

2021

# A review of neurophysiological mapping procedures of the brain and spinal cord

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BOSTON UNIVERSITY  
SCHOOL OF MEDICINE

Thesis

**A REVIEW OF NEUROPHYSIOLOGICAL MAPPING PROCEDURES OF THE  
BRAIN AND SPINAL CORD**

by

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B.A., University of Vermont, 2015

Submitted in partial fulfillment of the  
requirements for the degree of  
Master of Science

2021

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## **DEDICATION**

To my family and, most importantly, my mother, Robin. The support each of you has given me made this possible.

## **ACKNOWLEDGMENTS**

Thank you to all at the Boston University School of Graduate Medical Science. Through the challenges of the past year, your support has been critical.

I would also like to thank everyone I have worked with at Boston Medical Center, Memorial Sloane Kettering, and SpecialtyCare Inc. who trained and mentored me in the use of many of the techniques discussed in this thesis.

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BRAIN AND SPINAL CORD**

**TAYLOR M. STIVALI**

**ABSTRACT**

Surgical procedures of the brain and spine that require manipulation of, and near nervous structures, require unique considerations in their approach. Over the past 100 years, techniques have been developed and refined for localization of specific structures allowing for safer, more accurate interventions. These include the pre-operative use of Electroencephalography (EEG) in combination with radiographical imaging and intraoperative neurophysiological techniques rooted in electrophysiology.

Since the introduction of EEG and electrical cortical stimulation, physicians have had the tools to diagnose neurological conditions while also being able to complete surgical interventions with a level of safety. By the 1920's and 1930's, the efforts of Hans Berger and Frederic and Erna Gibbs to develop and utilize EEG led to accurate pre-operative diagnoses of epilepsy along with their associated foci. Within that same time, the efforts of Wilder Penfield to develop and implement electrical cortical stimulation in awake patients during neurosurgery led to broad understandings of the organization and function of regions of the brain. Both EEG and cortical stimulation in combination quickly became useful beyond research in mapping the regions of the brain and led to rapid improvements in the accuracy of epilepsy surgery.

Over preceding decades, these techniques continued to evolve with the latest research and technology. Additionally, their utilization has expanded from epilepsy surgery to resection for neoplasms of the central nervous system. In contemporary surgery, EEG and cortical stimulation still serve as the backbone of mapping techniques, but novel techniques are continually explored and improve patient outcomes. These advances include modern intraoperative neurophysiological monitoring, improved stimulation techniques, and additional utilization beyond the brain.

This review highlights the conceptual underpinning of electrical neurophysiological mapping techniques as well as their implementation and future considerations. The review covers the pre-operative mapping of the brain using EEG, intraoperative mapping of the brain using cortical and subcortical mapping, and spinal cord mapping of the dorsal column and anterolateral tracts. The techniques and theory of each are summarized along with discussions on implementation and efficacy. Additional emphasis is placed on the need for standardization of their use to improve patient outcomes and recommendations for future research and development.

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## LIST OF ABBREVIATIONS

BIS .....	Bispectral Index
CNS.....	Central nervous system
CT .....	Computer Tomography
CMR.....	Common Mode Rejection
CMRR.....	Common Mode Rejection Ratio
DC.....	Dorsal column
DMS .....	Dorsal median sulcus
DTI.....	Diffuse tensor imaging
ECoG.....	Electrocorticography
EEG.....	Electroencephalography
EOR.....	Extent of Tumor Resection
fMRI.....	Functional Magnetic Resonance Imaging
GBM .....	Glioblastoma Multiforme
GTR.....	Gross total resection
HD-EEG.....	High-Definition Electroencephalography
IMSCT .....	Intramedullary spinal cord tumor
IONM.....	Intraoperative neurophysiological monitoring
LMA.....	Laryngeal mask airway
PFS .....	Progression free survival
SNR.....	Signal-to-noise ratio
SSEP .....	Somatosensory evoked potential

STR ..... Subtotal Resection

TceMEP ..... Transcranial motor evoked potential

## INTRODUCTION

While uncommon, neurosurgical procedures of the brain and spine present a unique set of complexities. The anatomy and pathophysiology of nervous structures are complex, variable, and often difficult to approach. For these reasons, techniques to map the central nervous system (CNS) are critical to minimize side-effects, maximize efficacy, and develop new surgical approaches.

Of neurosurgical procedures of the brain and spinal cord, all pose direct risk to eloquent nervous structures. Manipulation of potentially eloquent structures is necessary and requires avoiding particular cortical or subcortical regions while also gaining access to a particular location. As medical science has advanced, techniques to map the nervous system in the pre-operative and intra-operative phases have proven effective at minimizing the risks to patients who undergo these procedures.

### *Background*

In 1895, Wilhelm Röntgen serendipitously discovered the use of cathode ray tubes to produce Röntgen Ray, later defined as X-rays. Days after discovering how these rays illuminated a barium platinocyanide screen after striking it, he produced the first radiograph of a human hand. After viewing the image, Anna Bertha, Röntgen's wife, exclaimed that she had "...seen [her] death." These early radiographs were remarkable

for the era and difficult to conceptualize for the general public, but it only took one year before its first clinical application.

By 1896, staff at Massachusetts General Hospital acquired an X-ray tube and began working on clinical applications. In October of that year, Dr. Harvey Cushing, who was completing his internship at Massachusetts General Hospital, took the tube with him to Johns Hopkins Hospital where he refined his work. Within the year, Cushing had published his first work of a patient who had suffered a gunshot wound to the cervical spine. The bullet had become lodged in the C<sub>6</sub> vertebra and, in this case, was clearly visualized before surgical intervention was considered. This case is widely considered one of the first case where pre-operative planning based on a visual image map of the spine.

While imaging techniques were first to map the body prior to surgical intervention, electrophysiological techniques soon became commonplace.. Electroencephalography (EEG) emerged as a useful tool to diagnose many neurological conditions and assist in preoperative evaluation.

Through the 1920's, efforts by Hans Berger to record EEG required overcoming many challenges. Using technology of the time, recordings using 3 channels with sufficient

resolution to record low voltage activity of the cortex proved difficult. That is, until Berger showed success in 1924 by successfully recording EEG waveforms from a 17 year-old boy (Kennett, 2012).

Across the world, physicians and scientists began exploring the possibility of utilizing EEG as a tool in diagnosing or detecting neurologic and psychiatric disorders. By the 1930's, Drs. Frederic and Erna Gibbs and found success in using EEG to identify and categorize epileptiform activity in patients suffering from seizure disorders (Gibbs et al., 1937). Their success in characterizing grand mal, petit mal, and psychomotor seizure activity served as the start a first step in the use of electroneurophysiology in diagnosing and planning for surgical procedures (Gibbs et al., 1943).

Aside from EEG, electrical cortical stimulation became an early tool used for intraoperative surgical mapping. Around the same time Hans Berger was discovering the utility of EEG, Wilder Penfield developed cortical stimulation methods that remain widely used today. His initial efforts were to identify epileptic foci during surgical resection of epileptic centers, but soon moved to characterizing regions of the brain during neurosurgical intervention. Efforts to identify cortical representation of the brain made tumor resection and epilepsy surgery safer and more accurate.(Penfield & Boldrey, 1937)

*Brain*

Surgical intervention of the brain frequently requires manipulation of potentially eloquent structures. For the scope of this thesis, the focus will be on tumor resections and functional neurosurgical interventions..

In the United States, the incidence of primary malignant neoplasms of the brain is 47.6 per 100,000 individuals. In 2010 alone, that left approximately 103,634 total diagnoses in the country with a great percentage being candidates for resection (Barnholtz-Sloan et al., 2018).

Tumors of the brain are greatly variable in their etiology and long-term survival. For this reason, resection strategies differ depending on the pathophysiology of the neoplasm and the quality of life of the patient. In regard to glioblastoma multiforme (GBM), the extent of tumor resection (EOR) favors gross total resection (GTR) to improve progression free survival in patients (Brown et al., 2016). Overall, early surgical intervention and EOR  $\geq$  78% is prognostic of greater 5-year survival and patient outcomes emphasizing the need to cortical mapping to surpass this threshold (Brown et al., 2016; Jakola et al., 2012; Sanai et al., 2011).

In a more complicated example, central nervous system lymphoma (CNSL) has different considerations for management. More recent studies have revealed that there is some benefit to surgical or radiosurgical intervention when larger lesions can be identified and are accessible (Kumar et al., 2015; Rae et al., 2019). If the paradigm for treatment for

CNSL continues to shift toward surgical intervention when possible, there is no doubt that mapping techniques will be critical when determining if surgery is possible.

While CNSL and GBM require different considerations in management, one attribute they have in common is the need for safe surgical access when warranted. These classifications of lesions of the brain make up a significant proportion of total brain tumors, but others share the need for a safe surgical approach. In order to achieve GTR while preserving the neurologic status of the patient, both pre-operative and intra-operative mapping techniques become crucial. In such cases, a combination of computed tomography (CT), magnetic resonance imaging (MRI), and intraoperative neurophysiological mapping becomes necessary.

In addition to brain tumor resection, many functional neurosurgical interventions require significant mapping of a patient's anatomy and physiology. These procedures include DBS or selective lesioning for conditions such as Parkinson's Disease, epilepsy, and a variety of psychiatric disorders. These treatment options are considered in the event such conditions cannot be controlled medically. Often, for optimal efficacy, pre-operative electrophysiological studies, function magnetic resonance imaging (fMRI), CT imaging, and diffuse tensor imaging (DTI) are utilized in planning the procedure, while stereotactic navigation and intraoperative neurophysiological mapping is utilized during the intra-operative phase. In doing so, the appropriate location can be targeted within the brain while mitigating risk to surrounding structures.

### *Spinal Cord*

Of procedures of the spine, only a small fraction require direct manipulation of the spinal cord. Two types of procedures that require detailed mapping of neuronal structures of the spinal cord include tumor resections and chronic pain treatment.

With respect to spinal cord tumors, intramedullary spinal cord tumors (IMSCT) are those where spinal cord mapping is most critical. IMSCTs are rare, often non-malignant lesions that grow within the medullary spinal cord. According to epidemiological analysis, between 2004 and 2007 there were only 2576 cases of malignant spinal cord tumors and 9136 cases of non-malignant spinal cord tumors in the United States. This equates to an incidence rate of 0.22 and 0.76 per 100,000 individuals respectively. For malignant tumors, the distribution is even between men and women with a generally low incidence rate across all age cohorts (0.14-0.33 per 100,000 individuals) (Table 1). For non-malignant tumors, 61.9% of cases occur in women with 38.1% in men. There is also significant differences in the incidence rate of non-malignant tumors by age with the lowest incidence in children aged 0-9 years at 0.09 per 100,000 individuals and highest in adults aged 70-79 years at 2.22 per 100,000 individuals (Table 1) (Duong et al., 2012).

Table 1: Adapted from Duong et al. (2012). Descriptive statistics of spinal cord tumor epidemiology.

Characteristic	Total		Malignant		Nonmalignant	
	Count <sup>a</sup> (%)	Rate <sup>b</sup> [95% CI] <sup>c</sup>	Count (%)	Rate [95% CI]	Count (%)	Rate [95% CI]
Total	11,712 (100.0)	0.97 [0.96-0.99]	2576 (100.0)	0.22 [0.21-0.22]	9136 (100.0)	0.76 [0.74-0.77]
<b>Age at diagnosis, years</b>						
Birth-9	364 (3.1)	0.23 [0.21-0.25]	229 (8.9)	0.14 [0.13-0.16]	135 (1.5)	0.09 [0.07-0.10]
10-19	505 (4.3)	0.30 [0.28-0.33]	208 (8.1)	0.13 [0.11-0.14]	297 (3.3)	0.18 [0.16-0.20]
20-29	774 (6.6)	0.47 [0.44-0.51]	227 (8.8)	0.14 [0.12-0.16]	547 (6.0)	0.34 [0.31-0.37]
30-39	1277 (10.9)	0.79 [0.75-0.83]	331 (12.8)	0.20 [0.18-0.23]	946 (10.4)	0.58 [0.55-0.62]
40-49	2059 (17.6)	1.15 [1.10-1.20]	507 (19.7)	0.28 [0.26-0.31]	1552 (17.0)	0.87 [0.82-0.91]
50-59	2348 (20.0)	1.57 [1.50-1.63]	466 (18.1)	0.31 [0.28-0.34]	1882 (20.6)	1.25 [1.20-1.31]
60-69	1883 (16.1)	2.01 [1.92-2.10]	313 (12.2)	0.33 [0.30-0.37]	1570 (17.2)	1.67 [1.59-1.76]
70-79	1601 (13.7)	2.53 [2.41-2.66]	197 (7.6)	0.31 [0.27-0.36]	1404 (15.4)	2.22 [2.10-2.34]
≥80	901 (7.7)	2.09 [1.96-2.23]	98 (3.8)	0.23 [0.18-0.28]	803 (8.8)	1.87 [1.74-2.00]
<b>Sex</b>						
Male	4791 (40.9)	0.83 [0.81-0.86]	1312 (50.9)	0.23 [0.21-0.24]	3479 (38.1)	0.61 [0.59-0.63]
Female	6921 (59.1)	1.09 [1.06-1.11]	1264 (49.1)	0.21 [0.20-0.22]	5657 (61.9)	0.88 [0.86-0.91]

Keeping in mind that, of these numbers, IMSCTs are an even smaller proportion with only 20% classified as intradural, intramedullary tumors in adult populations. These are most often astrocytomas, ependymomas, gangliogliomas, hemangioblastomas or metastatic neoplasms. Individuals with IMSCTs often present with non-specific radicular pain, gait instability, paresthesia, bowel and/or bladder incontinence, and Brown-Séquard Syndrome (Dauleac et al., 2019).

Clinical management of IMSCT is largely dependent on resection. While adjunct therapies are recommended as well, GTR is often the goal and increases 5-year survival rates significantly. In pediatric patients, GTR is associated with an 86% increase in progression-free survival and evidence suggests that long-term complications following successful resections are limited to post-laminectomy changes and kyphotic instability (Ahmed et al., 2014; Hsu et al., 2009). In all patient demographics, GTR is associated with survival rates that are 5.37 times higher than in patients where subtotal resection

(STR) is achieved (Hamilton et al., 2019). For these reasons, effective mapping techniques in the pre- and post-operative phases are critical to safely approach such lesions and identify lesion margins to achieve GTR (Cheng et al., 2014; Deletis et al., 2018; Verla et al., 2016).

### *Techniques of Interest*

There is a wealth of well established and emerging techniques that can be utilized in the pre- and intra-operative phases of neurosurgical interventions. For the purposes of this discussion, techniques that identify nervous structures based on their physiology will be considered. This will include intraoperative neuromonitoring, pre-operative electrophysiology, fMRI, and DTI. Each of these techniques and tools are capable of revealing nervous structures based on local changes in electrical activity, metabolic activity, or the unique structure of axons (Kennett, 2012; Moseley et al., 1990; Ogawa et al., 1990; Verla et al., 2016).

### **SPECIFIC AIMS**

1. Comprehensive review of techniques and theory of pre-operative and intraoperative neurophysiological mapping techniques of the brain and spine.
2. Investigation in utilization and efficacy of each modality
3. Conclusions and recommendations for the utilization of modalities explored

## **ELECTROENCEPHALOGRAPHY AND ELECTROCORTICOGRAPHY**

EEG has been the primary method of diagnosing seizure activity for over a century. Following Berger and Gibbs' refinement of EEG technique to characterize epileptic waveforms and their distinct patterns, clinicians began using EEG to identify the focus of seizure defined as the origin of seizure activity or the specific location of a focal seizure (Nadler & Spencer, 2014). When considering treatment options, the use of EEG to identify specific cortical zones of interest becomes important as surgical resection of an epileptogenic zone can be considered a curative measure for patients who do not respond to medical management of their epilepsy (Rosenow & Lüders, 2001).

### **Technique**

#### *The 10-20 System*

Since its inception, EEG recordings have increased the number of channels that could be recorded from at any one time. In the time of Frederic Gibbs, recording was limited to 3 channels, but as technology advanced, recordings moved from pen on paper to computerized systems that allowed for recordings well beyond 16 channels (Gibbs et al., 1937). This necessitated standardization of electrode placement and recording parameters.

By 1958, the American Clinical Neurophysiological Society (ACNS) recommended the use of the 10-20 System for all EEG recordings. The 10-20 system was meant to standardize electrode placement to create uniformity between recordings of patients. By

using landmarks of the skull and measurements proportional to skull size, it was understood that electrodes would be placed in approximately the same location for a given patient regardless of the clinician that placed the electrodes (Jasper, 1958).

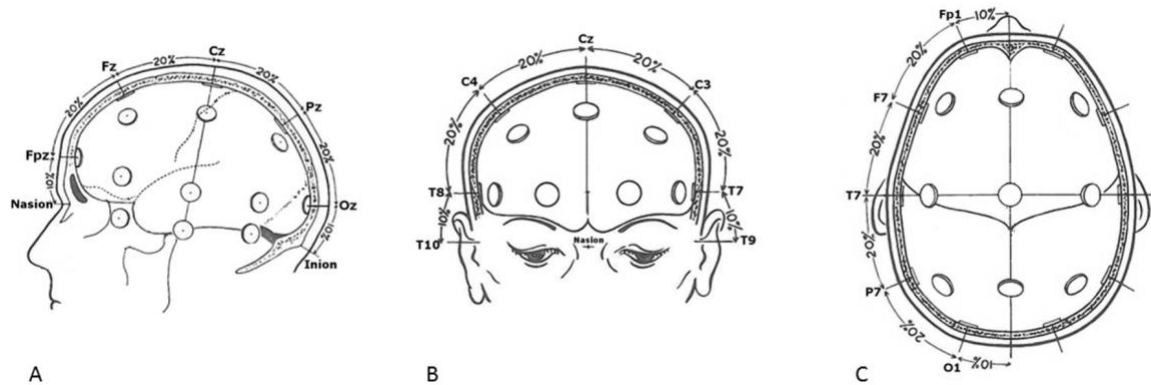


Figure 1: Standard electrode placement under the 10-20 system. A. lateral view B. anterior view C. top view (adapted from (Klem et al., 1999))

According to the 10-20 system of standard electrode placement, all locations are to be referenced to cephalometric landmarks. These are the nasion, inion, and the left and right preauricular points. With these four physical landmarks, electrode locations can be measured and the neurologic structures beneath approximated with each electrode referring to the lobe of the brain they are placed above alphanumerically. For example, the Cz electrode location is considered to be 50% the circumferential distance between the preauricular points and between the nasion and inion in the coronal and axial planes respectively. Moving laterally to the left and right in the coronal plane 20% of the circumferential distance identifies C3 and C4 respectively and an additional 20% of the circumferential distance identifies T7 and T8 respectively. From there, the remaining

10% of the circumferential distance returns to the preauricular points identified as T9 and T10 respectively (Fig 1B) (Klem et al., 1999).

For a standard 10-20 system EEG setup, the same process is completed in the axial plane and additional electrodes are added at regular intervals of 10 and 20% distances from one another (Fig 1). The resulting setup will contain 19 electrodes and has long been considered the standard for clinical EEG where technical limitations preclude additional channels (Seeck et al., 2017). This occurs in situations where amplifiers or software does not have the ability to interpret more than the 19 inputs recommended.

The 10-20 system proved effective in standardizing EEG recordings and allowed for comparison of studies for a single patient; it has significant limitations. Use of 19 electrodes leaves many regions of the brain unrecorded. Most notably, regions of the inferior and anterior regions of the temporal lobe may be excluded using this limited system which is of particular interest in cases of temporal lobe epilepsy related to hippocampal sclerosis (Koessler et al., 2015; Seeck et al., 2017). Additional studies have compared EEG recording locations to MRI of the same patient in an effort to ascertain the accuracy in localization of regions of the brain using electrodes placed using external landmarks. It was determined that, due to patient variability, it cannot be accurately determined which anatomical region is mapped beneath the scalp using the 10-20 system alone. Evidence presented emphasized difference in central sulcus location in the coronal

plane, central sulcus orientation in reference to the vertex-preauricular axis, and location of the sylvian fissure (Fig 2) (Steinmetz et al., 1989).

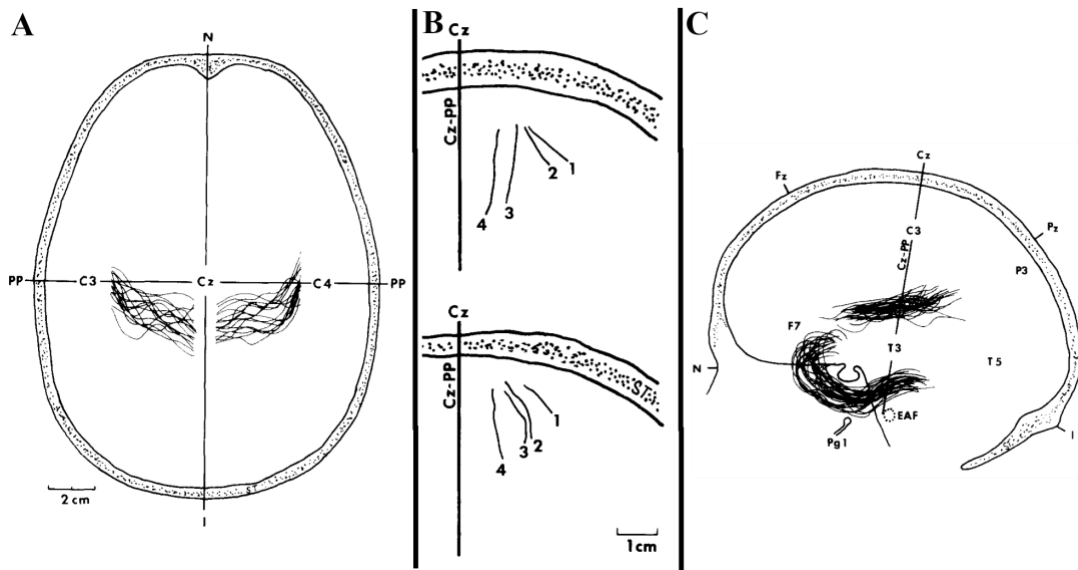


Figure 2: Aggregate locations of the central and lateral sulcus visualized by MRI. A. Coronal view of central sulcus location for 16 healthy individuals showing absolute location variability. B. Longitudinal view of orientation of the central sulcus relative to vertex-preauricular axis at distances of 5, 10, 15, 25 mm from midline in lines 1-4 respectively in two healthy patients. C. Lateral view of lateral sulcus location for 16 healthy individuals showing absolute location variability. Adapted from (Steinmetz et al., 1989)

### *The 10-10 System*

Limitations on the efficacy of the 10-20 system for diagnostic EEG led to the need for more electrode locations and improvements in computing to allow for simultaneous computation of multiple montages from each channel. Initial improvements added 2-6 electrodes to cover the inferior temporal chain for a total of 25 recording electrodes in the *modified* 10-20 system (J. N. Acharya et al., 2016; Seeck et al., 2017). According to the American Clinical Neurophysiology Society (ACNS), such modified version of the 10-20 system there are accepted for clinical evaluation of most patients, but exceptions are

made. For patients that do not have clear ictal or interictal epileptiform discharges or for those undergoing pre-surgical evaluation, additional spatial resolution is desirable (J. N. Acharya et al., 2016; Rosenow & Lüders, 2001). In these cases it is recommended the modified EEG electrode placement using the 10-10 system or other electrode placement be used to achieve the desired level of resolution (Oostenveld & Praamstra, 2001).

Increases in electrode density are shown to increase resolution, reduce variability in error detection and provide more accurate localization of epileptiform source which is critical in pre-operative mapping for epilepsy surgery (Song et al., 2015)

The 10-10 system similarly utilizes the same gross anatomical landmarks that the 10-20 system uses, but contains additional electrodes. Starting from the same four locations, all electrodes of the 10-20 system are placed with the addition of Nz (nasion), Iz (inion), AFz, FCz, CPz, and POz in the axial plane between inion and nasion and C1, C2, C5, C6, T9, and T10 in the coronal plane between pre-auricular points. From these landmarks, additional electrodes are placed at intervals of 10% of circumferential distance effectively resulting in the 10-20 system with an additional electrode between each of the earlier system (Fig 3) (Oostenveld & Praamstra, 2001).

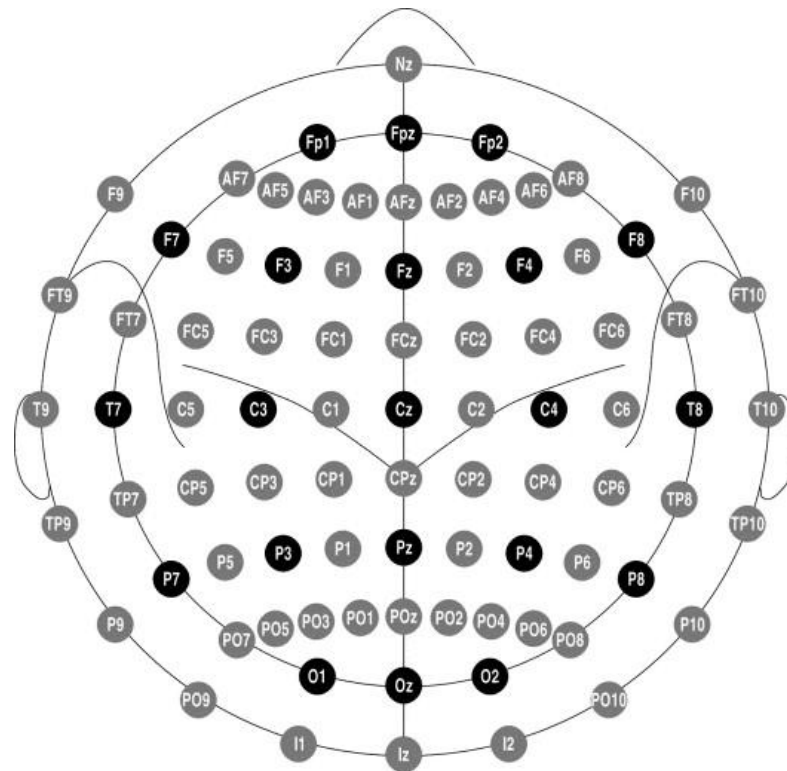


Figure 3: Standard electrode placement for the 10-10 System. Standard 10-10 electrode placement locations with combinatorial nomenclature. Dark circles indicate electrode locations shared with the 10-20 system. Adapted from Oostenveld & Praamstra, 2001.

### *Beyond the 10-10 System*

There are alternative methods that further increase spatial resolution beyond what is typically clinically indicated. These include the modified 10-5 system, geodesic electrode systems, and general high-density EEG (HD-EEG). Within the 10-5 system there is an additional electrode between each of the 10-10 system, but that is without a generally accepted system of nomenclature (Oostenveld & Praamstra, 2001). Geodesic systems also lose some of their generalizability as they also do not have standardized nomenclature for electrode locations and do not follow a prescribed mathematical pattern

in their placement. Instead, electrodes are placed equidistant from one another across the entirety of the skull (Seeck et al., 2017). The increased electrode density, when combined with other imaging techniques, such as MRI, can help clinicians map the focus of seizure activity and related it with great resolution to region of the cortex.

### *Electrocorticography*

From a technical perspective, electrocorticography (ECoG) does not share many of the challenges that EEG does related to regional specificity and nomenclature. Because ECoG is utilized intraoperatively, electrodes can be placed directly on cortical structures as they are visualized. This is typically achieved by placing a grid or strip of electrodes directly over the cortex made of platinum electrodes approximately 5 mm in diameter spaced 1 cm apart (Yang et al., 2014). Recent advances in material science have allowed for new electrodes to be lower profile, trade metals for conductive nano particles, and be safer for the patient. Recent work at the Martinos Center for Bioimaging in Boston, MA have produced such a grid that can be placed intraoperatively, causes less image artifact under CT, and does not significantly increase in temperature under 3T MRI (Ahmadi et al., 2016).

### **Theory**

Scalp electrodes placed during EEG setup function to detect changes in voltage and transfer these waveforms to a detector. At the level of the cortex, neuronal activity fluctuates with cortical location, anesthetic presence, state of awareness, motion,

sensation, and epileptic activity (Vakani & Nair, 2019). As individual neurons depolarize, they change the local voltage of the surrounding region. For the purposes of EEG and ECoG, the aggregate change in voltage, termed the local field potential, of many neurons is detected using large surface or subdermal electrodes. As these electrodes increase in size, they respond to larger areas containing more neurons and thus have lower spatial resolution (Huang, 2016). EEG electrodes record small changes in voltage while contending with insulating tissues of the meninges, vasculature, the skull, and dermal layers.

### *Differential Amplification*

Recording of these waveforms utilizes differential amplification. In an effort to maximize the signal to noise ratio (SNR) for these low amplitude waveforms, data is collected from an active and reference electrode where the difference between the two is presented. In its simplest form, a differential amplifier will take this difference and multiply it by the amplifier gain (Equation 1). The simplified expression for amplifier exists in a perfect system where noise is perfectly rejected as opposing polarity waveforms zero themselves out.

In reality, differential amplifiers are imperfect, and the common mode rejection ratio (CMRR) characterizes how effectively a differential amplifier can eliminate signals common to both inputs at any instance (Equation 3). CMRR varies and, in a perfect system, is infinite where the amplifiers common mode gain ( $A_c$ ) is equal to zero. This

eliminates the second term in Equation 2 resulting in the ideal amplifier in Equation 1 and depicted in Figure 4.

Equation 1: Output voltage of an idealized differential amplifier where the CMRR is infinite

$$V_{out} = A_d (V_{in}^+ - V_{in}^-)$$

Equation 2: Output voltage of a differential amplifier with known CMRR

$$V_{out} = A_d (V_{in}^+ - V_{in}^-) + A_c \left( \frac{V_{in}^+ + V_{in}^-}{2} \right)$$

Equation 3: Definition of CMRR where  $A_d$  is equal to the gain of the differential amplifier and  $A_c$  is equal to amplifiers common mode gain

$$CMRR = 10 \log_{10} \left( \frac{A_d}{A_c} \right)^2$$

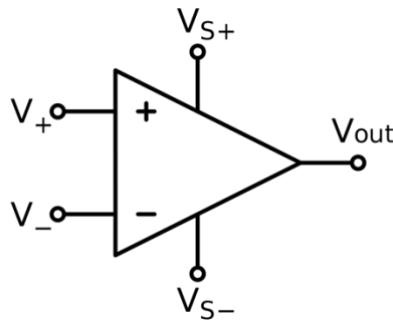


Figure 4: Schematic representation of an idealized differential amplifier with theoretical infinite CMRR. Source: Creative Commons license

### *Recording Montages*

The use of differential amplification allows for a number of different recording techniques that have individual benefits. These typically include bipolar or referential recordings. In regard to bipolar recordings, the goal is to understand the near-field electrical activity that is occurring just under two neighboring electrodes (e.g. F1-F3 montages). Because both electrodes are close to one another, they will experience similar levels of ambient and physiological electrical noise and the resultant output will be a low amplitude waveform specific to that region. In addition, their close proximity helps cancel out higher voltage, large waveforms, that would be collected if greater distance was between the electrodes (Lesser et al., 1985). This makes bipolar montages particularly useful when identifying small focal changes in waveform making them invaluable for pre-surgical mapping and evaluation (Kutluay & Kalamangalam, 2019).

The use of referential recordings has its own benefits. Where bipolar montages excel at identifying low amplitude focal patterns, they may miss larger, more dispersed waveforms due to common mode rejection (CMR). In these cases, a referential recording montage may be more appropriate when detecting high amplitude discharges spread over a larger area (Kutluay & Kalamangalam, 2019). Referential recording requires that all active electrodes be referenced to a common reference that is, ideally, electrically inactive. This is often the ear lobe or Cz under the 10-20 convention. Alternatively, an average reference, the average voltage across all recording electrodes, can be created as a

universal, common reference for all recording electrodes that, theoretically, experiences the same ambient electrical noise.

However, if discharges are particularly dispersed or high amplitude, there is a risk of contamination of the average reference (Kutluay & Kalamangalam, 2019). When a sufficiently high number of recording electrodes become influenced by such diffuse activity leading to potential difficulty when identifying regions of interest. In such cases, a quiet reference is preferred (Seneviratne, 2014).

Presentation of EEG and ECoG data is aided by computer programs. Modern EEG software has the ability to present the clinician with real-time data from a number of different montages. By presenting this, along with real-time video, clinicians have the ability to reference different montages to localize the focus of seizure activity.

## **Application**

EEG and ECoG serve similar, albeit unique functions, in mapping the brain. Their role in detecting seizure activity is critical for diagnosing and for localizing the focus of a seizure. In instances of epilepsy that cannot be treated medically, surgical intervention may be warranted and considered curative. EEG alone will likely never be the only tool used to identify a target of the cortex. Particularly when planning a surgical intervention, EEG will be used in conjunction with a non-simultaneous MRI to better visualize cortical structure (Klein et al., 2015).

### *Pre-surgical Evaluation*

EEG as a modality does play a crucial role in localizing cortical activity in pre-surgical evaluation. For those that suffer from focal epilepsy, 30-40% cannot be treated with anti-convulsant medical therapy alone. For these individuals with intractable epileptic episodes, surgery may be a curative option (Kwan et al., 2010; Rugg-Gunn et al., 2020).

During the pre-surgical phase, identification of the epileptogenic zone must take place. This region is defined as the smallest region of cortex that must be resected to eliminate seizure activity (Rosenow & Lüders, 2001; Rugg-Gunn et al., 2020). During this phase, ictal and interictal EEG activity must be recorded for a prolonged period of time in conjunction with neurocognitive testing to appropriately localize the epileptogenic zone (Beniczky et al., 2016). Using EEG in this way is an effective method of mapping the approximate location of the epileptogenic zone allowing for further studies to identify if where to resect and if such an approach is possible.

### *Intraoperative Evaluation*

For cases where the epileptogenic zone is not easily identified, more advanced forms of electrophysiological mapping can be utilized. These cases can include multifocal epilepsies and often benefit from ECoG recording over the suspected region or depth electrode placement. Grid electrodes can be easily placed through burr holes or a craniotomy can be completed to place a larger array over the suspected region. Depth

electrodes are placed stereotactically through the skull. These electrodes can be left in place with a 1.3% morbidity rate for upwards of 10-14 days to monitor the interictal and ictal phases (Mullin et al., 2016). In combination with imaging, this technique can result in precise localization of epileptogenic centers at the expense of being more invasive.

ECoG is also of great importance for detecting intraoperative seizures following stimulation of the cortex. Seizure activity that occurs secondary to electrical stimulation of the cortex presents with epileptiform activity known as after discharges (ADs). For this reason, ECoG is indicated for use even when a patient does not present with pre-operative seizure history. ADs can kindle into a seizure that result in additional risk to the patient and staff. This is the leading causes of aborted procedures that require mapping with 66% of aborted cases resulting from repetitive seizure in a retrospective study of 859 patients who underwent awake brain tumor surgery (Hervey-Jumper et al., 2015).

AD epileptiform can be classified as a number of different waveforms and may or may not kindle broad seizure activity (Hirsch et al., 2013). Following seizure activity, a period of ECoG monitoring will look for a new, focal waveforms that are typically rhythmic and contain either simple spikes or polyphasic spikewaves. This will appear to be time locked with termination of electrical stimulation (Fig. 5) (Tatum et al., 2020). It is of great importance that such activity be caught early such that an intervention can take place. The accepted intervention for continued AD activity or intraoperative seizure is administration of cold saline or Ringer's lactate solution (Alimohamadi et al., 2016;

Sartorius & Berger, 1998). This emphasizes the importance of utilizing ECoG during and procedure involving cortical mapping.

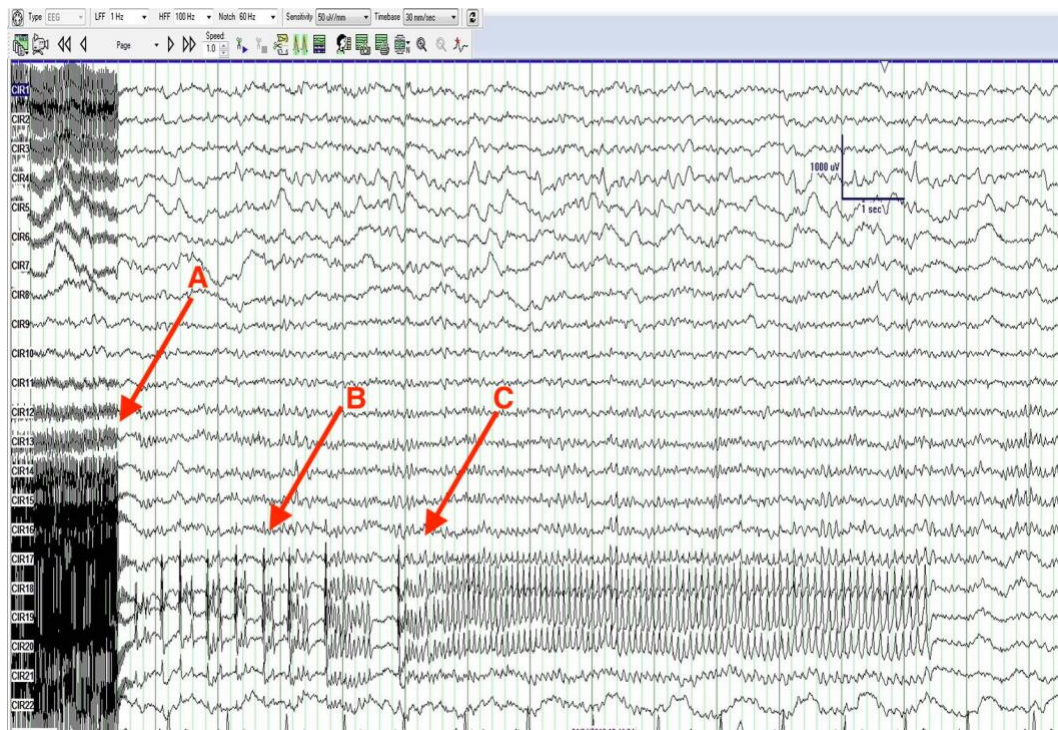


Figure 5: 13 second recording of AD activity secondary to direct cortical stimulation. (A) End of direct cortical stimulation. (B) Onset of polyspike burst AD activity. (C) Onset of continuous sequential spike without interpike pauses. Adapted from Tatum et al. 2020.

## CORTICAL AND SUBCORTICAL MAPPING

During a number of open procedures of the brain, mapping eloquent regions of the cortex and subcortical structures becomes critical. Of particular interest, mapping during tumor resections often requires mapping of eloquent regions of the cortex and subcortical regions to achieve GTR. This technique becomes critically important when attempting

GTR in an effort to improve progression free survival (Brown et al., 2016; Jakola et al., 2012; Sanai et al., 2011).

## **Technique**

Current accepted techniques follow one of two approaches: bipolar, also known as Penfield, or monopolar stimulation. The former has been long accepted and can effectively evoke local, seizure-like, activity over a region for a period of time making it particularly useful for language mapping. The latter has become the gold-standard for localizing specific regions of the cortex near the primary motor cortex where surgical decisions on EOR are determined by the risk of insult to motor eloquent areas.

Furthermore, evidence suggests that monopolar mapping techniques are more reliable in evoking responses during subcortical mapping than bipolar stimulation (A. Szelényi et al., 2011). Recent studies and evidence have gone further in recommending the utilization of monopolar stimulation in mapping and recommend the inclusion of transcranial motor evoked potentials (TceMEPs) along with direct cortical motor evoked potentials (dcMEPs) if the size of the exposure allows (Schucht et al., 2017).

### *Stimulation*

Penfield stimulation is often preferred due to the lack of current spread caused by the creation of a homogeneous electrical field between the poles of the electrode (Fig. 6). Its application was first described in the 1930's and has remained largely the same since (Penfield & Boldrey, 1937). Current is applied at 50-60 Hz and is biphasic in its

waveform. Responses can be evoked with a stimulation intensity of less than 10 mA when measured peak to peak where lower intensities provide more focal stimulation and decrease the risk of intraoperative seizure (Sandhu et al., n.d.). However, accepted protocols allow for stimulation intensities up to 20 mA measured peak to peak (Jahangiri et al., 2020). Once the probe is activated, the surgeon can move the probe throughout the surgical field stimulating for a period of 1-5 sec at each area of interest (Table 2) (Bello et al., 2014; Jahangiri et al., 2020; Schucht et al., 2017). From a surgical perspective, this makes visualizing tumor margins simple. The tissue that lies between the poles of the electrode is depolarized and the surgeon can move quickly between areas of concern without having to communicate with a technologist.

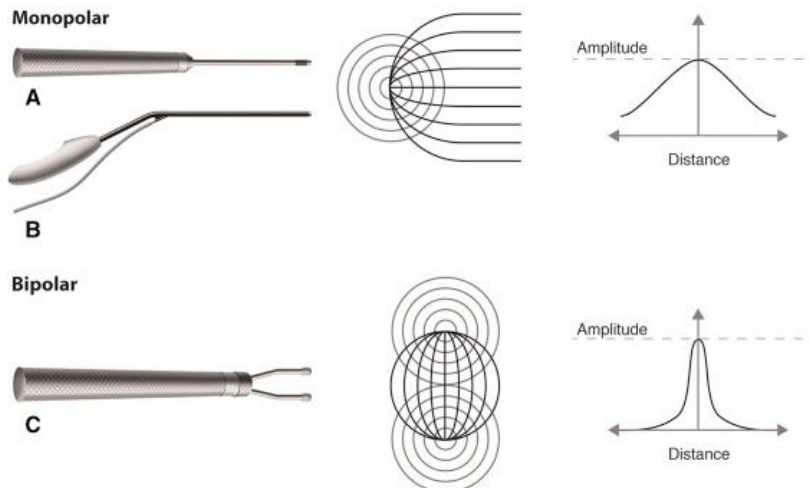


Figure 6: Illustration of cortical stimulation probes and their current spread. (A)(B) Depiction of monopolar probes and visualization of current to a far reference. (C) Depiction of a bipolar stimulation probe with current spread visualized. Note the uniform and high charge density of bipolar stimulation. Adapted from Schucht et al. (2017)

Monopolar stimulation utilizes a different technique to this continuous stimulation that Penfield stimulation can provide. Rather than a continued low-frequency (50-60 Hz)

discharge, accepted monopolar techniques utilize a train of stimuli consisting of 4-9 high-frequency square discharges at 250-500 Hz (Table 2) (Jahangiri et al., 2020; F. Sala & Lanteri, 2003; Taniguchi et al., 1993). Similar to TceMEPs, this method utilizes temporal summation to achieve local depolarization of the cortex with less total charge than bipolar stimulation. Similar to TceMEPs, stimulation cannot be achieved continuously. Rather, volleys are elicited when required necessitating communication between a surgeon and a technologist and adding complexity to mapping.

Table 2: Accepted stimulation parameters for both bipolar and monopolar techniques. Adapted from Jahangiri et al. 2020

Stimulation Parameters		
Specification	Penfield	Taniguchi
Type of Stimulator	Bipolar	Monopolar
Type of Pulse (Phase)	Biphasic or Monophasic	Monophasic Anodal
Frequency	50 Hz	250-500 Hz
Pulse width	300 - 1000 $\mu$ s	500 $\mu$ s
Intensity	2 - 20 mA	2 - 20 mA
Duration of stimulation	2 - 5 s	20 $\mu$ s

The polarity of monopolar stimulation is critical to achieve appropriate levels of neuronal activation. Over the cortex, anodal stimulation is favored as the active electrode. Anodal current is favorable as its use requires less charge to reach excitation threshold for neurons that are oriented perpendicular relative to the electrode. For grey matter, this approach achieves focal stimulation at lower stimulation intensities. The opposite is true for subcritical stimulation where neurons are often oriented near parallel to the probe in

use. Cathodal stimulation is favored in these cases where excitation can be achieved at a lower stimulation threshold (Manola et al., 2007).

If the anatomic structures in question are assumed to be components of Broca's or Wernicke's language centers, there are additional considerations for interpreting responses. First, it is best practice to use fMRI to localize the lateralization of these centers. While 80% of the population have language centers localized to the left side of the brain, this is not the case for all (Hugdahl & Westerhausen, 2016). For this reason, fMRI imaging is commonly used preoperatively if surgical targets are within the temporal or lateral frontal lobes. If it is found that language centers are ipsilateral to the surgical site, language mapping during an awake craniotomy is indicated. In this case, bipolar Penfield stimulation or monopolar stimulation can be effective (Morshed et al., 2020; Verst et al., 2018).

### *Recording*

Direct cortical stimulation benefits from the inclusion multimodality neuromonitoring as it utilizes similar recording. Like TceMEPs, cortical mapping of motor eloquent structures requires recording from distal muscles. When using bipolar stimulation, twitch responses are expected to be recorded as the electrode is placed over the primary motor cortex. Twitches are then recorded using spontaneous electromyography (sEMG) channels in muscle groups that are innervated by the pyramidal tracts associated with the stimulated region of cortex. When using monopolar stimulation, the applied pulse is time

locked with recording producing a compound muscle action potential (CMAP) waveform that can be compared to recordings throughout the duration of the procedure in morphology, latency, and amplitude.

Monopolar cortical mapping in this style allows for the possibility of continuous motor mapping throughout the duration of a procedure. Using a grid electrode, direct cortical motor evoked potentials (dcMEPs) can be monitored continuously. By using the same stimulation parameters as monopolar mapping, MEPs evoked from the cortex serve as an additional modality that is diagnostic of postoperative patient outcome. It serves as a warning when resection has strayed into cortical or pyramidal tracts associated with the muscle group of the evoked response. While it cannot replace continuous TceMEP monitoring, it can provide feedback about the integrity of corticospinal tracts without the need for high intensity stimulation that results in patient movement that can be disruptive to the surgeon at critical phases in a procedure.

During cortical stimulation, it is critical to record ECoG. Electrical stimulation of the brain can induce seizure which may have significant implications of the continuation of the procedure. A temporary surface grid electrode must be placed over the cortex near the surgical site of interest. Continuous monitoring of ECoG activity can inform surgical staff of epileptiform activity, known as after discharges (AD), before a patient begins showing the physical signs of a seizure (Jahangiri et al., 2020). In the event ADs are noted ice cold lactated ringers solution should immediately be introduced into the

surgical site and antiepileptic drugs administered. ECoG can be critical for the early identification of intraoperative seizure and rapid control.

### *Interpretation*

Commonly, intraoperative neurophysiological mapping will be utilized with continuous, multimodality neuromonitoring (Cabreja et al., 2009; Kombos et al., 2001; Moiyadi et al., 2018). With the inclusion of TceMEP monitoring, noninvasive electrical stimuli above the scalp are utilized to record time-locked twitch responses from distal muscles. During TceMEP monitoring these are often monitored throughout the duration of the procedure where recorded amplitudes falling below a predetermined criterion constitute an alert. However, if the primary role of stimulation is simply mapping motor eloquent cortex or white matter, the presence or absence of a response is sufficient. This is shared between both bipolar and monopolar stimulation techniques though the time-locked recording following monopolar stimulation serves as a clearer snapshot of which muscle groups were activated.

Studies have also begun adding continuous dcMEPs during resection and cortical and subcortical mapping after motor eloquent cortex has been identified. In such cases, a grid electrode can be placed over the identified cortical area and dcMEPs can be evoked throughout the procedure to assess the integrity of both the cortical region and pyramidal tracts beneath. Current accepted standards indicate that a decrease in amplitude of 50-80% of baseline amplitudes indicate possible insult to the motor cortex and new post-

operative motor deficit if unresolved (Lee et al., 2014). However, it is possible that tailoring alert criteria to the lesion in question may be an appropriate strategy in decreasing incidences of false-positive alerts (Kombos et al., 2009; Obermueller et al., 2015).

### *Anesthetic Consideration*

As with many protocols involving intraoperative neuromonitoring (IONM), total intravenous anesthesia (TIVA) is widely considered to be necessary in mitigation of false-positives (Tamkus et al., 2014; Ushirozako et al., 2019). When general anesthesia is allowed, sedation should be achieved using a combination of propofol at doses < 150 µg/kg/min and remifentanyl with non-depolarizing neuromuscular blockade only administered at induction. When measured with intraoperative bispectral index (BIS), patients should be kept between 40 and 60 on a scale from 0-100 to allow for accurate monitoring, reliable ECoG, and limited patient movement (Chen, 2004; Finger et al., 2016). Intravenous adjuncts such as ketamine, dexmedetomidine, and lidocaine may also be considered as appropriate when maintain sedation in an effort to keep propofol doses low (Walker et al., 2020). Continuation of anti-epilepsy drugs is recommended for patients presenting with seizure history. Volatile inhalational agents should be avoided at any dosage. At doses of 0.5% inhalational volume isoflurane can obliterate TceMEP amplitude and increase the rate of false-positive motor alerts (Tamkus et al., 2014; Zhou & Zhu, 2000). These findings are similar across all fluorinated ether anesthetic agents.

During traditional TceMEP monitoring, false-positives can result in changes to the surgical approach as true decreases in TceMEP amplitude indicate the need for surgeon intervention. If volatile inhalational agents were utilized during mapping of motor eloquent regions, stimulation would likely not result in depolarization sufficient to activate of neurons in the corticospinal tract and responses would not be seen. This would increase the chance of unsuccessful mapping and decrease the success of GTR. While the exact mechanism of action for volatile inhalational agents is not fully elucidated, it is understood that its broad action on various chloride and potassium channels lends to its ability to provide analgesia, amnesia, and paralysis effectively. Their action on pathways containing muscarinic acetylcholine, cholinergic acetylcholine, glutamine, and serotonin receptors is the both the reason it is favored anesthetically, but a challenge for evoking motor potentials (Akk et al., 2008; Miller et al., 2021).

For procedures that require the patient to be awake, as in language mapping, special anesthetic considerations must be made. There are multiple accepted approaches: the asleep-awake-asleep method, monitored anesthesia care (MAC), or conscious sedation (Stevanovic et al., 2016). In the former, induction utilizes a combination of intravenous anesthetic agents such as propofol, remifentanyl, and/or dexmedetomidine and the patient can continue on this regimen throughout the duration of the craniotomy (Kulikov & Lubnin, 2018; Morshed et al., 2020). In the latter, the patient anesthetic considerations become increasingly complex. While there is no accepted standard for premedication, administration of a benzodiazepine is widely considered acceptable and antiemetic agents

should be available due to the risk of intractable nausea related to surgical manipulation of the dura or cerebral blood vessels (Piccioni & Fanzio, 2008). Nerve blocks prior to exposure and craniotomy are considered effective and the use of dexmedetomidine and opioids have proven to be an effective alternative to propofol under MAC (Kulikov & Lubnin, 2018; Piccioni & Fanzio, 2008)

Additional concerns during awake craniotomies include airway maintenance and patient cooperation. During asleep-awake-asleep craniotomies, anesthesiologists must be able to maintain an airway during the asleep portion of the procedure, and remove an endotracheal tube or laryngeal mask airway (LMA). They must also feel that the patient is positioned in a way where they can access the airway if needed during the awake portion of the procedure, and where the patient can communicate with surgical staff. It is also important to consider that patients who undergo the procedure with the asleep-awake-awake are less likely to experience intraoperative seizure. In a case series of 64 patients, it was found that those 19% of patients in the conscious sedation group experiences intraoperative, post-stimulation seizure. The asleep-awake-asleep group experienced 0 seizures throughout emphasizing that this approach is likely safer for the patient ( $p < 0.05$ ). Furthermore, patients are less likely to experience agitation during asleep-awake-asleep craniotomy versus conscious sedation making management easier for surgical staff ( $p < 0.05$ ) (Dilmen et al., 2017).

Overall, the anesthetic plan of preference should be based on a multidisciplinary analysis of patient safety, surgical considerations, and anesthesiologist preference (Morshed et al., 2020). That being said, a recent meta-analysis study has indicated that the sleep-awake-asleep method and MAC is considered safe and is widely accepted. Full awake techniques, while applicable, are generally not favored due to challenges of patient compliance and intraoperative hypertension. In the analysis, of all patients who underwent a craniotomy and were awake throughout the duration of the procedure, 44% experienced intraoperative hypertension and a higher proportion of seizures relative to other anesthetic techniques (Stevanovic et al., 2016).

## **Application**

### *Tumor Resection*

Resection of primary neoplasms or metastatic lesions of the brain presents a host of challenges. Depending on location of the lesion, there are any number of specific regions of the brain that are at risk during a procedure. Mapping of cortical and subcortical structures becomes critically important if it is believed that the margin of a tumor exists near an eloquent region of cortex or its underlying white matter.

When the concern is the primary motor cortex, cortical mapping is indicated and should contain any variation on the application of stimulation explained above. After identification of the central sulcus using somatosensory phase reversal (PR) (see section on Somatosensory Evoked Potential Phase Reversal) the approximate location of the

motor cortex can be approximated (Yingling, 2011). Intraoperative motor mapping becomes critically important due to changes in the tumors mass effect. While pre-operative imaging techniques in combination with transcranial magnetic stimulation (TMS) can provide the surgical team with a detailed view of the patients anatomy, the surgical field will deviate from imaging as the tumor is debulked (Zakaria & Prabhu, 2017).

One concern when selecting stimulation type for mapping of eloquent motor structures is intraoperative seizure risk. Application of electrical stimuli directly to the cortex or subcortical regions is known to evoke seizures in 9.5% and 1.2% of procedures where bipolar and monopolar stimulation is utilized respectively (Yingling, 2011). There is no statistically significant difference in the occurrence of intraoperative seizure between those presenting with symptomatic epilepsy and those that do not during pre-surgical evaluation (Andrea Szelényi et al., 2007). Furthermore, application of monopolar stimulation has been shown to be more effective in than bipolar stimulation during subcortical mapping of pyramidal tracts. Monopolar techniques were found to elicit responses in 92% of attempts versus 54% when bipolar stimulation was utilized and with lower stimulation intensity thresholds (A. Szelényi et al., 2011). This style of stimulation can be completed in tandem with resection to alert the surgeon to proximity of the CST (Fig. 7).

If there is concern for language centers or for the arcuate fasciculus near tumor margins, eloquent language mapping is indicated (A. B. Acharya & Maani, 2021; Morshed et al., 2020). Regardless of anesthetic approach, a patient will be awake during the most critical portions of resection and stimulation is applied using either bipolar or monopolar techniques. However, recent studies have shown that high-frequency monopolar mapping can be equally as effective in language mapping while being less likely to induce seizure. In a recent prospective cohort study, differences in sensitivity and specificity were noted where bipolar stimulation was more sensitive than monopolar stimulation at 45.8% versus 36.7% and more precise at 66.5% and 58.2% for both groups respectively. These values were calculated from a total of 1,603 total responses elicited during awake craniotomies but were from a cohort that is too small to statistically analyze. Though these differences do exist, language arrest was established in all patients regardless of stimulation type with and the mean EOR across the entire cohort was  $95.3 \pm 15.6\%$  with 5 patients experiencing ADs and intraoperative seizure which only occurred during monopolar stimulation (Riva et al., 2016). It is believed that, high-frequency monopolar stimulation is effective for cortical and subcortical language mapping during awake craniotomy with a lower risk of seizure mirroring what is known about the use of monopolar motor mapping (Bello et al., 2014; Seidel et al., 2012).

In a recent series of neuro-oncology patients who underwent tumor resections, approximately one quarter of all patients received some form of intraoperative mapping (Giamouriadis et al., 2020). When indicated, such mapping, even at increased cost,

results in better patient outcomes. In a 2013 cost-benefit analysis of patients diagnosed with WHO grade II glioma who received intraoperative mapping versus those who did not, it was found that there was that the mean cost per quality adjusted life year (QALY) was significantly lower in patients who received mapping. The mean cost per QALY for those that received mapping was found to be \$12,22.30 (USD) versus \$31,927,10 (USD) in the group that did not (Martino et al., 2013).

Based on the available research, it would appear that the use of monopolar stimulation serves as a more well-rounded approach with sufficient efficacy during cortical motor mapping, subcortical motor mapping, cortical language mapping, ad subcortical mapping of the arcuate fasciculus. Being able to achieve these results with a decreased incidence of intraoperative AD and seizure also proves to be beneficial for patient safety and decreases the chance of aborted procedure (Bello et al., 2014; Riva et al., 2016; Seidel et al., 2012; A. Szelényi et al., 2011).

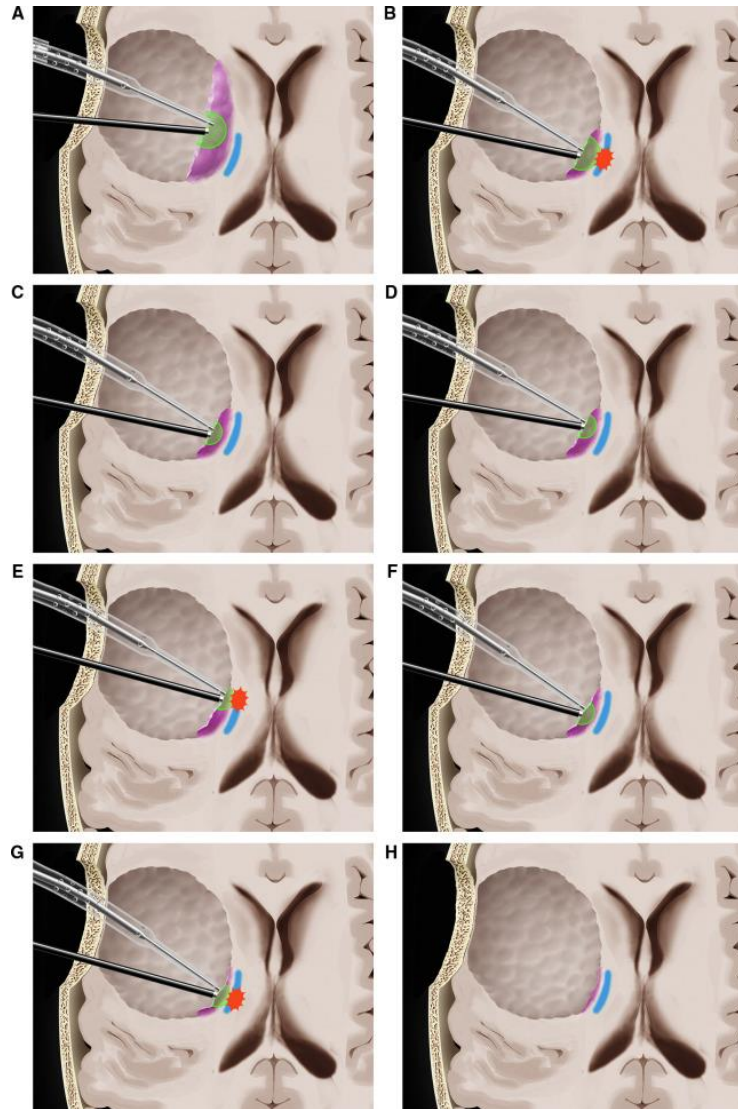


Figure 7: Illustration of subcortical resection using ultrasonic aspirator and continuous high frequency monopolar stimulation. Purple represents lesion. Blue represents eloquent CST. Adapted from Schucht et al. 2017

## SOMATOSENSORY EVOKED POTENTIAL PHASE REVERSAL

Pre-operative evaluation of the location of the primary motor cortex is critical in planning the surgical approach for tumor resection. While the results of pre-operative MRI, MEG,

and TMS evaluation can highlight the location of the motor cortex, intraoperative evaluation is still critical due to tumor mass-effect and anatomic shift during craniotomy and resection (Korvenoja et al., 2006). To emphasize this, a case series revealed that pre-operative MRI data differs from intraoperative neurophysiological findings approximately 12% of the time (Cedzich et al., 1996). Even with modern imaging techniques, the use of phase reversal (PR) is an effective tool in orienting the surgeon to the anatomical structures of the brain (Yingling, 2011).

## **Technique**

Many of the considerations for phase reversal rely upon the use of somatosensory evoked potential (SSEP) monitoring. SSEPs are commonly used during procedures that may risk insult to the CNS and PNS and can be diagnostic of the integrity of the dorsal column of the spinal cord, peripheral nerves, medial lemniscus, and sensory cortex. Their use involves the stimulation of peripheral nerves and recording of activity over the sensory cortex, cervical spine, and a peripheral recording location. The information conveyed from these recordings can provide surgical teams with information related to surgical changes intraoperatively to structures of the sensory tract.

### *Stimulation*

The most common peripheral nerve utilized for PR mapping is the median nerve. The median nerve benefits from having larger cortical representation than many other peripheral nerves that are commonly utilized during IONM (Allison et al., 1991). Thus,

high amplitude cortical responses can be recorded with better SNR relative to other potential stimulation sites. SSEP recording are completed using scalp electrodes to collect baseline values, confirm acceptable waveform and morphology, and assess the utility of phase reversal.

Once the craniotomy is complete and the location of the central sulcus approximated, the median nerve is stimulated. Electrodes are placed over the median nerve contralateral to the craniotomy, 2 cm proximal to the crease of the wrist between the tendons of the palmaris longus and the flexor carpi radialis. Stimulation parameters are consistent with standard SSEP stimulation and require approximately 250-1000 trials averaged to achieve an acceptable SNR. Commonly accepted repetition rates are 1.41, 2.79, 3.11, and 3.17 with a rectangular, monophasic pulse duration of 300  $\mu$ Sec, and a stimulation intensity between 20 and 30 mA for a neurologically intact patient (American Clinical Neurophysiology Society, 2009; Simon et al., 2014).

#### *Recording and Interpretation*

Recording phase reversal signals is most commonly completed using a grid electrode placed over the cortex longitudinally over the approximate location of the central sulcus. Grid electrodes come in a number of sizes with the most common for phase reversal being a 1 x 6 strip electrode made with platinum contacts. Similar to EEG, recording montages use differential amplification of an active electrode over the cortex referenced

to a common electrode at Fz. Data analysis and visualization is completed digitally where software averages all recorded, time locked responses and averages the results.

The waveform of interest begins with a positive deflection visualized in recording with a peak named the N20 response. Following the N20, there is a reversal of recorded stimulation phase with a negative deflection for the P30 response (American Clinical Neurophysiology Society, 2009; Legatt & Kader, 2000). This positive to negative biphasic morphology is typical when recording directly over the somatosensory cortex along the post central gyrus and corresponds closely with Brodmann area 3b (Anzellotti et al., 2016). The further posterior an electrode is placed after crossing the central sulcus, the lower the recorded amplitude will be as the generator of the response becomes further away from the active electrode.

Over the primary motor cortex of the precentral gyrus, the described morphology inverts to include the P20, visualized as a negative deflection, followed by a change in polarity with the N30, seen as a positive deflection. If an electrode is placed directly over the central sulcus, amplitude will be notably low due to destructive interference from the opposing phase of the pre and postcentral sulcus. With this information, recorded data from a number of active electrodes placed over the cortex will yield waveforms that differ in phase and in amplitude where the central sulcus exists between the electrodes where the phase inverts. The anatomic cause for the reverse in phase can be visualized in Fig. 8 where a simplified dipole originating from the postcentral gyrus can be seen

moving along the central sulcus resulting in inverted polarity when recording anterior to the central sulcus (Jung et al., 2003). PR results can be easily visualized in practice as in Fig 9 where there is a clear inversion of the peak and trough highlighted by the red and yellow arrows.

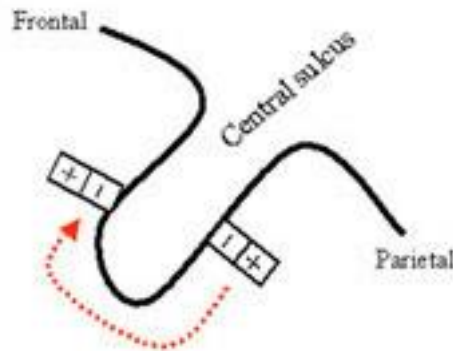


Figure 8: Simplified dipole propagation from postcentral gyrus to over the central sulcus. Adapted from Jung et al. 2003

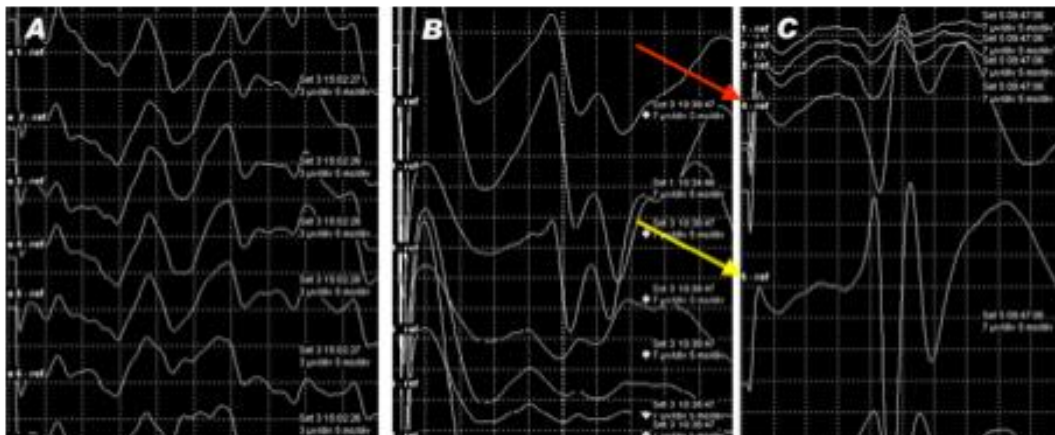


Figure 9: Visual representation of recorded phase reversal data recorded from a 1 x 8 grid electrode following stimulation of the median nerve. (A) Recording from the grid electrodes before placement over the central sulcus. Note that all channels show uniform morphology. (B) Recordings after initial grid placement. Montages 1-3 show clear N20 to P30 reflection indicating likely placement of the postcentral gyrus. Montages 4-7 show the same polarity but with notably decreased amplitude with increasing distance from generators of the somatosensory cortex. (C) Recordings after repositioning of the recording grid. Montages 1-4 show clear P20 to N30 deflection with montage 4 likely over the primary motor cortex (Red Arrow). Montage 5 shows an abrupt change in phase presenting with a distinct N20 and P30 (Yellow Arrow). Adapted from Simon et al. 2014

## **Application**

In procedures that require manipulation of the cortex near the motor eloquent structures of the brain, PR can be an effective tool in lucidating a patient's surgical anatomy. As previously highlighted, there are cases where fMRI data does not paint a clear picture of the location of the motor cortex.

Modernization in recording of PR is critical to allow for utilization of the technique in these instances. One approach has been to utilize a ball tip electrode as the active recording input and moving the electrode across the surface of the cortex. This approach may be slower in that multiple waveforms across a single area of cortex cannot be recorded at once increasing the time to central sulcus identification, but is validated for use with small craniotomies (Bharadwaj & Venkatraghavan, 2016).

Time in the operating room is of immense value. In a study published in the Journal of the American Medical Association, it was found that each minute of operating room time costs between \$36 and \$37 (USD) (Childers & Maggard-Gibbons, 2018). In another study, it was determined that, when PR was utilized prior to beginning motor mapping that the total time required for mapping was reduced by 48.6% (Simon et al., 2014). With this in mind, PR should be considered a critical modality for use during all motor mapping procedures.

## DORSAL COLUMN MAPPING

Intraoperative dorsal column mapping is an excellent tool that confirms the localization of the dorsal median sulcus (DMS)—a non-eloquent structure that lies between tracts of the dorsal column (Diaz & Morales, 2016; Jacquesson et al., 2014). This anatomic structure is of great importance when approaching the spinal cord during a surgical intervention. Presently, dorsal column mapping is indicated for use during intramedullary spinal cord tumor resections where the eloquent aspects of the dorsal column of the spinal cord are at risk during approach. When considering that the only effective curative intervention for many spinal cord tumors is resection, avoiding neurological sequelae during resection of the utmost importance.

### **Theory**

#### *Anatomical Considerations*

Sensory afferents ascend predominately rostrally via the dorsal column of the spinal cord. Within the dorsal column exists the structures of the cuneate fasciculus and gracile fasciculus which carry sensory information from the upper extremities/upper thoracic spine and the lower extremities/midthoracic spine respectively. The axons collected within these tracts synapse caudally in the ipsilateral dorsal root ganglion and rostrally in the medulla (Diaz & Morales, 2016). Between the left and right components of the dorsal column is the DMS, which is non-eloquent and generally considered the safest location to

enter the spinal cord for resection of IMSCT (Fig 10). The composition of the PMS differs from that of spinal cord white matter and is largely a layer of collagen that extends from the pia mater (Jacquesson et al., 2014).

Distal to the brainstem, all sensory tracts ascend ipsilateral to the activated sensory neuron. At the level of the medulla, the neurons of the fasciculus gracilis and cuneatus synapse at the nucleus gracilis and cuneatus respectively. The interneurons that these neurons synapse to project their axons through the sensory decussation and ascend via the medial lemniscus to the posterolateral nucleus of the thalamus where they synapse with pyramidal sensory neurons that project to the cortex contralateral to the source of sensation (Standring, 2021).

Dorsal column mapping takes advantage of these anatomical considerations to define the location of the DMS. Techniques that stimulate or record from the dorsal column involve activate axons of the dorsal column at the operative level or recording orthodromic responses that ascend the dorsal column in response to peripheral stimulation. Because these two techniques do not differ in their efficacy, it is important that surgical teams utilize the process that they deem to be the most efficient.

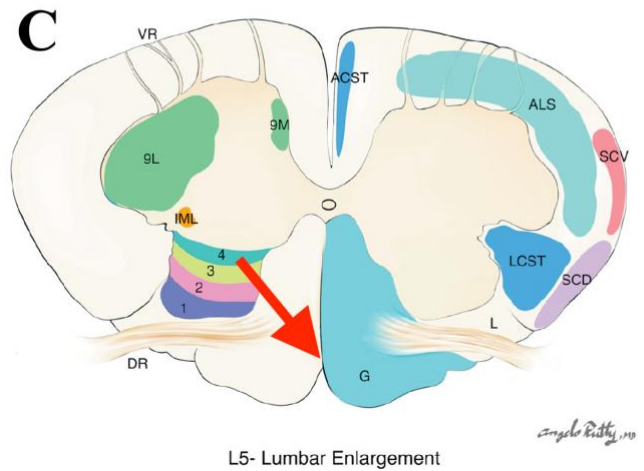
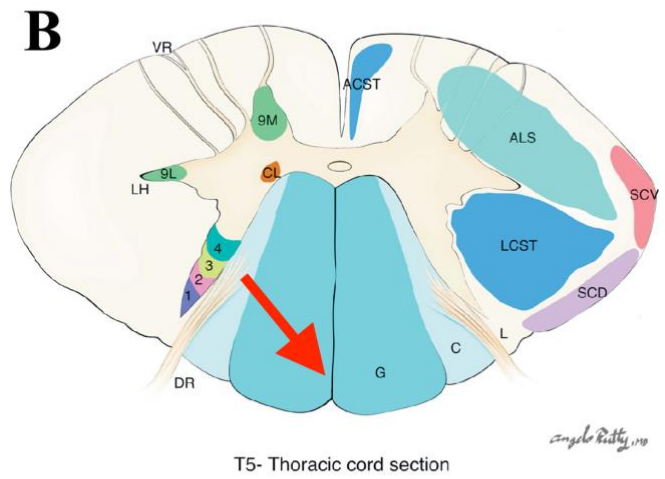
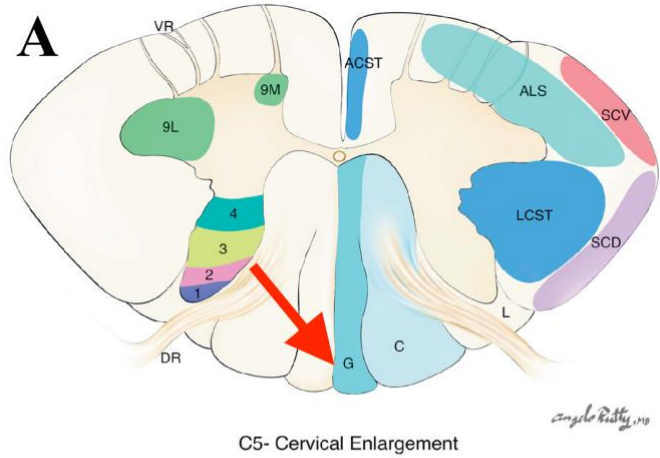


Figure 10: Anatomy of the spinal cord viewed in axial cross-section. Red arrow approximates the location of the dorsal median sulcus (A) cervical spinal cord. (B) Thoracic spinal cord. (C) Thoracolumbar spinal cord superior to cauda equina. Adapted from Diaz and Morales 2016

### *Action Potential Conduction*

Under normal circumstances, sensory input travels from peripheral nerves, to the dorsal root ganglion, where there is an additional synapse to a neuron whose axon projects up the dorsal column. Using the principals of SSEP monitoring, that are typically already in place during most IMSCT procedures, options exist for stimulating and recording that can be manipulated to provide information related to laterality of the dorsal column.

One common technique involves recording of orthodromic evoked potentials stimulated directly from the posterior spinal cord. Often referred to as orthodromic DCM, recordings are similar to SSEP recordings where the contralateral recording over the scalp results in a distinct N20 peak or P37 trough initial waveform from the median nerve or posterior tibial nerve (American Clinical Neurophysiology Society, 2009; Simon et al., 2012). However, the latency will be significantly lower and dependent upon the level of the surgical exposure and the differentiating factor will be the recorded polarity of the response. Alternative techniques can take advantage of antidromic action potentials that are stimulated at the cord and recorded from recording sites over peripheral nerves (Quinones-Hinojosa et al., 2002).

### **Technique**

#### *Orthodromic DCM*

Stimulation of the spinal cord at the level of the procedure, action potentials will travel rostrally along the dorsal column. Using recording montages shared with SSEP

monitoring, cortical activation initiated by the ascending action potentials from the cord are recorded. Typical stimulation parameters are between 0.5 and 2 mA in intensity, a pulse width of 200  $\mu$ Sec, and a frequency similar to that SSEP stimulation (American Clinical Neurophysiology Society, 2009; Simon et al., 2012). Stimulation can be achieved using a monopolar, bipolar, or bipolar concentric probe. Evidence suggests that utilization of an electrode with a guarded electrode produces stimulation at a lower intensity (Ramasubbu et al., 2013). Stimulation is made safer and more focal using a shielded electrode similar to a concentric bipolar probe mitigating risk to the cord and making mapping more accurate.

Recording utilizes the C3-C4 transcortical montage where the recording is not inverted depending upon where stimulation takes place. Effectively, stimulation to the right of the DMS results in a negative peak seen as an upward deflection when recorded and stimulation left of the DMS results in a positive peak seen as a downward deflection. When action potentials are evoked directly over the DMS, the SNR should be poor and there should be no prevailing deflection (Fig 11) (Nair et al., 2014).

#### *Antidromic DCM*

As an alternative to orthodromic DCM, the antidromic technique achieves mapping without the need for electrodes over the scalp. In this approach, a stimulation is achieved using the same methodology as previously mentioned, but rather than relying on the ascending action potential, we monitor the descending action potential that is traveling

antidromic to its intended path. Recoding is achieved over a peripheral nerve and is most commonly recorded from the posterior tibial nerve 2 cm distal to the medial malleoli (Quinones-Hinojosa et al., 2002). When using typical multimodality IONM, this requires removing the input leads from the posterior tibial nerve SSEP stimulating electrode from a stimulator and placing them into an amplifier manually.

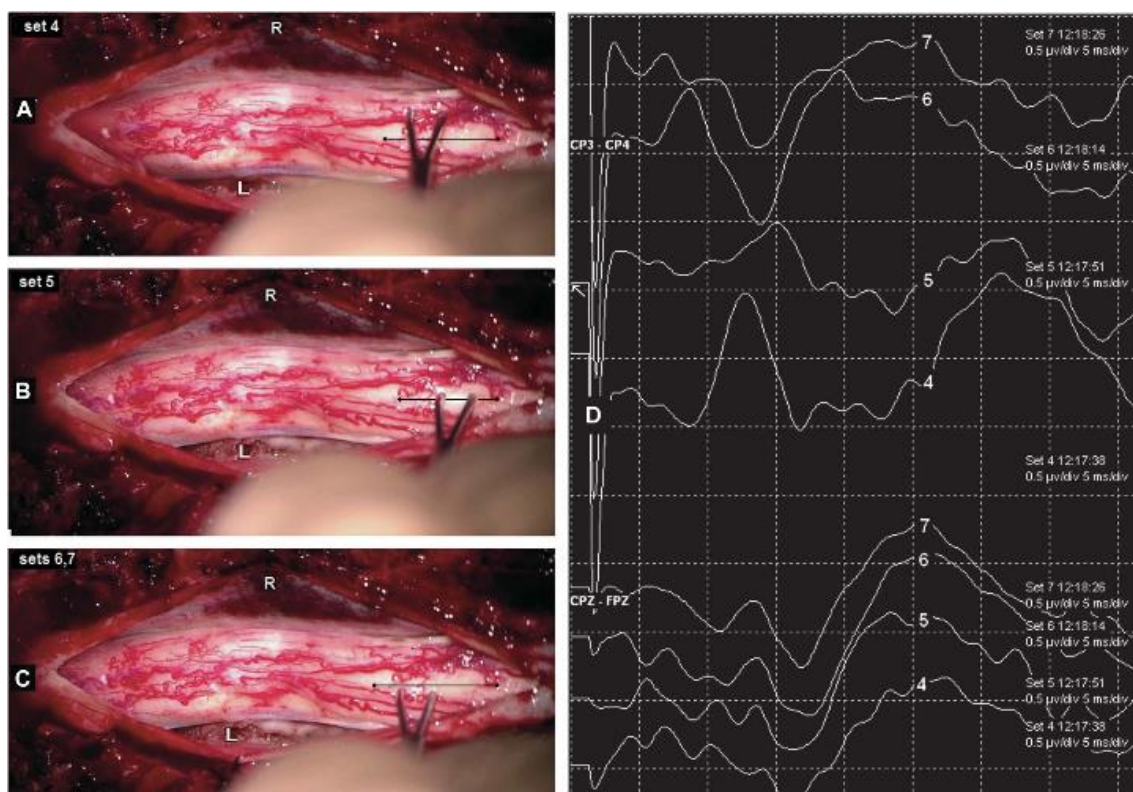


Figure 11: DCM stimulation technique and visualized results in both CP3-CP4 and CPz-FPz montages. (A) bipolar stimulation right of estimated PMS. Corresponding stimulation seen in Trace 4 with high SNR negative peak. (B) Bipolar stimulation directly over predicted PMS. Corresponding stimulation seen in Trace 5 with a small negative peak with poor SNR. (C) bipolar stimulation left of estimated PMS. Corresponding Trace 6 and 7 with high SNR positive peak. (D) Waterfall view of Traces 4-7 in CP3-CP4 and CPz-FPz montages. Adapted from Nair et al. 2014

As in other methods, recordings are averaged over many trials, similar to SSEP recording, requiring the surgeon to maintain stimulator position for the duration of trialing. Once a clear waveform has been visualized, the surgeon can move the probe

laterally across the cord to the next stimulation location. Recordings that are equal in amplitude, or bilaterally absent, indicate likely positioning over the DMS. Lateralization in amplitude between the left and right recording indicate that stimulation is being applied ipsilateral to the DMS relative to the side with higher amplitude.

### *Collision Studies*

An effective method of assessing lateralization can be achieved by providing destructive interference. SSEP collision studies act based on principles of spinal cord stimulators (SCS) that reduce the symptoms of chronic, intractable pain by providing continuous electrical stimulation to the dorsal column epidurally. SCS electrodes are typically multi-contact paddle electrodes that are placed in the epidural space over in the cervicothoracic spine. To maximize the effect of the SCS implant, stimulation must be provided over the dorsal columns bilaterally or unilaterally in the case of unilateral chronic pain. Collision studies have become a useful intraoperative test that is diagnostic of lateralization of the electrode or contacts utilized.

Lower extremity posterior tibial nerve SSEP baseline recordings are achieved using standard IONM protocols with monophasic rectangular pulses of 20-30 mA, a pulse duration of 300  $\mu$ Sec and 250-1000 trials averaged to achieve an acceptable SNR at a repetition rate of 1.41, 2.79, 3.11, and 3.17 (American Clinical Neurophysiology Society, 2009). Once the electrode has been positioned and is ready to be trialed, baseline responses are reset, reject settings are deactivated, and the SCS implant is activated.

Stimulation is increased incrementally with a trial of SSEPs run at each stimulation intensity. If the electrode is placed midline and central contacts on the paddle electrode are selected, action potentials will be evoked locally at the level of the electrode causing action potentials to propagate in the orthodromic and antidromic directions. The antidromic action potentials will collide with the ascending action potentials traveling orthodromic from the posterior tibial nerve caudally. The collision will result in a decrease in SSEP amplitude as recorded over the somatosensory cortex. Bilateral and uniform decreases in response amplitude below 70% of baseline is sufficient criteria for acceptance of midline placement (Fig. 12) (Balzer et al., 2011; Choi et al., 2015).

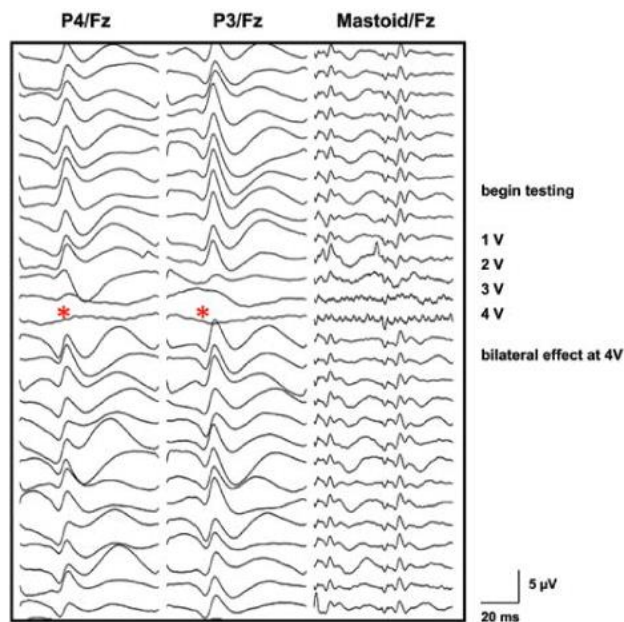


Figure 12: Example of bilateral median nerve collision following activation of bilaterally placed SCS paddle electrode over the dorsal cervical spinal cord. (\*) Note the increase in stimulator intensity and subsequent obliteration of recorded SSEP amplitude in from both left and right recording montages. Adapted from Blazer et al 2011.

### *Variations*

Orthodromic and antidromic techniques for DCM are well understood and variable in their application. The basis for both lies in basic understanding of SSEPs and the anatomy of the dorsal column. With some modification, a variation on the orthodromic method can yield similar results by recording from the spinal cord rather than stimulating. This has been explored by some surgical teams by utilizing a recording array and stimulating for a peripheral nerve. While its efficacy has been proven, many have struggled to find an electrode array that is both small enough to fit over the posterior aspect of the spinal cord and is appropriate for recording responses with sufficient focal resolution. Yanni et al. found that this method was successful in a case series of 10 patients who presented with IMSCT. During this series, surgeons effectively identified the dorsal column using a grid style electrode in all ten patients, and did so faster than using techniques requiring a handheld probe as described above (Yanni et al., 2010).

## **Application**

### *IMSCT Resection*

In the literature, dorsal column mapping is most practically used during IMSCT resection where a myelotomy is required. While risky, posterior midline myelotomy remains the safest approach with the highest likelihood of achieving GTR (Katsigiannis et al., 2020; Samartzis et al., 2016). This approach can be achieved based on visual assessment, but there is an associated risk as the anatomy is commonly distorted due to the tumor itself, edema, vascularization, and scar formation (Yanni et al., 2010). Combined with the fact

that imaging techniques have not yet achieved an effective method of visualizing the dorsal column of the spinal cord pre-operatively, DCM is critical to mitigate risk of insult to the dorsal column.

In a retrospective cohort study that studied the efficacy of DCM in 91 IMSCT patients that underwent resection, those that received DCM were significantly less likely to emerge with new postoperative dorsal column dysfunction. 9% of those with DCM suffered from new neurologic sensory deficit compared to 50% in the group that did not have DCM ( $p = 0.01$ ). These results effectively demonstrated the importance of DCM and the need to implement effective strategies to make DCM an easy to use tool at any institution regularly attempting IMSCT resections (Mehta et al., 2012).

### *Spinal Cord Stimulator Placement*

Placement of SCS paddle electrodes under general anesthesia has been proven to be safe and effective. Earlier techniques required conscious sedation such that the patient could be responsive to describe where they felt paresthesia during electrode activation.

Numerous problems were associated with this approach including airway access while the patient is prone. To alleviate this concern, neurophysiological techniques to test SCS location under general anesthesia have been validated. In a retrospective cohort study of 172 SCS electrode placement procedures, it was found that the use of general anesthesia and neurophysiological testing to confirm laterality of the SCS electrode was as effective as placement in an awake patient (Shils & Arle, 2012).

When considering collision studies specifically, as an adjunct to multimodality monitoring and testing, has shown efficacy in confirming SCS paddle electrode placement. In a retrospective review of 25 patients who had SCS electrodes placed for treatment of chronic pain at a single institution, all patients had successful electrode placement with no incidence of subsequent revision procedures (Choi et al., 2015).

### **ANTEROLATERAL TRACT MAPPING**

Like subcortical mapping of the brain, stimulation of the corticospinal tract (CST) can be an effective tool in preserving the axons of spinothalamic tract. Multimodality IONM does serve a vital role in providing real-time information regarding the integrity of the of the nervous system, but it cannot convey instantaneous data that will drive clinical decision about margins of resection. For IMSCT resections where GTR is critical after an inherently complicated surgical approach, mapping throughout a resection is beneficial in defining the tumors margin while preserving eloquent regions of the spinal cord (Francesco Sala et al., 2007).

#### **Theory**

##### *The corticospinal tract*

The majority of fibers of the corticospinal tract arise from the cortex of the brain and project distally. Brodmann area 4 is the primary region of the cortex where these neurons originate before descending through the subcortical brain and enter the internal capsule.

Corticospinal fibers form the pyramid along the ventral surface of the medulla before decussating rostral to the spinomedullary junction. This bundle contains 90% of axons that originated from the cortex where the remaining 10% do not decussate. As fibers descend through the spinal cord, 50% terminate in the cervical spine, 20% in the thoracic spine, and the final 30% in the lumbosacral spine (Standring, 2021).

Like axons of the dorsal column, the axons of the CST can be depolarized along their axon sending action potentials in both the orthodromic and antidromic directions. During resection, it is likely that additional fibers are being activated due to the high density of axons and the close distances between eloquent regions of the spinal cord. Mapping of this region is largely meant to alert the surgeon in of real-time proximity to motor eloquent structures and likely does not show any specificity to CST only. In a letter to the editor of the Journal of Neurosurgery related to specificity in anterolateral tract mapping, Deletis et al. emphasized that stimulation of the dorsal column alone can evoke responses from distal muscle groups. Stimulation of the dorsal column evokes action potentials in both the orthodromic and antidromic direction. The descending antidromic action potentials can synapse on to alpha motor neurons distally an initiate a response via the Hoffman Reflex (Fig. 13) (Deletis et al., 2017). For this reason alone, it should be noted that stimulation of fibers within the spinal cord do not activate CST neurons only.

## Technique

During resection of IMSCTs, the pathology of the lesion can make GTR challenging. Cystic lesions or those that are well infiltrated can be particularly challenging when

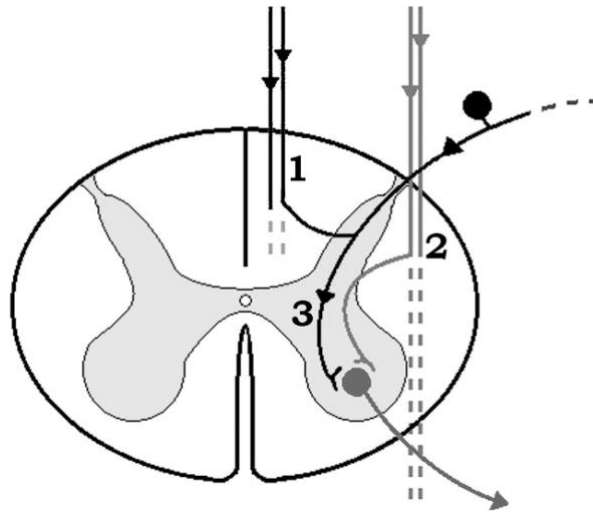


Figure 13: Simplified diagram of the central H-reflex. (1) dorsal column with antidromic action potentials. (2) Axons and projections of the CST. (3) Synaptic projection from branch of the dorsal root ganglion. Adapted from Deletis et al. 2017

attempting to define a margin of resection. Direct stimulation can be an effective strategy after completing the DMS myelotomy and once the lesion has been located.

It is important to note that there is no widely accepted stimulation method with multiple case studies utilizing different techniques. During resection, continuous stimulation can be achieved with a number of stimulation probes. Similar to subcortical mapping, it is likely that the type of stimulation applied may play a role in how effective stimulation is at evoking a response (Manola et al., 2007). However, sufficient intraoperative data does not exist to provide validation of differences between monopolar and bipolar mapping during anterolateral tract mapping.

Like cortical mapping, recoding of mapping responses is achieved using bipolar muscle recording of CMAPs. This is similar to EMG or TceMEP monitoring. Stimulation is then applied at intensities of 0.1-1 mA and time-locked EMG records subsequent responses (Gandhi et al., 2015). For monopolar techniques, a pulse train style of stimulation can also be utilized where 2-3 pulses are recommended (Barzilai et al., 2017).

### **Application**

Gandhi et al. found success with the use of bipolar stimulation using a concentric bipolar probe. In an illustrative case report, they effectively mapped the surgical field with significant precision and were able to isolate regions with specific motor responses (Gandhi et al., 2015). While these cannot be completely validated to be stimulating via the CST, it proved an effective tool in expanding the margin of resection.

Alternative stimulation techniques that utilize monopolar stimulation have shown significant efficacy. In a retrospective series review of 6 cases illustrated by Barzilai et al., the utility and versatility of monopolar mapping was highlighted. In this particular series, Monopolar stimulation was evoked through an electrified ultrasonic aspirator tip. This method has been explored as a method of mapping using the same tool used for resection and suction. By eliminating the need for an additional tool for stimulation,

eloquent regions that are activated in response to stimulation can be avoided and tumor margins can be easily avoided (Barzilai et al., 2017).

## **FUTURE CONSIDERATIONS AND RECOMMENDATIONS**

The neurophysiological mapping modalities described have been developed over decades and incrementally improved. For this reason, it is critical that each continue to evolve to best serve patients. The discussion below highlights areas of current and future research regarding the utilization of these modalities.

### **Pre-Operative Brain Mapping**

EEG is a long-standing tool that is well understood, cost effective, and widely applicable. It will continue to be a mainstay diagnostic modality, but in combination with others. In support of this, past and current research continues to highlight the importance of EEG use in combination with MEG and fMRI for pre-operative mapping of the brain. In a model to determine the cost-effectiveness of adding MEG or utilizing MEG in pre-operative intracranial EEG assessment, it was found MEG is not more cost effective per QALY. This model determined that the addition of MEG to the standard assessment for epilepsy surgery results in a clear increase in cost over time per year of life. However, they did assert that the validity of MEG is a reasonable expense (Berrigan et al., 2016).

However, there is little doubt that as MEG technology continues to advance, the efficacy of MEG to locate epileptogenic zones targeted for resection will surpass that of EEG recording. In a 1999 study, this relationship was already well understood. MEG was only second to invasive, intracranial EEG recording for targeting epileptogenic zones. For those with temporal lobe foci, MEG was worse than intracranial EEG with 57% and 62% success in identification of foci respectively. When removing invasive recording approaches, MEG surpasses the efficacy of scalp recorded EEG with 52% success when using MEG compared to 45% success for EEG during the interictal phase (Wheless et al., 1999).

This study may be dated, but it is illustrative of how rapidly advancing MEG technology is proving more successful at identifying epileptic foci when targeting for surgical resection. Just five years later, an additional study showed that, while MEG and scalp EEG were comparable in their efficacy in 32.3% of cases, MEG was able to identify more specific localization in 40% of patients. Of additional interest was that MEG was able to localize epileptogenic zones in 58.8% of patients for whom EEG was unable to identify a focus and was 72.8% effective in identifying the focus when EEG was non-localizing (Pataria et al., 2004).

These results clearly identify differences in the utility of EEG and MEG in a very specific use case, but it is critical to emphasize that both are important tools for different use cases. In the clinical setting, EEG is well understood and provides excellent spatial

resolution while being technically simple to setup. In combination with fMRI, it can be utilized to analyze a wide range of situations including task-related and resting state recording. By adding MEG recording, there is the added benefit of being able to assess fast changes in resting-state networks that will prove to be critical in understanding underlying networks related to epilepsy. As epilepsy is now understood as a whole brain disease, such understanding beyond the focus of seizure will require continued advancement and integration with traditional EEG recording (Pittau et al., 2014; Youssofzadeh et al., 2018).

### **Intraoperative Cortical Mapping and Phase Reversal**

Methods used to map the cortex and subcortical region intraoperatively are generally well studied and there is little debate related to their efficacy or theory. However, there is still continued debate in the United States about which stimulation modality to use. When comparing bipolar stimulation to monopolar stimulation, a transition to monopolar cortical and subcortical stimulation is recommended. Evidence continues to suggest that monopolar, high-frequency train stimulation is able to elicit cortical activation at lower stimulation intensities while inducing seizure at lower rates than bipolar stimulation. Even for language mapping, for which bipolar stimulation is still considered the standard, monopolar mapping has been proven to be effective and safe (Morshed et al., 2020; Riva et al., 2016; Verst et al., 2018).

One area of continued interest is the differences in intraoperative seizure activity between monopolar and bipolar language mapping. Some case studies have already revealed that,

for motor mapping, there is a clear benefit to using monopolar stimulation without significant seizure risk. Even among subcortical mapping, the incidence of seizure is only 4% when utilizing monopolar stimulation (Raabe et al., 2014). However, in the cohort of patients studied by Verst et al., they showed an incidence of intraoperative seizure of 7.3%. This is consistent with the literature which reports the risk of seizure activity anywhere between 2 and 67%. This reference range is not specific to stimulation method (Verst et al., 2018). Large retrospective studies do not exist comparing monopolar and bipolar stimulation for this use case and is an important area of future study.

Similarly, PR methodology has been carefully elucidated and applied. The method of identification of the central sulcus is widely accepted when indicated and provides excellent intraoperative feedback to the surgeon. Additionally, the use of fMRI exclusively cannot be relied upon during the intraoperative phase. Even with recent imaging and excellent stereotactic navigation, the results of fMRI to highlight the primary motor cortex are not perfect. In a prospective evaluation of 15 patients presenting with supratentorial lesions of the primary sensorimotor cortex, fMRI performed worse than MEG where 4 of the patients had fMRI results that differed from intraoperative PR findings (Korvenoja et al., 2006).

One final area of continued interest is in validating electrical subcortical mapping with distance to eloquent structures. Nossek et al. was able to illustrate an approximation of 1mm radius of tissue activation for every 1 mA of increased stimulation. Using

intraoperative ultrasonography, stimulation results were correlated with pre-operative DTI imaging (Nossek et al., 2011). These results have been widely accepted, though additional computational models and intraoperative validation using high resolution intraoperative stereotactic navigation may be beneficial.

Overall, the future of brain mapping requires additional study to compare the efficacy and safety of existing modalities. As indicated, there is sufficient evidence to favor monopolar over bipolar mapping for improved efficacy and patient safety. It is time that surgeons compare both on their merits and shift towards safer monopolar stimulation.

### **Spinal Cord Mapping**

During procedures of the spinal cord, there are a number of areas of interest that will be critical in expanding our understanding of intraoperative mapping. These include improving data interpretation of DCM and validating stimulation techniques for SCT stimulation.

As illustrated by Barzilai et al., introducing a monopolar stimulator into resection tools is a valid approach for IMSCT resection. This method allows for continued stimulation and mapping while continuing to resect and improve margins of resection. While this was a small cohort technical demonstration, there is a clear benefit to this approach (Barzilai et al., 2017). Others have found similar methods effective during brain lesion resection with

stimulating suction tips which proved to maximize resection with acceptable morbidity (Moiyadi et al., 2018).

Regarding interpretation of DCM, few studies have attempted to assess the amount of time required to complete DCM and alternative approaches in presenting data. A common anecdote from surgical teams is that DCM adds time to a resection and, when the DMS is clearly visible and sensory deficit generally acceptable, DCM may be unnecessary. However, as was highlighted by Mehta et al. and mentioned above, there is a significant difference in sensory outcomes when DCM is utilized (Mehta et al., 2012). This cannot be ignored, and DCM should be considered the gold standard for IMSCT resection approach. What can and should be explored is how to make the application easier and faster. Improvements will likely require advancements in grid electrode arrays for recording orthodromic responses. Current arrays can be cumbersome and challenging to keep in place with sufficiently low impedance. However, if this is achieved, DCM could be completed with one trial of interleaved peripheral nerve stimulation rather than multiple trials across the entirety of the spinal cord.

This technique recommended for future advancement of dorsal column mapping could have implications outside of IMSCT resections. Similarly, implantation of SCS paddle electrodes benefits from dorsal column mapping using collision studies or the H-reflex. Similar anecdotes related to the increase in surgical time prevail in this space as such testing can be time consuming. However, if the SCS paddle were to be utilized as an

array and an automated system interleaving peripheral nerve stimulation were utilized, a map of the dorsal spinal cord in relation to the current electrode placement could be utilized. This techniques, and similar methods should be explored as the introduction of DCM techniques to SCS placement procedures has allowed for placement to be equally as effective without requiring awake placement procedures (Shils & Arle, 2012). The addition of recommended automated DCM would promote faster and more accurate SCS placement.

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## CURRICULUM VITAE

