(B) Source localizationof SEF on the SPL,L (C)Source localization of SEF on the PCG,R. The cross-hair intersection denotes the voxel of maximum activation overlay with IBASPM 71 region atlas (D) The source had localized on SPL,L . (E) Spatial source distribution of a time varying dipole model with the strength of ECD was 43.7 nAm for RH and (F) 23.0 nAm for LH.

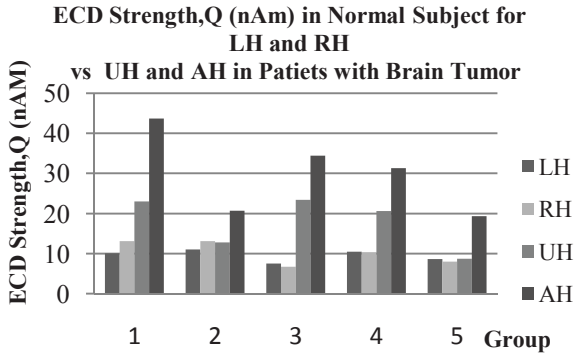


Figure 4: show the equivalent current dipole strength in patient with a brain tumor as compared with affected hemisphere (AH) and unaffected hemisphere (UH) and right and left hemisphere for the normal subjects.

V. Discussion

In the present study, we have localized the cortical somatosensory network to median nerve stimulation in patients with tumor near or in the somatosensory cortex and compared with the normal group as a control group in this study. We found that, there are increases in dipole strength for the N20M component in the affected hemisphere of patients with tumor in the somatosensory cortex (shown in Figure 4). This is believed that this situation occurs due to the tumor[11-13]. Tumor near or in the somatosensory cortex may attack the normal sensory brain tissue and cause damage to the brain. Tumor surgery is an important treatment of brain tumors but patients are often at the risk of neurological deficits owing to aggressive resection which easily causes damage to somatosensory cortex, and of shorter survival owing to partial tumor resection and [14-16] and [17] used SEF for neurosurgery. SEF used before surgery to localize the central sulcus since the space in the brain was occupied with tumors that frequently shifted the central sulcus. In recent studies, MEG has been exclusively applied to investigate the changes in cortical response to sensory stimulation in patients with brain lesions. It is believed that different lesions affect the somatosensory network in different ways. Therefore the knowledge about the structural and functional changes of the network due to presence of tumors has potential clinical significance for presurgical planning[13]. However,[18] also found that MEG had demonstrated the tumor lesion expected sensory motor cortex location in various degrees of displacement and deformations for the 36 patients. The authors also claimed that through evoked magnetic fields accurate localization of functional cortex is obtained and the relationship of brain tumor and important function cortex can be displayed which provides guidelines for brain surgery. Due to tumors they also found that 12 patients who had neurological deficits or lack of ability to cooperate could not localize the central sulcus with MEG. The reason is that the tumor which had constricted the functional cortex or damaged of the white matter tissue which had a negative impact on the success of the examination. Furthermore for the success of presurgical planning magnetic source imaging approach is important to provide localization information of functional cortex and discovered the relationship

between functional cortex and brain tumor and provides reference for the neurosurgeon to evaluate the risk of tumor resection. In addition, increasing of the equivalent current dipole strength in patient with tumor as compared with UH and normal subjects, it was shown that the dipole strength can be considered as a valuable quantitative index of the cortical response to somatosensory stimuli in patients with tumor or even in different neurological diseases. Some authors[11, 19] believed that the study of dipole strength is about the study of excitatory and inhibitory influences of cerebral lesions.It has been suggested that increased dipole strength in patients with tumors close to the central sulcus is a result of hyperactive and more synchronized neurons in surrounding tissue resulting from altered concentrations of inhibitory and excitatory neurotransmitters[20]. As part other valuable findings, our present findings can be used for further studies describing the somatosensory network changes in the presence of tumors near the somatosensory cortex in combination with clinical findings.

VI. CONCLUSION

In conclusion, we confirmed that displacement may occurs for the source location, N20m SEF peak latency in P1-P5 with enlarged of ECD strength of the N20m SEF in patients with brain tumor when we compare the results with affected and unaffected area of the brain. From the literature our present results can be used for further studies elucidating the N20m somatosensory network changes and displacement in the presence of tumors in combination with clinical findings. However for the future work the differential effects of source location and types of lesion on cerebral displacement are needed to elucidate the mechanism involved in cortical displacement.

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