Real-time delineation of the central sulcus with the spatial profile of SSEPs captured with high-density ECoG grid*

Priscella Asman, Sujit Prabhu, Sudhakar Tummala, and Nuri F. Ince*, *Senior Member, IEEE*

Abstract— **Cortical mapping is widely employed to define the sensorimotor area and delineate the central sulcus (CS) during awake craniotomies. The approach involves the gold standard somatosensory evoked potentials (SSEPs) recorded with electrocorticogram (ECoG) strip electrodes. However, the evoked response can be misconstrued from the manual peak interpretation due to the poor spatial resolution of the strip electrode or when the electrode does not precisely cover the desired cortical area. This can lead to unintentional damage to the eloquent cortex. We present a soft real-time computer based visualization system that uses recorded SSEPs with a subdural grid to aid in cortical mapping. The neural data during electrical stimulation of the median nerve at 0.6Hz are picked up with a bio-amplifier at 2.4kHz. The stimulation artifact recorded from the bipolar electromyogram (EMG) is used as the stimulation onset. The ECoG data are assessed online with MATLAB Simulink to process and visualize the SSEPs waveform. The visualization system is programmed to display the SSEPs peak activation as a heat map on a 2D grid and projected onto a screen, showcasing the nature of the cortical activities over the contact surface area. Since the grid occupies a large cortical surface, the heatmap is able to delineate the central sulcus. The map can be viewed at any time point along the SSEP trace without the need for peak interpretation. With the goal to provide additional information during cortical mapping and facilitate interpretation of ECoG grid data, we believe that this visualization system will aid in rapid definition of the sensorimotor area during surgical planning.**

Clinical Relevance—**This real-time visualization system can be used to delineate the central sulcus in a short time during awake craniotomies.**

I. Introduction

Intraoperative cortical mapping has long been used to spare the eloquent cortex during resection surgeries [1]. One of the techniques used to identify the sensorimotor cortex involves the gold standard median nerve somatosensory evoked potential phase reversal technique (MSSEP-PRT)[2]. The approach comprises the phase reversal termed N20/P20 seen between two adjacent electrodes, 20ms after stimulation onset recorded generally with strip electrodes (such as the 1 × 8 and 1 × 4 array with 5–10 mm electrode spacing) [2]. However, the evoked response can become ambiguous and challenging to interpret either due to the poor spatial resolution of the strip electrode, the anatomical variability of the hand area position, or the complexity of the exposed brain during surgery [3]. When there is unsolvable doubt, the strip electrode is relocated, or direct cortical stimulation (DCS) is employed [4]. Although DCS ensures a thorough investigation of the cortical function, it prolongs the surgical planning and poses an increased risk for induced pathological brain activity such as after-discharges or seizures [5].

Other visualization techniques have been employed to aid the neurosurgeons during surgical planning to prevent increasing neurological deficits from extended resections. One of which is the functional neuronavigation which displays the position of the eloquent areas of the brain in the operative field. Another is intraoperative magnetic resonance imaging (iMRI) which assists in evaluating the extent of resection. However, neuronavigation approach is time-consuming and inevitably affected by brain drift [6]. Whilst the intraoperative MRI substentially lengthens the operation time [7]. Therefore, tumor boundary identification is not enough; accurate brain mapping is highly recommended. Passive cortical mapping with ECoG activities is shown to provide information on the cortical activations in the areas considered for preservation [8]. Studies have shown that passive functional mapping with ECoG signals in the broadband gamma range can safely and rapidly localize the eloquent cortex in only a few minutes during repeated hand movements [9]. However, this approach relies heavily on patient participation and cooperation.

We present a triggered visualization system that delineates the sensorimotor areas based on SSEP responses using a high-density ECoG grid without the need for patient involvement. The system is designed in Simulink/MATLAB (MathWorks, Inc. USA) to assess the distinct waveforms of the ECoG SSEP trace at any desired time point and project its distribution over a 2D grid. By visualizing the cortical SSEPs response as a heat map in 2D plane, we were able to delineate the CS vividly with a high spatial resolution. We anticipate that this approach will provide objective feedback to the neurosurgeon in a short time and in real-time for surgical planning. We used the visualization system in three patients' awake craniotomies. We compared the heat map with the OR images and sensorimotor delineation by the neurosurgeons. Below, we present a schematic diagram and discuss the application of the system.

II. Materials and Methods

A. The behavioral and data collection

Three patients (P1-3) with an average age of 47.5±2.1 years old with brain tumors adjacent to the peri Rolandic area consented to participate in this study. The study was approved by the Institutional Review Boards (IRB) of the University of

* Research supported by the National Science Foundation (Grant 2124705).

Priscella Asman and Nuri F. Ince are with the Clinical Neural Engineering Lab, Biomedical Engineering Department, University of Houston, Houston, TX USA. (e-mail:peasman@uh.edu, nfince@uh.edu).

Sujit Prabhu and Sudhakar Tummala are with the Department of Neurosurgery, University of Texas MD Anderson Cancer Center, ,Houston, TX, USA.

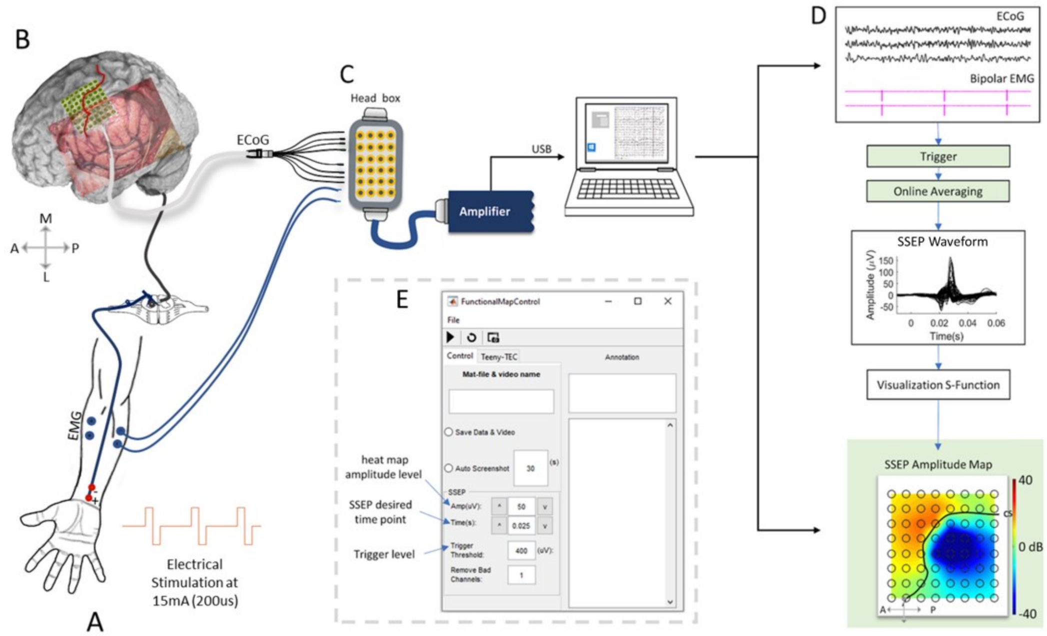

Figure. 1: Pipeline of real-time visualization system: (A)-The electrical stimulus pathway from the periphery. The electrical stimulation is applied to the median nerve at 0.6 Hz and recorded the EMG from the flexor and extensor muscles. (B)The 3D cortical rendering from the preoperative MRI shows the electrode coregistration on the brain. The location of the CS is shown with a red line. (P) Posterior, (A) anterior, (M) medial, (L) lateral. The pink area is the image of the craniotomy. (C) The recording system consists of the bio-amplifier and headbox receiving the touch-proof ends of the electrodes. The amplifier is connected to the computer via USB. (D) Schematic of the visualization system for SSEP temporal amplitude map. The CS is shown as the black line of the 2D grid. (E) The Simulink GUI of the controller that sets and adjusts the parameters for visualization.

Texas MD Anderson Cancer Center and the University of Houston. From P1, we recorded the neural data with a 64-channel high-density grid with 5 mm spacing and 2.3 mm contact exposure (Ad-Tech, Michigan, MI), Fig. 1B. From P2 and P3, we recorded with a 25-53-channel hybrid grid (CorTec GmbH, Freiburg Germany) with 10 mm spacing and 1–2.7 mm contact exposure. A pre-op thin slice MRI scan of the patient with an average repetition time of 6.8s, echo time of 101.6ms, slice thickness of 1mm with 262,144 pixels was used to create a 3D cortical rendering of the brain in MATLAB (MathWorks, Natick, MA, USA) using [9]. Based on the craniotomy images with electrode placements, we co-registered the electrodes on the 3D cortical mesh and iteratively interpolated contacts not visually exposed from the neighboring contacts offline using an in-house developed electrode registration software [10] as shown in Fig. 1B. The CS and sensorimotor borders were defined on the 3D rendering by the neurosurgeon, blinded to electrophysiology. We recorded a bipolar surface EMG from the patient's forearm, Fig. 1A. We applied electrical stimulations of 0.6 Hz frequency, 200 µs pulse width, and a current intensity up to 15 mA to the patient's median nerve, Fig. 1A The stimulation onset was captured as a spike artifact from the EMG and was used as the stimulation trigger onset in Fig. 1D(top).

B. Hardware Interface Module

We used a multichannel bio amplifier (gHIamp: 256 channels, g.tec medical engineering GmbH, Graz Austria) at a sampling frequency of 2.4 kHz with a 24bit A/D resolution as shown in Fig. 1C. A 2 × 4 clinical grid (10 mm spacing), flipped, and placed under the dura, was used as the reference and ground. We used a clinical two or four-channel EMG/EP Measuring System (Neuropack S1 MEB-9400) to provide the electrical stimulations to the median nerve.

C. Simulink Online Processing Module

The ECoG data were recorded and processed online in Simulink/MATLAB (MathWorks, Inc. USA). For the visualization of the raw ECoG trace and generation of stimulation onset aligned data, g.Hisys Simulink Highspeed Library (v3.16.01, gTec, Graz, Austria) was used, Fig. 2A. In particular, Simulink is a graphical programming environment comprising a rich set of signal processing and visualization libraries for modeling, simulating, and analyzing dynamic systems. The raw neural data was streamed through USB into the Simulink environment (gHIamp driver block of gHIsys library Fig.1 C) and visualized dynamically. Additionally, high-speed Simulink online library blocks, 'Trigger' and 'Online Averaging' was applied to compute the overlap plot of the average SSEPs trace online, Fig 1D (middle). The incoming ECoG data is high pass filtered at a cut-off frequency of 30 Hz as recommended by the ACNS (2015)[11] using 2nd order Butterworth filter. The Trigger block receives the incoming ECoG data and trigger onset from the EMG channel. The controller graphic user interface (GUI), Fig. 1E, allows us to determine the level of the trigger. There it creates an epoch of the data with a 50ms time window and then transmits the epoch to the Online Averaging block. The Online Averaging block receives and stacks the epoch data and applies Steiner's algebraic law to continuously calculate the average SSEPs (g.tec Simulink Highspeed Library user manual v3.16.01), thus creating the SSEPs waveform, Fig. 1D (middle). A MATLAB system function (S-function) was programmed to pick up the SSEPs as it updates from the online averaging. The S-function is a computer language written in MATLAB that enables the interaction with the Simulink engine. In the S-function, at a particular time point along the SSEP trace, the peaks of the SSEP are projected onto a 2D grid as a heat map,

Fig. 1D(bottom). The controller GUI allows input commands to change the time point along the SSEPs at which to view the heat map and the amplitude level of the map.

III. Results

SSEPs were recorded in the OR during the awake craniotomy of three male patients (P1, P2 and P3). About 100±20 electrical stimulations were delivered to the median nerve for the SSEP waveform to be observed. Using the real-time visualization system, we generated the 2D heat map using the MATLAB Simulink from the recorded data. We compared the results with the OR image and electrode co-registered 3D rendering of the brain. Fig. 2 shows the instance of the recorded SSEP of P2. The controller GUI is used to set the time point where the most negative peak is noted (N20). In Fig. 2A, the Simulink model generates the SSEP waveform (Fig. 2B) from the recorded data(Fig. 2C) and computes the heat map shown in Fig. 2D. The red patches showed the P20, and the blue patches showed the N20. Fig. 2C shows the stimulation spikes (bottom) synchronized with the raw ECoG data (top). The raw data alone was not enough to assess the ECoG activities. With the visualization system, the 2D heat map at the N20/P20 in Figure 2D showed a clear delineation of the CS, which correlated with the 3D rendering and OR image in fig 2E. Using the color-coding of the heat map to pick up the anterior and posterior channels at N20, we quantified the separation accuracy by calculating the area under the receiver operative charismatics curve (AUC). There we noted a consistently high accuracy of separation (mean ± SD: 99.7±0.25) in each patient, Fig 2F. We observed the SSEPs amplitude heat map for each patient at different time points along the SSEP trace in Fig. 3. In Fig. 3A, the time update is shown as the brown bar over the SSEP waveform. The heat map also showed the temporal cortical activities of the SSEPs in Fig. 3B as the time changed across the SSEP trace. The time update of the heat map in each patient showed the dipole propagation of the SSEPs from anterior to posterior regions

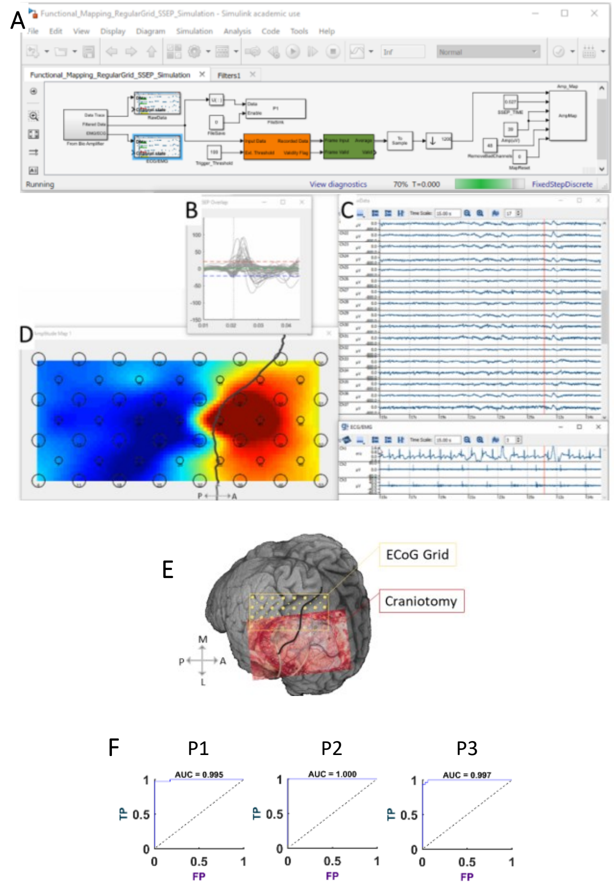

Figure. 2: A screenshot of the running instance of the Simulink real-time system that collects ECoG, ECG, and EMG data simultaneously. (A) The Simulink model was used to create the heatmap. (B) The SSEP waveform shows the nature of the phase reversal. (C) The raw map shows the nature of the ECoG activities, ECG, and EMG in real-time (D) The 2D heat map shows the spatial activities of the SSEP and CS delineation at the N20 time point. (E) The 3D rendering was used to compare the orientation of the SSEPs. (F) The ROC curves for each patient at N20.

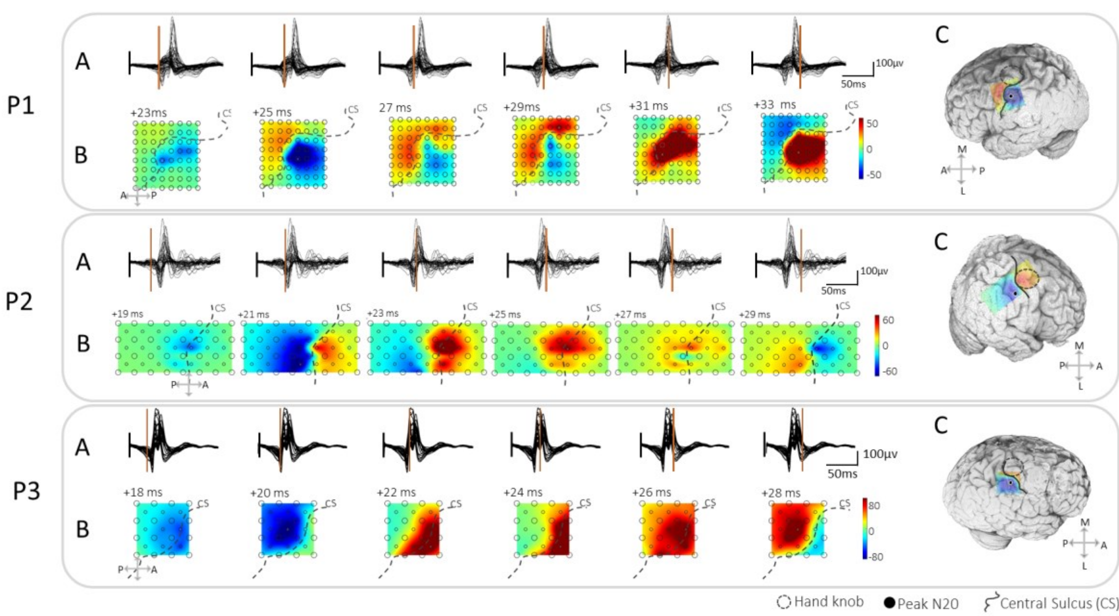

Figure. 3: SSEPs spatial heat map at multiple time points: (A) The temporal propagation of the SSEPs is shown with the brown bar unique to each patient. (B) Updated heat map showing the cortical activity at each time point observed from the brown bar in (A). (C) The cortical orientation of the SSEP on the 3D rendering of the brain where the maximum (peak) N20 is shown with the black dot about the hand knob (dotted circle).

[12]. We noted the peak activities at the N20/P20 time point showed a lateral orientation to the hand knob in each patient, Fig. 3C.

IV. Discussion

In this study, we present the use of a visualization system to assess SSEPs. The system was designed in MATLAB Simulink. MATLAB Simulink is a simple, user-friendly software tool used to develop, simulate, analyze, and graphically study any system. The library allows us to drag and drop blocks to represent any system instead of writing tedious code from scratch. We used g.tec library blocks (g.tec medical engineering GmbH, Graz Austria) and Simulink blocks to develop our visualization system shown in Fig. 1 and Fig 2A. There, we captured the ECoG data in real-time and processed them online. We recorded ECoG data from three patients' awake craniotomies. With the visualization system, we recorded SSEPs. SSEPs are generated from the bombardments of the cerebral impulse responses to the electrical stimulation at the median nerve [3]. These responses create the complex waveform whose peaks represent the incoming afferent volley[2]. Cortical distribution of the SSEPs was first demonstrated by [13] who showed the temporal propagation of the SSEPs from 18ms to 30ms as a heatmap on a 2D grid, based on his model of electrogenesis. This approach of 2D visualization of the SSEP was also employed by [14] who showed that the N20 was distributed diffusely around the primary hand sensorimotor area. We provided cortical distribution of the SSEPs in real-time using the visualization system. The system generates and updates the waveform as the number of electrical stimulations given increases, which becomes more apparent and reveals a distinct negative deflection, N20, at the 20ms time point. At this point, the system showcases the SSEPs peak activities on the 2D grid as a heat map.

Neurosurgeons have also used intraoperative navigation and intraoperative MRI to define the sensorimotor area in the OR. While intraoperative navigation presents real-time intuitive tumor detection, it is time-consuming and inevitably affected by brain drift [7]. iMRI may be good at detecting tumor boundaries and avoiding brain shifts. However, it substantially lengthens operation time [7]. With ECoG SSEPs, the neurosurgeon relies on the phase reversal of the SSEPs to locate the somatosensory and motor area on the cortical surface using electrode strips. However, the strip electrodes have poor spatial resolution and usually require multiple electrode placements or relocation [3]. This study used a high-density grid that occupied a larger surface area with high spatial resolution. With a single placement of the ECoG grid, we can identify the different parts of the craniotomy with the animated heat map to target the active areas with ease and use the spatial orientation to assess the anterior and posterior regions and delineate the CS. Based on the color contrast of the map, we saw a lateral direction of the peak N20 to the hand knob [12], and a clear definition of the sensorimotor area. We believe that our proposed approach of an unambiguous delineation of the CS with the heat map can be easily executed intraoperatively and in a short time using the visualization system.

Conclusion

This real-time visualization system can provide objective feedback to the neurosurgeon during sensorimotor delineation. The system shows the SSEPs amplitude alterations over the cortical surface as a heat map which clearly delineates the CS. We believe the clinical application of this system will improve the cortical mapping in awake craniotomies.

Acknowledgment

We are indebted to the three patients, the neurological team of MD Anderson Cancer Center and Dr. Jeremy Schultz, who made this work possible.

References

[1] DW. Gross, I. Merlet, W. Boling, J. Gotman. “Relationships between the epileptic focus and hand area in central epilepsy: combining dipole models and anatomical landmarks”. Journal of neurosurgery. 2000 May 1;92(5):785-92.

[2] JP. Lavrador, I. Gioti, S. Hoppe, J. Jung, S. Patel. “Altered motor excitability in patients with diffuse gliomas involving motor eloquent areas: the impact of tumor grading”. Neurosurgery. 2021 Jan;88(1):183-92.

[3] FR. Jahangiri, K. Pautler, K. Watters, SS. Anjum, GL. Bennett. “Mapping of the somatosensory cortex”. Cureus. 2020 Mar;12(3).

[4] AM. Taplin, P. Brunner, D. Hermes. JC. Dalfino, MA. Adamo, AL. Ritaccio, G. “Schalk. Intraoperative mapping of expressive language cortex using passive real-time electrocorticography”. Epilepsy & behavior case reports. 2016 Jan 1;5:46-51.

[5] JA. Corley, P. Nazari, VJ. Rossi, NC. Kim, LF. Fogg, TJ. Hoeppner, TR. Stoub, RW. Byrne. “Cortical stimulation parameters for functional mapping”. Seizure. 2017 Feb 1;45:36-41.

[6] DA. Orringer, DR. Vago, AJ. Golby. “Clinical applications and future directions of functional MRI”. In Seminars in neurology. 2012 Sep (Vol. 32, No. 04, pp. 466-475). Thieme Medical Publishers.

[7] H. You, H. Qiao.” Intraoperative Neuromonitoring During Resection of Gliomas Involving Eloquent Areas”. Frontiers in Neurology. 2021 Jun 23;12:952.

[8] KJ. Miller, P. Shenoy, JW. Miller, RP. Rao, JG. Ojemann. “Real-time functional brain mapping using electrocorticography”. Neuroimage. 2007 Aug 15;37(2):504-7.

[9] J. Ashburner, G. Barnes, CC. Chen, J. Daunizeau , G. Flandin, K/ Friston, S. Kiebel, J. Kilner, V. Litvak, R. Moran, W. Penny. “SPM12 manual”. Wellcome Trust Centre for Neuroimaging, London, UK. 2014 Jun 26;2464.

[10] T. Jiang, H. Siddiqui, S. Ray, P. Asman, M .Ozturk, NF. Ince. “A portable platform to collect and review behavioral data simultaneously with neurophysiological signals”. In2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2017 Jul 11 (pp. 1784-1787). IEEE.

[11] American Clinical Neurophysiology Society 2015 Guideline 11B: recommended standards for intraoperative monitoring of somatosensory evoked potentials. 2009 (available at:ACNS.org)

[12] P. Asman, S. Prabhu, D. Bastos, S. Tummala, S. Bhavsar, TM. McHugh, NF. Ince. “Unsupervised machine learning can delineate central sulcus by using the spatiotemporal characteristic of somatosensory evoked potentials.” Journal of Neural Engineering. 2021 Apr 29;18(4):046038.

[13] TR. Allison, GR. McCarthy, CC. Wood, TM. Darcey, DD. Spencer, PD. Williamson. “Human cortical potentials evoked by stimulation of the median nerve. II. Cytoarchitectonic areas generating short-latency activity.” Journal of neurophysiology. 1989 Sep 1 ,62(3),pp.694-710.

[14] Y. Maegaki, I. Najm, K. Terada, HH. Morris, WE. Bingaman, N. Kohaya, A. Takenobu, Y. Kadonaga, HO. Lüders. “Somatosensory evoked high-frequency oscillations recorded directly from the human cerebral cortex”. Clinical neurophysiology. 2000 Nov 1;111(11):1916-26.