

## Case Report

## Passive real-time identification of speech and motor cortex during an awake craniotomy

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## ABSTRACT

Precise localization of eloquent cortex is a clinical necessity prior to surgical resections adjacent to speech or motor cortex. In the intraoperative setting, this traditionally requires inducing temporary lesions by direct electrocortical stimulation (DECS). In an attempt to increase efficiency and potentially reduce the amount of necessary stimulation, we used a passive mapping procedure in the setting of an awake craniotomy for tumor in two patients resection. We recorded electrocorticographic (ECoG) signals from exposed cortex while patients performed simple cue-directed motor and speech tasks. SIGFRIED, a procedure for real-time event detection, was used to identify areas of cortical activation by detecting task-related modulations in the ECoG high gamma band. SIGFRIED's real-time output quickly localized motor and speech areas of cortex similar to those identified by DECS. In conclusion, real-time passive identification of cortical function using SIGFRIED may serve as a useful adjunct to cortical stimulation mapping in the intraoperative setting.

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## 1. Introduction

An unresolved challenge in the practice of neurosurgery is to identify and avoid injury to eloquent areas of the brain that may lead to permanent neurological deficit if disturbed. The interindividual variation in functional anatomy mandates extensive cortical mapping prior to surgical resection of lesions located adjacent to eloquent cortex [1]. The gold standard for cortical mapping, direct electrocortical stimulation (DECS), has a long history of application in the practice of neurosurgery. Its utility in improving functional outcomes in glioma surgery has been demonstrated [2], but potential side effects remain a significant concern. Specifically, afterdischarges, seizures, and distant site stimulation may result in false information leading to complete failure of the procedure or other morbidities. Intraoperative stimulation-induced seizures can be seen in 1.2–9.5% of patients, depending on the type of stimulation used [3]. Although several less invasive alternatives to DECS have been explored, such as fMRI [4] and PET [5], they are not yet practical enough for widespread routine use. Furthermore, technical constraints further impede the utility of these methods in the intraoperative setting. In this study, we demonstrate the first use of a real-time mapping procedure called SIGFRIED [6], which is based on passive electrocorticography (ECoG). This procedure may serve as an adjunct to DECS such that the operating neurosurgeon can

target direct cortical stimulation to the most relevant areas first. Thus, this technique may reduce morbidity and increase the efficiency of intraoperative cortical stimulation mapping.

The brain generates oscillating electrical potentials at a broad range of frequencies that show characteristic task-related changes. Commonly, these have been described in the context of sensorimotor cortical activation. The notable frequencies comprise mu (8–12 Hz), beta (18–26 Hz), and gamma (>30 Hz) oscillations [7–9]. The lower frequencies of mu and beta are thought to be produced by thalamocortical circuits that decrease in amplitude in association with actual or imagined movements [10–13]. In general, these changes in lower-frequency bands tend to have a large spatial distribution and, hence, are only modestly specific to the type of function. Activity in gamma frequencies (>30 Hz) is thought to be produced by smaller cortical circuits [14]. These frequencies increase in amplitude with cortical activation and tend to have a more cortically focal anatomic distribution for signal change. On a functional level, several studies have revealed that higher frequencies carry highly specific information about cortical processing with respect to speech, motor movements, and motor intention [15–19]. Changes in these frequency rhythms have been used in offline analyses for brain mapping [16,17,20] and compared with the gold standard of DECS [18,21,22]. Although these studies demonstrated the general feasibility of passive functional mapping, the methods used required expertise in signal analysis and cortical physiology and, thus, were not readily applicable in clinical settings.

A procedure known as SIGFRIED (signal modeling for real-time identification and event detection) has recently been developed for

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motor and speech mapping during extraoperative brain mapping [6] to reduce this need for expert oversight. SIGFRIED accomplishes increased efficiency of localization by implementing a detection-based approach based on a gaussian mixture model of recorded brain signals. Rather than using a discrimination-based approach, where an active condition is alternated with a rest condition and then subsequently analyzed, SIGFRIED creates a statistical model of baseline brain activity and then subsequently detects significant deviations from that baseline. This is done in an automated process that does not require the definition of any signal processing parameters by the clinician. The process requires three steps: (1) recording a baseline signal in the absence of overt motor or speech activity, (2) building a statistical model based on the baseline signal, and (3) detecting significant differences from the baseline signal model during cue-directed activity. This enables a real-time assessment of cortical changes that is shown on a topographical display and, as a result, obviates the need for post hoc analysis by an expert. This software is based on the BCI2000 software suite [23], a general-purpose brain-computer interface system for data acquisition, stimulus presentation, and cortical monitoring. It supports acquisition from a number of hardware devices, can process different types of brain signals, and can relay the output to a variety of devices. In the context of brain mapping, it supports programmable presentation of auditory/visual stimuli and receipt of device input. BCI2000 associates the timing of these stimuli with recorded ECoG signals, which facilitates time-locked analyses. The combination of SIGFRIED and BCI2000 has been shown to be useful in the extra-operative setting for localization of eloquent cortex with implanted subdural electrode arrays [24].

Thus far, the use of real-time passive ECoG mapping has not been reported in the setting of awake craniotomies. Because of the short times required for mapping, the real-time identification of functional sites, and the automated nature of the process, the SIGFRIED methodology is well suited to the needs of intraoperative cortical mapping. Here we demonstrate for the first time the application of SIGFRIED in the setting of an awake craniotomy for cortical mapping prior to tumor resection. We report two cases in which passive mapping with SIGFRIED successfully identified areas of cortex associated with hand motor, tongue motor, and speech activity. These data were available to the surgeon within minutes. Additionally, these passively identified speech and motor loci correlated well with sites identified with standard DCES. In summary, our preliminary experience suggests that SIGFRIED can be used practically and with good results in the intraoperative setting. Because of its ease of use and encouraging results, SIGFRIED may find wide adoption by neurosurgeons in the future.

## 2. Methods

Two patients with brain tumors localized to eloquent cortex underwent standard awake craniotomies with cortical mapping and tumor resection (Fig. 1). After initial dural opening and hemostasis, an ECoG electrode array (Ad-Tech, Racine, WI, USA) was placed on the surface of the brain to record cortical surface potentials. The array was covered by wet lap pads to prevent movement of the array during mapping and maintain contact between the electrodes and the cortical surface. The array consisted of 48 platinum electrodes embedded in Silastic and arranged in a  $6 \times 8$  rectangular grid. The electrodes were 4 mm in diameter, with 2.3 mm exposed and 1-cm interelectrode spacing. The electrode leads were connected to three optically isolated 16-channel USB biosignal amplifiers. A similarly configured six-electrode strip was placed at a distant site for use as a ground and reference channel. The signal was sampled at 1200 Hz and collected by a Dell Optiplex computer (Dell, Houston, TX, USA) running the BCI2000 [23] and SIGFRIED software [6].

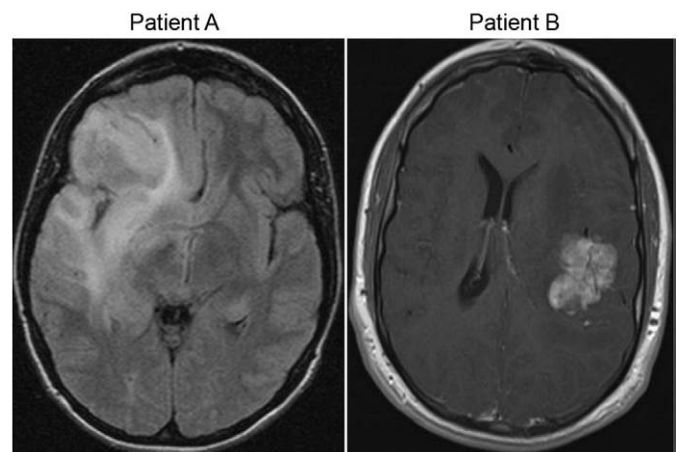


Fig. 1. Clinical MRI scans. Axial MRI images of patient A's right frontotemporal tumor and patient B's left parietal tumor.

Once each patient was deemed awake and cooperative, we recorded 6 minutes of rest activity using BCI2000. The software then used these data to build a model of that rest activity (i.e., one model for each location) [25]. Specifically, after re-referencing the brain signals to the common average, it then extracted spectral estimates of the 70–115 Hz band (starting at 70 Hz and with bin width 5, the last bin ends at 115 Hz) at each location using an autoregressive model. Activity in this frequency range has previously been shown useful for functional localization [22,26]. The software then fit a gaussian mixture model to the distribution of spectral estimates extracted from the baseline recording. This modeling process was fully automated and required less than 1 minute for each patient.

The patients engaged in different tasks following visual cues that were presented on an LCD monitor placed at eye level. Each trial was cued by display of the word *Hand*, *Tongue*, or *Speak* to indicate continuous opening and closing of the contralateral hand, protrusion and retraction of the tongue, and recitation of the alphabet (patient A) or part of the Pledge of Allegiance (patient B), respectively. In addition to the visual cue, an audible tone indicated the beginning and end of each trial for patient B. Each cue was presented for 15 seconds and was followed by a rest period of the same length before proceeding to the next trial (see [Appendix: Supplementary Video](#)). The three activity types proceeded in order and this sequence was repeated five times. This actual mapping procedure lasted a total of 7.5 minutes ( $[15 \text{ seconds} + 15 \text{ seconds}] \times 3 \times 5/60 \text{ seconds/minute}$ ).

As the patient performed the different tasks, BCI2000 acquired signals from the g.USBamp amplifier systems. The resulting time-series ECoG signals were first re-referenced to the common average and transformed into the frequency domain using an autoregressive model. In real time, the SIGFRIED component in BCI2000 determined, for each location, the negative log likelihood that the 70- to 115-Hz spectra at that location differed from the spectral distribution during the baseline period. Finally, the software determined the coefficient of determination ( $r^2$ ) between the distributions of negative log likelihood values for the task and interleaved rest periods. This procedure resulted in one  $r^2$  value (that was continuously updated during data collection) for each location and task. These  $r^2$  values were presented in an easily interpreted display (Fig. 2) on a second monitor. This display showed, for each task, a circle at each location whose diameter was proportional to the  $r^2$  at that location. All of these computations were performed in real time with an update frequency of 20 Hz.

After passive identification of hand motor, tongue motor, and speech cortex, standard DECS mapping proceeded as normal. To

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