Technical Standards for Electrical Stimulation with Intracranial Electrodes for Functional Brain Mapping and Seizure Induction

Authors: Ravindra Arya¹, Fiona Baumer², Patrick Chauvel³, Birgit Frauscher⁴, Prasanna Jayakar⁵, Ammar Kheder⁶, Bradley Lega⁷, Ronald P. Lesser⁸, Kai J. Miller⁹, Marc R. Nuwer¹⁰, Nigel P. Pedersen¹¹, Anthony L. Ritaccio¹², David Sabsevitz¹³, Saurabh Sinha¹⁴, Elson L. So¹⁵, William O. Tatum IV¹⁶, Jessica W. Templer¹⁷, Stephan U. Schuele¹⁸

¹Comprehensive Epilepsy Center, Division of Neurology, Cincinnati Children's Hospital Medical Center, and Departments of Neurology, Pediatrics, and Computer Science, University of Cincinnati, Cincinnati, OH
²Division of Child Neurology, Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, CA
³Department of Neurology, University of Pittsburgh School of Medicine, Pittsburgh, PA
⁴Department of Neurology, Duke University Medical Center, and Department of Biomedical Engineering, Duke Pratt School of Engineering, Durham, NC
⁵Brain Institute, Nicklaus Children's Hospital, and Florida International University, Miami, FL
⁶Department of Neurology and Pediatric Institute, Emory University School of Medicine, Atlanta, GA
⁷Department of Neurological Surgery, University of Texas Southwestern Medical Center, Dallas, TX
⁸Departments of Neurology and Neurological Surgery, Johns Hopkins Medical Institutions, Baltimore, MD
⁹Department of Neurosurgery, Mayo Clinic, Rochester, MN
¹⁰Department of Neurology, David Geffen School of Medicine at UCLA, and Department of Clinical Neurophysiology, Ronald Reagan UCLA Medical Center, Los Angeles, CA
¹¹Department of Neurology, Comprehensive Epilepsy Center, and Center for Neuroscience, University of California Davis School of Medicine, Davis, CA
¹²Department of Neurology, Mayo Clinic, Jacksonville, FL; and, Department of Neurosurgery, Albany Medical College, Albany, NY
¹³Departments of Psychiatry and Psychology, Department of Neurological Surgery, Mayo Clinic, Jacksonville, FL
¹⁴Epilepsy Division, Department of Neurology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA
¹⁵Department of Neurology, Mayo Clinic Alix School of Medicine, Rochester, MN
¹⁶Department of Neurology, Mayo Clinic, Jacksonville, FL
¹⁷Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, IL
¹⁸Departments of Neurology, and Physical Medicine and Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL

Note: Except first and senior authors, all authors are listed alphabetically.

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1. INTRODUCTION
Electrical stimulation mapping (ESM) to localize cortical areas, sometimes including subcortical tracts, supporting sensorimotor and speech/language functions, and delineation of epileptic network with electrical stimulation-induced seizures (EIS), are important for neurosurgical decisions. However, there is a lack of consensus regarding the methodology of ESM for localization of cerebral functions and epileptic network. These technical standards by the American Clinical Neurophysiology Society (ACNS) describe best practices for ESM, including both intraoperative and extra-operative stimulation, of subdural electrodes (SDE) and stereotactic electroencephalography (SEEG) electrodes (including conventional depth electrodes and hybrid implants), and for mapping brain function and elicitation of seizures. Specific brain functions include somatic motor, somatosensory, and language (in this manuscript “language” represents both speech and language function).

2. METHODS
Clinicians from diverse backgrounds (clinical neurophysiology, epilepsy, neuropsychology, and neurosurgery) with expertise in ESM were recruited. Initial meetings were held to formulate the scope and outline of the document, and assign sections based on contributor’s expertise. Authors of each section prepared a draft based on literature review, clinical experience, and manufacturers’ monographs for stimulators and electrodes. PubMed searches were performed to identify pertinent peer-reviewed literature. Relevant sections of the American Academy of Neurology Clinical Practice Guidelines Manual were applied to ensure completeness of the literature review and avoidance of bias\(^1\). Subsequent meetings reviewed progress, built consensus by discussion, and developed evidence-based recommendations to the extent possible. The document is based on class III and class IV evidence and reflects practice patterns in North America. These technical standards were developed over a period extending from January 2022 to April 2024. Hence, we could not adhere to the recent ACNS methodology for guideline development.

3. EQUIPMENT
3.1. Electrodes
Electrodes used for ESM are the same (extra-operative) or fairly similar (intraoperative) to those used for recording spontaneous seizures. The metallic contacts that interface with the brain tissue are commonly made of platinum/platinum-iridium alloy (for extra-operative use) or stainless-steel (for intraoperative use). Both SEEG electrodes and SDE are available in many different configurations (Table 1).
Commonly used SDE have disc-shaped contacts with 4mm diameter, 2.3mm exposed surface, 5-10mm inter-contact spacing, and 2-64 contact grid/strip configuration. Commonly used SEEG electrodes have cylindrical contacts usually with 2mm length, 0.8mm diameter, 3.5mm inter-contact spacing, and 5-18 contacts.
Surface area of the individual electrode contacts is a determinant of charge density, which is important in deciding appropriate ESM settings. The aforementioned common configurations yield contact surface areas of 4-7mm\(^2\). Impact of atypical electrode configurations (such as ring electrodes, electrodes with smaller surface areas, or with high contact density) on charge density should be incorporated when deciding ESM settings for individual patients.
3.2. Recording Equipment
The equipment used during ESM is the same as that for recording intracranial EEG. Commonly used amplifiers should have a minimum of 64 channels but can have over 256 channels. Sampling rate should be at least 512 Hz/channel and rates of 1-2 kHz/channel are common. High input impedances and high common mode rejections ratios (CMRR) are necessary for good quality recordings. Typical systems have input impedances >100 MΩ and CMRR >80 dB. The recording system should have the ability to display live EEG data at the bedside, including a monitor with adequate size and resolution to display all intracranial channels of interest. This is necessary to identify after-discharges (ADs) and EIS that may occasionally occur at sites remote from the stimulated site.

3.3. Stimulators
Commercial electrical stimulators are available as stand-alone, integrated, or hybrid systems (Table 1). Stand-alone systems require manually connecting the contacts to be stimulated to the stimulator and selecting the stimulation settings. Integrated systems allow control of ESM (stimulated contacts and stimulation settings) from the recording software. Hybrid stimulators provide some control within the recording software, for example, the contacts being stimulated, while stimulation settings are manually chosen on the stimulator. Both constant current and constant voltage stimulators are available, with output specifications ranging from 0 to 20 mA (up to 0.1 mA increments) current strength, 50 to 1000-2000 µs pulse duration, and 1 to 450 Hz pulse frequency, able to deliver single pulse, recurrent pulse, and train stimulations. Stimulators should have means to interrupt a stimulus train and to inject an additional disrupting pulse (ictal disrupt mechanism). If prolonged ADs or unwanted EIS are provoked, injecting short-duration electrical current at the stimulation site may abort the discharge.

4. SAFETY CONSIDERATIONS
Successful ESM requires that recognizable and reproducible behavioral change(s) can be attributed to stimulation of specific brain region(s). With false negative ESM, the patient is at risk for functional deficit(s) from resection of unidentified eloquent cortex; conversely, false positive results may lead to inadequate resection of the epileptogenic zone or tumor. The success of ESM also depends on patient’s cooperation and the ability to perform task(s) needed to evaluate the function(s) of interest.

4.1. Clinical risks associated with intracranial electrodes. Risks associated with placement of intracranial electrodes and extra-operative monitoring mainly include intracranial hemorrhage, elevated intracranial pressure, neurological and skin/soft tissue infections, cerebrospinal fluid (CSF) leak, electrode fracture/dislocation/mispositioning, and new neurological deficits. These risks are not directly related to ESM and are outside the scope of these technical standards.

4.2. ADs and unwanted EIS. ADs are rhythmic epileptiform discharges that are clearly distinct from pre-stimulation electrographic activity and occur immediately following electrical stimulation. ADs can raise doubt whether an elicited behavioral response is due to local versus a broader network effect and can also evolve into seizures. ADs are reported in up to 75% of patients.
12-40% of SDE stimulations, and 32-43% of SEEG stimulations, with test-retest and inter-individual variability. ADs can occasionally involve electrodes remote from the stimulated site with variability on repeat stimulation. Different studies have reported higher incidence of ADs with short inter-stimulus interval (<1 minute), male sex, and negative brain MRI; and lower AD thresholds in patients with malformations of cortical development and longer duration of epilepsy. However, these findings have not been consistently reproduced, probably due to heterogeneity in the included sample and ESM settings across studies.

In extra-operative ESM, unwanted EIS have been reported in up to 35% of the patients with over 35% of the EIS requiring rescue medication. The incidence of EIS in intraoperative ESM has varied from 4%-24%. No consistent risk factors for unwanted EIS have been identified across studies. With SEEG, elicitation of habitual seizures with electrical stimulation may be a desired endpoint (see 5.6).

Strategies to address evolving ADs or unwanted EIS include giving an additional stimulation pulse (although stimulation has been shown to abort evolving ADs/EIS, optimal settings for such stimulation have not been clearly established), using the ictal disrupt function of the stimulator, rescue medication, or in the intraoperative setting, cold saline irrigation.

4.3. Premedication to mitigate the risks of ADs and unwanted EIS. There is variability in the literature on whether premedication should be routinely used before ESM and the best premedication. Different practices include (1) administering an intravenous anti-seizure medication (ASM), (2) starting regular ASMs, or (3) no pre-medication. Isolated studies have shown utility of benzodiazepines in patients with frequent ADs and fosphenytoin to decrease the incidence of EIS with SDE ESM but not with SEEG ESM. Some studies suggest that preoperative ASMs may reduce the risk of unwanted EIS with intraoperative ESM in tumor patients. Effect of premedication on functional or AD thresholds has not been reproduced consistently. Therefore, premedication may be considered before SDE ESM but there is insufficient data to make any recommendations about premedication before SEEG ESM.

5. STIMULATION SETTINGS

5.1. Electrical safety considerations inform choice of ESM settings. ESM settings should allow focal and reproducible perturbation of neurological function while avoiding neuronal injury. However, the current propagation, both local and distant through axonal connections, and the interaction of injected current with cortical cells to generate the observed behavior, are not sufficiently known to inform specific stimulation settings. A key determinant of the likelihood of neuronal injury is charge density, which is defined as charge delivered (current x duration) per unit surface area of the electrode contact (Figure 1). However, there is paucity of human data regarding the relationship between charge density and neuronal injury.

A maximum charge density of 52-57 μC/cm\(^2\)/phase is suggested for SDE ESM. This is based on absence of histological abnormalities in three temporal lobectomy specimens after prolonged electrical stimulation. It is difficult to extrapolate this value to SEEG, because of the heterogeneity in the electrical properties of tissues surrounding an SEEG electrode compared to SDE, and because up to 87% of the current may be shunted by CSF in case of SDE unlike that for SEEG. The FDA approved limit for deep brain stimulation (DBS) of 30 μC/cm\(^2\)/phase is based...
on postmortem neuropathologic evaluations in movement disorder patients with up to 12 years of DBS implants where charge densities above $40 \ \mu\text{C/cm}^2/\text{phase}$ were associated with tissue damage\textsuperscript{32}. However, extrapolation of this limit for shorter-duration ESM remains unclear, and safe charge density limit for SEEG ESM is not established.

Another electrical consideration is the use of biphasic versus monophasic pulses. Biphasic pulses are charge-balanced and probably less likely to cause neuronal injury\textsuperscript{33}.

5.2. Extra-operative SDE ESM.
Commonly, SDE ESM is performed with 50 Hz biphasic pulses with 200-300 µs pulse duration. Stimulation is usually begun at 1 mA and increased in 0.5-1.0 mA increments until a functional response, ADs, or the ceiling of the stimulation device (10-20 mA) is reached, constrained by safe charge density limits as described above. Stimulation is applied for 2-8 seconds, with longer-duration trains typically for testing complex functions such as language (Table 2).

5.3. Extra-operative SEEG ESM.
There are two common modes for performing SEEG ESM, called low-frequency (1 Hz) and high-frequency (50 or 60 Hz) stimulations, sometimes also called “shock” and “train” stimulations respectively. Previous studies have shown heterogeneity in the maximum current strength and pulse duration, mostly reflecting institutional practice, rather than a rigorous neurophysiologic or biophysical basis\textsuperscript{26}. The proposed protocol for SEEG ESM is provided in Table 2.

In addition, the following suggestions may be considered: (1) For functional mapping, it may be desirable to avoid stimulating electrode contacts in the seizure-onset zone (SOZ), or to stimulate them in the end, if necessary. (2) On a given SEEG electrode, it may be preferable to stimulate from deep to superficial contacts. Because of the preferential orthodromic conduction of the stimulation impulse, this approach theoretically protects against deeper contacts being refractory after stimulation of more superficial contacts. (3) For language ESM, it may be better to stimulate in the presumptive anterior (frontal) language area before stimulating posterior (temporo-parietal) language area, because of possible directional connectivity from temporal to frontal language areas\textsuperscript{34}.

Certain issues remain unresolved, and no specific recommendations can be offered for them, including: (1) time interval between successive stimulations, (2) stimulation of alternate versus successive contacts on a given electrode, (3) bipolar stimulation of contacts lying on different SEEG electrodes, and (4) monopolar stimulation (usually with respect to a remote non-eloquent reference). Herein, we have used “polarity” to describe a stimulation configuration and not the current direction.

5.4. Intraoperative ESM

5.4.1. Motor ESM in awake/asleep patients.
Somatosensory evoked potentials may be used for preliminary localization of central sulcus, however, details of that technique are outside the scope of these technical standards.

There are two common protocols for intraoperative motor ESM\textsuperscript{35}. The conventional protocol (also called Penfield’s or Ojemann’s technique) uses 50 (or 60) Hz biphasic square wave pulses of 250-1000 µs for 1-2 seconds delivered using a handheld stimulator (Table 2). The current strength varies from 2-12 mA, however, many times a threshold current that elicits consistent response in
primary motor cortex is identified and followed throughout the ESM (constant current stimulation). The Tanaguchi protocol uses high-frequency (250-500 Hz), 300-500 μs monophasic pulses of anodal stimulation with the cathode being a peripheral subdermal needle, delivered in trains of 5 every second with 2-4 ms inter-stimulus interval[36]. The Taniguchi technique does not elicit observable movements, and electromyography (EMG) is required on the side contralateral to the stimulated hemisphere to monitor for motor evoked potentials.

No definite guidance can be offered regarding the choice between conventional and Taniguchi protocol. However, conventional protocol allows resection close to eloquent cortical margins in tumors with limited infiltration of corticospinal tract and having well-defined margins in patients with good seizure control, without significant preoperative motor deficits, and without previous radiotherapy (“low-risk” tumors)[35]. However, Taniguchi protocol is regarded as more versatile, particularly for “high-risk” tumors, and less prone to cause EIS even in patients with altered cortical excitability[36]. Intraoperative cortical motor mapping is typically followed by mapping of subcortical tracts to define resection boundaries and preserve fibers involved in motor control[35].

5.4.2. Language ESM in awake patients. Language ESM is typically performed with bipolar stimulation using 50 (or 60) Hz biphasic pulses of 250-1000 μs for 2-4 seconds. The initial current intensity is often 2 mA whereas the maximum current intensity is typically kept below the AD threshold. Particularly for tumor neurosurgery, subcortical mapping of white matter tracts involved in language networks, is also desirable in addition to localization of cortical language areas.

5.5. Variation in ESM settings

Certain areas of the brain may be more susceptible to the emergence and propagation of ADs and EIS, including amygdala, hippocampus, primary sensorimotor, and calcarine cortices. Also, ADs or EIS may be provoked more easily within malformations of cortical development and cortical areas with frequent epileptiform discharges[37]. In such situations, it may be desirable to start stimulating at a lower current strength such as 0.5 mA, use smaller increments, or (with SEEG) first perform 1 Hz stimulation.

Also, for language mapping, it may be desirable to stimulate below AD and sensorimotor thresholds, so that language responses are not obscured by ADs or sensorimotor responses.

5.6. Seizure Stimulation

In contrast to wide use of electrical stimulation for functional mapping with intracranial EEG, its use for defining the epileptogenic zone is less well established. No definitive recommendations can be offered for seizure stimulation with SDE due to limited experience[38, 39]. However, since the beginning of SEEG practice, seizure stimulation is considered useful to disentangle the primary epileptogenic area from areas of propagation, and, to mitigate time constraints involved in recording sufficient spontaneous seizures. SEEG studies have shown a concordance in SOZ between spontaneous and stimulated seizures in 33-100% of cases, more so when the complete semiology was reproduced[40-42]. Two recent large studies have shown that[43, 44]: (1) EIS are evoked in 57%-75% of patients, (2) occurrence of EIS, particularly with low-frequency stimulation, predicts favorable surgical outcome, (3) surgical outcomes are better if the resections encompass EIS electrode contacts. Hence, seizure stimulation should be considered an integral part of SEEG evaluation.
Failure to elicit EIS may be due to subthreshold simulation, insufficient sampling of the true SOZ including a more widespread SOZ than initially anticipated. Occurrence of ADs suggest that the stimulation threshold of a certain structure has been achieved, although thresholds may vary with repeat testing\textsuperscript{13}.

5.6.1. High-frequency vs low-frequency stimulation. Studies have shown a higher incidence of EIS with 50 Hz stimulation (40-55\%) compared to 1 Hz stimulation (7-18\%)\textsuperscript{43,45}. Furthermore, EIS elicited with high-frequency stimulation may be less likely to resemble habitual semiology and probably less likely to determine post-surgical outcomes. Therefore, we suggest starting with 1 Hz stimulation and using 50 (or 60) Hz stimulation only if required. Also, non-habitual seizures appear to occur more frequently in the hippocampus and primary sensorimotor cortex, so for these regions 1 Hz stimulation, or 50 Hz stimulation at lower current strengths may be considered for seizure stimulation.

5.6.2. Initial current intensity and increments. The initial intensity for seizure stimulation is chosen depending on the pulse duration, electrode type, anatomical structure or pathology (lower intensities for primary sensorimotor cortices, mesial temporal lobe, and dysplastic tissue), current ASMs, history of generalization, and time since the last seizure\textsuperscript{43,46}. An increase in intensity is recommended only for 50 (or 60) Hz stimulation until ADs are evoked. An increase in intensity is not desirable for 1 Hz stimulation, where a gradual increase in current intensity may result in slowing of the regional electrographic activity due to exhaustion of the neuronal pool. In practice, 1 Hz stimulation is usually performed at constant current intensity of 3-5 mA depending on the pulse duration.

5.6.3. Timing of seizure stimulation during SEEG monitoring. In practice, most centers perform seizure stimulation after at least one spontaneous seizure has been recorded, however, it can also be performed without a prior spontaneous seizure. No overarching recommendations can be offered.

5.6.4. Premedication. No general recommendations can be offered, although many centers perform seizure stimulation with the patient on some ASM(s) to mitigate risks of focal-to-bilateral seizures or non-habitual seizures when the patient is completely off ASMs.

5.6.5. Selection of electrode contacts for stimulation. No recommendations can be offered for stimulating all contacts vs a select subgroup, although this is a relevant consideration for high-volume centers. Also, no general recommendation can be made regarding starting the stimulation from channels outside the SOZ moving to those suspected to be involved in the epileptogenic network (periphery-to-center) or vice versa, although the former appears to be more common in practice.

5.6.6. Stimulation-induced ADs or auras without accompanying EEG changes. Studies have not shown a consistent relationship between the site(s) of ADs and the SOZ for spontaneous seizures\textsuperscript{6,10}. Sites which show only ADs without habitual electroclinical features are unlikely to be the key drivers of the epileptogenic network. Similarly, elicitation of auras without corresponding electrographic changes may indicate the symptomatogenic zone rather than the epileptogenic zone.

6. FUNCTIONAL MAPPING
Locations for stimulation should be selected based on the functional neuroanatomy of the planned resection (cortical areas and white matter tracts) and information from other presurgical functional
modalities (Figure 2). This data is used to formulate a priority list of mapping tasks that also incorporates vocational or social factors specific to the patient (e.g., arithmetic tasks for an accountant when stimulating the dominant angular gyrus). To obtain the most informative functional map with ESM, close attention should be paid to the (1) cognitive or motor demands of a particular task, and (2) nature of errors or responses elicited by ESM.

6.1. Language ESM
Language is a complex cognitive function and involves many conceptually distinct but interacting subsystems including object recognition, visual decoding of symbols (orthography), auditory processing, semantics, lexical access, phonemic representation, speech motor planning, articulation, fluency, syntactic structure, verbal working memory, and others. These cognitive subcomponents of language are represented as dynamic networks with time-varying functional connections among different brain areas.

For the purposes of ESM, it is important to recognize that different tasks used in clinical practice to map “language” typically engage several of these functional subsystems to varying extents and therefore have different cortical topography (Table 3). For the same reason, using only a single task to perform language ESM is likely to under-detect language sites.

Tasks used for language ESM include relatively simpler tasks such as phoneme identification and repetition (word/non-word), as well as higher-level tasks such as picture naming (visual naming, object naming), auditory description naming, category-specific naming (e.g. proper nouns), verb generation, word rhyming, reading comprehension, short-term verbal recall, and automatic speech (e.g. counting, reciting alphabet or a nursery rhyme).

We suggest that a visual naming task be performed in all patients able to do it. Depending on the patient cooperation, we suggest using additional task(s) for language ESM based on location of the planned resection, patient’s baseline language function, vocational or other goals, and time constraints (Table 3). This can be planned in consultation with a neuropsychologist.

Finally, in multilingual patients, it is desirable to test each language separately, guided by patient’s baseline proficiency, personal goals, time constraints, and availability of valid testing materials.

6.2. Motor ESM
Motor ESM relies on observation of responses during stimulation. Movements localized to a single joint or in a single direction, contralateral to the ESM side, are typically seen with stimulation of the primary motor cortex (precentral gyrus). More complex movements involving multiple joints, bilateral quasi-purposive movements, or tonic/dystonic posturing, usually involving proximal joints, may be elicited on stimulation of premotor and supplementary motor areas. There may be variability in responses elicited at a particular site within and between patients, depending, in part, on the stimulation settings.

 SEEG, and less often SDE, can allow mapping negative motor areas. This is one situation where task interruption is used for motor mapping. The patient is usually instructed to perform repetitive and rapid movements of hands and fingers, for example, synchronous and asynchronous rotations of hands and thumb, finger pinches, or opposing thumb to different digits. A negative motor response is defined as cessation of movement without loss of consciousness.

We do not routinely recommend using surface EMG to capture subtle muscle contractions during extra-operative ESM. A typical ESM session may stimulate multiple muscle groups and/or
movements, hence, it will require application of EMG electrodes to several different muscles, which may be challenging. In highly selected cases, where the goal is to test a single or a limited number of muscles/movements, application of surface EMG electrodes may be considered. Surface EMG electrodes are typically placed in a bipolar montage, with 2 Hz to 1 kHz bandpass, and 200-2000 µV/cm sensitivity.

6.3. Sensory ESM
Sensory ESM relies on patient reporting.

6.4. Surgical Lesion Boundaries
Based on studies of intra-operative functional mapping, a distance of >1 cm from nearest naming site is suggested for lesion boundary with SDE\textsuperscript{50}. No definite recommendation can be made for a safe distance in primary sensorimotor cortices and for subcortical tracts. For SEEG, sulcal margins around functional areas are commonly used. The decisions regarding lesion margins should incorporate several other variables, such as, current thresholds for functional responses, regional anatomy, pathology of lesion, etc.\textsuperscript{35}

7. DOCUMENTATION AND REPORTING
7.1. Response Documentation
A tabulated datasheet for recording ESM responses is provided (Table 4). The behavioral state of the patient and stimulation settings should be recorded initially and when making any changes to the stimulation settings. Any extenuating circumstances (such as pain or distraction) should also be recorded. Reproducibility of functional responses (consistency of elicited semiology on repeat stimulation at a particular setting) and if responses were seen in some but not all trials of a task/stimulation should be documented.

7.1.1 Motor Responses. (1) Whether the response elicited was positive (induction of a new movement) or negative (inhibition of a sustained or repetitive movement). (2) Body region and preferably the specific joint(s) involved. (3) Description of the specific movement observed (example: adduction and internal rotation of left shoulder with flexion of left elbow).

7.1.2. Sensory Responses. (1) Location(s) of the sensation on the body. (2) Sensation(s) experienced (for example: tingling, numbness, buzzing, burning). (3) Location(s) and quality of phosphenes (for primary visual cortex stimulation) or more complex apparitions (for secondary/associative visual cortex stimulation). (4) Pure tones/sounds (for core auditory cortex stimulation) and complex auditory phenomenon (for auditory association cortex stimulation).

7.1.3. Language Responses. (1) Type of deficits including speech arrest/anomia, paraphasic errors (semantic or phonemic), circumlocutions or neologisms, and performance errors (dysarthria or apraxia)\textsuperscript{51}.

7.1.4. ADs. (1) Location: stimulated contacts and/or remote. (2) Any evolution in morphology, frequency, or extent (spread), (3) If ictal disrupt mechanism (see 3.3) needed to be used.

7.1.5. EIS. (1) Semiology: overlap with spontaneous habitual seizures. (2) Electrographic pattern.

7.2. Reporting
ESM report can be integrated with the intracranial video-EEG report or preferably as a separate encounter. The report should be divided into separate sections including the technical aspects, observations during stimulation, and the clinical impression. It may also be desirable to separate results of functional mapping and seizure stimulations into different sections. Developing an institutional reporting template is recommended. Documentation of procedure date and technologist and physician time is required for billing and medico-legal purposes. It is recommended to archive the entire video-EEG tracings of each stimulation session.

The clinical impression should attempt to place the ESM findings in context of SOZ information and other functional mapping modalities. A 2 or 3-dimensional map summarizing the responses at each electrode is helpful for surgical planning. It may be worth communicating that not all functions identified by ESM will incur the risk of permanent deficit if surgically lesioned.

8. SPECIAL CONSIDERATIONS IN PEDIATRIC PATIENTS

8.1. Relationship among functional thresholds, AD thresholds, electrode type, and age.

For SDE ESM in pediatric patients, studies have shown language thresholds to be higher than AD thresholds, whereas motor thresholds fall below AD thresholds during late childhood depending on the cortical region. This potentially increases the likelihood of false negative ESM sites in younger children. In contrast, motor and language thresholds for SEEG ESM have been shown to remain below AD thresholds in pediatric patients.

Hence, for pediatric ESM particularly with SDE: (1) Absence of a behavioral response before ADs are evoked does not necessarily mean absence of eloquent function. (2) Testing at current intensities approaching and even exceeding AD thresholds may be required to optimize sensitivity of language ESM in children. This may complicate interpretation of ESM results, especially when ADs are seen remote from the stimulation site, because whether the observed behavior localizes to the stimulated cortex or is attributable to a broader network effect, becomes ambiguous. (3) Protocols that alternately increase current intensities and pulse duration in a stepwise manner (dual-increment paradigm) may be required for pediatric language ESM to minimize the risk of EIS. (4) Age-wise safe charge density limits have not been established for pediatric patients.

8.2. Cerebral reorganization.

The topography of language and, to a lesser extent, motor sites may be altered in some patients. While not unique to pediatric population, children with developmental pathology are more susceptible to having atypical functional representation. Specifically: (1) Language sites may sometimes overlap with developmental lesions such as cortical dysplasia or polymicrogyria, whereas they are often displaced by encephaloclastic lesions, the reorganization depending on the nature, location, size, age of occurrence, and chronicity of the epileptogenic lesion. (2) Some patients with atypical language distribution may have more than one discrete area of language representation particularly in the temporal lobe. (3) Anterior displacement of temporal language sites or right hemispheric language dominance may be seen with left handedness and earlier age of seizure onset. (4) Naming sites may have a distributed topography and predominance in posterior language area in children with lower IQ.
The implications for ESM include: (1) Individualized ESM for defining functional cortical areas is more important in such patients. (2) Stimulation beyond anatomic boundaries of the canonical functional areas is often required.

**8.3. Behavioral considerations.**
Children, particularly those with developmental or attentional impairments, or adults with similar disabilities, may be challenging to test, requiring creativity on the part of the clinical team performing the ESM. Some examples are provided: (1) Some children may not be able to perform any structured language task. In such cases, clinician may try using spontaneous speech or even conversation with a parent for language ESM. (2) In some children, it may be challenging to distinguish between ESM-induced motor responses and voluntary movements. Reproducibility and stereotypic nature of the elicited response may be helpful. (3) Certain subtle responses may need to be highlighted such as using a pacifier to discern oral/tongue motor responses. (4) Patient-reported responses may sometimes be unreliable or difficult to interpret.

Intra-operative language ESM is rarely, if ever, performed in children. In highly selected older children, if it is attempted, then child-life professionals should be involved beforehand to offer walk-throughs to help alleviate anxiety and maximize cooperation.

**9. ANESTHETIC CONSIDERATIONS**
Anesthetic considerations for performing intraoperative ESM are similar to those for intraoperative electrocorticography (ECoG). In particular, intraoperative language mapping requires the patient to be awake and cooperative.

**10. PERSONNEL**
Intracranial electrodes are placed by a neurosurgeon often with real-time guidance from a clinical neurophysiologist. Cables are then connected from these electrodes to the acquisition machine by a trained EEG technologist. For intraoperative ESM, stimulator is connected to a handheld wand used by the neurosurgeon. The clinical neurophysiologist controls the stimulation settings and evaluates ECoG and behavioral responses. For extra-operative ESM stimulation is delivered by sequentially connecting implanted electrodes to the stimulator by clinical neurophysiologist or the EEG technologist. For both the scenarios, neurophysiologists presence in the room is required per definition of the services. The technologist preferably holds the Registered EEG Technologist qualification and optionally the Certification in Neurophysiologic Intraoperative Monitoring or Certification in Long-Term Monitoring. The neurophysiologist should have completed appropriate fellowship training with sufficient supervised ESM sessions.

**11. CONCLUSION**
ESM provides clinically useful information for neurosurgical planning and localizes cortical and subcortical sites involved in functional and epileptic networks. However, there is heterogeneity in practice regarding the methodology and interpretation of responses. To facilitate uniformity across institutions, best practices based on published literature and expert consensus are presented here. These technical standards can serve as a starting point for developing institutional protocols.
and should be viewed as suggestions which do not supersede clinical judgment for individual patients.
Table 1
Specifications of selected commercially available electrodes and cortical electrical stimulators

<table>
<thead>
<tr>
<th>Subdural Electrodes</th>
<th>Total Contact Diameter (mm)</th>
<th>2.0, 3.0, 4.0*, 4.5, 6.0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposed Contact Diameter (mm)</td>
<td>1.5, 1.8, 2.3*</td>
</tr>
<tr>
<td></td>
<td>Inter-contact Distance (mm)</td>
<td>5, 10*, 15</td>
</tr>
<tr>
<td></td>
<td>Number of Contacts</td>
<td>Strips: 2, 4, 6, 8, 10, 12, 14, 16; Grids: 8 to 256 (common: 8, 16, 64)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stereotactic Depth Electrodes</th>
<th>Diameter (mm)</th>
<th>0.8*, 0.86*, 1.12, 1.26</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Contact length (mm)</td>
<td>1.32, 2.0, 2.29*, 2.41*, 2.5, 5.0</td>
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<tr>
<td></td>
<td>Inter-contact Distance (mm)</td>
<td>2.2, 3.0, 3.5, 3.97, 4.0, 4.43, 5.0, 7.0, 8.0, 10.0;</td>
</tr>
<tr>
<td></td>
<td>Number of Contacts</td>
<td>4, 5, 6, 8, 10, 12, 14, 15, 16, 18</td>
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<tr>
<td></td>
<td>Other Configurations</td>
<td>3 sets of 5 or 6 contacts, inter-contact distance 3.5 mm, with 7 or 11 mm between sets</td>
</tr>
<tr>
<td></td>
<td>Recording Lengths (mm)</td>
<td>17 to 92</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stimulators</th>
<th>Output Range (mA)</th>
<th>0 to 20 mA (with 0.1-0.5 mA increments)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pulse Width (μs)</td>
<td>50 to 1000-2000</td>
</tr>
<tr>
<td></td>
<td>Frequency (Hz)</td>
<td>1 to 450</td>
</tr>
<tr>
<td></td>
<td>Train Duration</td>
<td>Single pulse to 300 seconds</td>
</tr>
<tr>
<td></td>
<td>Stimulation waveform</td>
<td>Biphasic square wave pulse (negative or positive leading), alternating square wave</td>
</tr>
</tbody>
</table>

*Used relatively commonly in clinical practice
### Table 2
Proposed protocols for electrical stimulation

<table>
<thead>
<tr>
<th>Setting</th>
<th>SDE ESM</th>
<th>SEEG ESM (High Frequency)</th>
<th>SEEG ESM (Low Frequency)</th>
<th>Intraoperative ESM (Conventional)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Intraoperative ESM (Taniguchi)&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polarity</td>
<td>Bipolar/Monopolar</td>
<td>Bipolar</td>
<td>Bipolar</td>
<td>Bipolar</td>
<td>Monopolar</td>
</tr>
<tr>
<td>Phases</td>
<td>Biphasic</td>
<td>Biphasic</td>
<td>Biphasic</td>
<td>Biphasic</td>
<td>Monophasic</td>
</tr>
<tr>
<td>Pulse frequency</td>
<td>50 (or 60) Hz</td>
<td>50 (or 60) Hz</td>
<td>1 Hz</td>
<td>50 (or 60) Hz</td>
<td>250-500 Hz</td>
</tr>
<tr>
<td>Pulse width</td>
<td>200-300 μs</td>
<td>300 μs (100-500 μs)</td>
<td>500 μs (300-500 μs)</td>
<td>250-1000 μs</td>
<td>300-500 μs</td>
</tr>
<tr>
<td>Train duration</td>
<td>For passive responses (e.g. motor): 2-4s</td>
<td>For passive responses (e.g. motor): 2-4s</td>
<td>Up to 30s</td>
<td>1-4 s</td>
<td>2-5 ms</td>
</tr>
<tr>
<td></td>
<td>For trial-based testing (e.g. naming): 4-8s</td>
<td>For trial-based testing (e.g. naming): 4-8s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current intensity&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1-20 mA</td>
<td>0.5-10 mA</td>
<td>1-10 mA&lt;sup&gt;4&lt;/sup&gt;</td>
<td>2-12 mA&lt;sup&gt;5&lt;/sup&gt;</td>
<td>2-16 mA&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Suggested use</td>
<td>Functional mapping</td>
<td>Functional mapping, seizure stimulation (outside primary sensorimotor cortex and presumptive excitable tissue)</td>
<td>Seizure stimulation (particularly in primary sensorimotor cortex, hippocampus, and within cortical dysplasia), cortico-cortical evoked potentials</td>
<td>Motor mapping, Language mapping</td>
<td>Motor mapping</td>
</tr>
</tbody>
</table>

<sup>1</sup>Also called Penfield’s or Ojemann’s technique
<sup>2</sup>Delivered in trains (inter-stimulus interval 2-5 ms) of 5, usually every second. EMG is required for detection of motor evoked potentials.
we have used polarity to describe a stimulation configuration and not the current direction
<sup>3</sup>Caution: higher limit of current intensity may not be safe depending on the surface area of the electrode contact. For high-frequency SEEG ESM, the usual maximum current is 6-7 mA for a pulse duration of 250-300 μs. We recommend calculating charge density based on the dimensions of the specific electrode contacts, particularly for stimulations with higher current intensities and pulse durations. Current intensity is usually limited to that below after-discharge threshold except in specific scenarios, for example, in children.
<sup>4</sup>Commonly performed with constant current intensity of 3-5 mA.
<sup>5</sup>Occasionally, intraoperative stimulation can start at 1 mA.
<sup>6</sup>Higher end of current strength is used in asleep mapping (typically 6-16 mA) compared to awake mapping (typically 2-8 mA).
Table 3
Sample tasks for language mapping based on the cortical area

<table>
<thead>
<tr>
<th>Anatomic Area</th>
<th>Language Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-sylvian region (IFG, STG, anterior IPL)</td>
<td>Visual naming, automatic speech</td>
</tr>
<tr>
<td><strong>Broca’s area:</strong></td>
<td></td>
</tr>
<tr>
<td>IFG pars opercularis and pars triangularis</td>
<td>Automatic speech, visual naming, verb generation, reading, auditory verbal comprehension</td>
</tr>
<tr>
<td><strong>Posterior language area:</strong></td>
<td></td>
</tr>
<tr>
<td>Posterior (±middle) STG, posterior MTG, angular gyrus, supramarginal gyrus (posterior limb)</td>
<td>Visual naming, automatic speech, auditory verbal comprehension, sentence completion during reading “fill in the blank”, reading, verb generation, arithmetic ability</td>
</tr>
<tr>
<td><strong>Basal temporal language area</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Visual naming (most common ESM induced disruption), auditory verbal comprehension “token test” (second most common impairment), auditory naming, reading</td>
</tr>
<tr>
<td><strong>Anterior temporal lobe</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Auditory naming</td>
</tr>
</tbody>
</table>

Note: all the tasks are not required. A selection should be made based on cortical areas to be stimulated, functional anatomy of planned resection, patient-specific factors such as ability to cooperate, post-operative vocational goals, and time constraints. The task-selection is better planned in consultation with a neuropsychologist.

Abbreviations: ESM Electrical Stimulation Mapping, IFG Inferior Frontal Gyrus, IPL Inferior Parietal Lobule, MTG Middle Temporal Gyrus, STG Superior Temporal Gyrus
Table 4
Datasheet for recording ESM responses

<table>
<thead>
<tr>
<th>Behavioral State</th>
<th>Pulse Frequency (Hz)</th>
<th>Pulse Duration (μs)</th>
<th>Train Duration (s)</th>
<th>Polarity (reference in case of monopolar)</th>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIS*</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Used</td>
<td>Seizure (Yes/No)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disruption</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Note: *document if habitual aura or elements of the semiology were reproduced during stimulation
FIGURE LEGENDS

Figure 1. Types of electrodes used for intracranial recordings and electrical stimulation are illustrated (A) including depth electrodes, subdural electrodes, and intra-operative probes. The surface area in contact with brain tissue is also illustrated (B) which determines charge density (C).

Symbols: $\sigma$ = charge density, $Q$ = charge, $A$ = surface area in contact with the brain tissue, $I$ = current strength, $t$ = pulse duration, $d$ = diameter of the electrode contact, and $l$ = length of the depth electrode contact, SDE = subdural electrodes, DE = depth electrodes (including stereo-electroencephalography electrodes)

Figure 2. Selected canonical cortical speech and language areas (A) and subcortical white matter tracts (B) supporting speech and language functions.

A: a = supplementary motor area, b = inferior frontal gyrus pars triangularis and opercularis (Broca’s area), c = inferior precentral gyrus, d = supramarginal gyrus, e = angular gyrus, f = temporal pole, g = superior temporal gyrus, h = middle temporal gyrus, i = basal temporal language area.

B: 1 = frontal Aslant tract, 2 = corticospinal tract, 3a = superior longitudinal fasciculus 2 (no direct relationship with language function according to current models, shown to differential from #3b), 3b = superior longitudinal fasciculus 3, 4, and arcuate fasciculus, 5 = middle longitudinal fasciculus (unclear relationship to language function, shown to differentiate from #6), 6 = inferior longitudinal fasciculus, 7 = uncinate fasciculus.
Appendix 1

Abbreviations used in the text

ACNS American Clinical Neurophysiology Society
ADs After-discharges
ASM Anti-seizure medication
CMRR Common mode rejections ratio
CSF Cerebrospinal fluid
DBS Deep brain stimulation
ECoG Electrodecephalography
EIS Electrical stimulation induced seizures
EMG Electromyography
ESM Electrical stimulation mapping
SDE Subdural electrodes
SEEG Stereotactic electrodecephalography
SOZ Seizure-onset zone
**Appendix 2**

Disclosures in addition to those on file with ACNS

<table>
<thead>
<tr>
<th>Author</th>
<th>Disclosures</th>
</tr>
</thead>
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<tr>
<td>Fiona Baumer</td>
<td>Research support: NINDS K23NS116110, Pediatric Epilepsy Research Foundation</td>
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<tr>
<td>Patrick Chauvel</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Birgit Frauscher</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Prasanna Jayakar</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Ammar Kheder</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Bradley Lega</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Ronald P. Lesser</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Kai J. Miller</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Marc R. Nuwer</td>
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</tr>
<tr>
<td>Nigel P. Pedersen</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Anthony L. Ritaccio</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>David Sabsevitz</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Saurabh Sinha</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Elson L. So</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>William O. Tatum</td>
<td>Patents held or pending: #62527896; #62770362 (intraoperative monitoring sensor devices).</td>
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<tr>
<td>Jessica W. Templer</td>
<td>No additional disclosures.</td>
</tr>
<tr>
<td>Stephan U. Schuele</td>
<td>No additional disclosures.</td>
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</tbody>
</table>
REFERENCES


22. xxx. Place Holder 1.

A

Depth electrodes

Subdural electrodes (grid)

Subdural electrodes

Spherical probe

Suction electrode

B

Depth electrode

Subdural electrode

Intraoperative spherical probe

Intraoperative cylindrical suction probe

\[ \sigma = \frac{Q}{A} = \frac{It}{A} \]

\[ A_{SDE} = \frac{\pi d^2}{4} \]

\[ A_{DE} = \pi dl \]
These technical standards suggest best practices for ESM, based on literature review and expert consensus, for:
- Intraoperative and extra-operative stimulation
- Of SDE and SEEG electrodes (including conventional depth electrodes and hybrid implants)
- For mapping brain function as well as elicitation of seizures

Amplifiers used during ESM should have:
- Number of channels ≥64
- Sampling rate ≥512 Hz/channel
- High input impedances
- High common mode rejections ratios

Live bedside display of EEG data should be available on a monitor with adequate size and resolution to show all intracranial channels of interest. Stimulators should have sufficient dynamic range for different stimulation settings, ability to interrupt a stimulus train, and to inject additional disrupting pulse(s) (*ictal disrupt mechanism*).

Charge density should be calculated for the specific electrodes and ESM settings used in clinical practice. Maximum safe charge density:
- For SDE ESM: 52-57 μC/cm²/phase
- For SEEG ESM: not established

**Seizure Stimulation**
- Start with 1 Hz stimulation and use 50 (or 60) Hz stimulation only if required
- In regions with higher cortical excitability use lower current strengths
- Stepwise increase in intensity should be used only with 50 (or 60) Hz stimulation, it is preferable to perform 1 Hz stimulation at a constant current

**Language ESM**
- A visual naming task should be performed in all patients able to do it
- At least one additional language task should be considered depending on:
  - Location (anatomy) of the planned resection
  - The patient’s ability to cooperate
  - Patient’s baseline language function
  - Vocational or other post-operative goals
  - Time constraints

**Sensorimotor ESM**
- Motor ESM relies on observation of responses during stimulation
- Surface EMG to capture subtle muscle contractions during extra-operative ESM is not routinely recommended
- Sensory ESM relies on patient reporting

**Polarities**

<table>
<thead>
<tr>
<th>Setting</th>
<th>SDE ESM</th>
<th>SEEG ESM (High Frequency)</th>
<th>SEEG ESM (Low Frequency)</th>
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<tr>
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<tr>
<td><strong>Phases</strong></td>
<td>Biphasic</td>
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<td>Biphasic</td>
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</tr>
<tr>
<td><strong>Pulse frequency</strong></td>
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</tr>
<tr>
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<td>2-12 mA</td>
<td>2-16 mA</td>
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<td>Functional mapping, seizure stimulation (outside primary sensorimotor cortex and presumptive excitable tissue)</td>
<td>Seizure stimulation (particularly in primary sensorimotor cortex, hippocampus, and within cortical dysplasia), cortico-cortical evoked potentials</td>
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*Caution: higher limit of current intensity may not be safe depending on the surface area of the electrode contact. For high-frequency SEEG ESM, the usual maximum current is 6-7 mA for a pulse durations of 250-300 μs. We recommend calculating charge density based on the dimensions of the specific electrode contacts, particularly for stimulations with higher current intensities and pulse durations. Commonly performed with constant current intensity of 3-5 mA. See text for additional details.
## PROTOCOLS FOR ELECTRICAL STIMULATION WITH INTRACRANIAL ELECTRODES

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<thead>
<tr>
<th>Setting</th>
<th>SDE ESM</th>
<th>SEEG ESM (High Frequency)</th>
<th>SEEG ESM (Low Frequency)</th>
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1. Also called Penfield’s or Ojemann’s technique
2. Delivered in trains (inter-stimulus interval 2-5 ms) of 5, usually every second. EMG is required for detection of motor evoked potentials.
3. Polarity describes stimulation configuration and not the current direction.
4. Caution: higher limit of current intensity may not be safe depending on the surface area of the electrode contact. For high-frequency SEEG ESM, the usual maximum current is 6-7 mA for a pulse duration of 250-300 μs. We recommend calculating charge density based on the dimensions of the specific electrode contacts, particularly for stimulations with higher current intensities and pulse durations. Current intensity is usually limited to that below after-discharge threshold except in specific scenarios, for example, in children.
5. Commonly performed with constant current intensity of 3-5 mA.
6. Occasionally, intraoperative stimulation can start at 1 mA.
7. Higher end of current strength is used in asleep mapping (typically 6-16 mA) compared to awake mapping (typically 2-8 mA).
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A:  
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- $c =$ inferior precentral gyrus,
- $d =$ supramarginal gyrus,
- $e =$ angular gyrus,
- $f =$ temporal pole,
- $g =$ superior temporal gyrus,
- $h =$ middle temporal gyrus,
- $i =$ basal temporal language area.

B:  
1. frontal Aslant tract,
2. corticospinal tract,
3a. superior longitudinal fasciculus,
3b. superior longitudinal fasciculus,
4. and arcuate fasciculus,
5. middle longitudinal fasciculus,
6. inferior longitudinal fasciculus,
7. uncinate fasciculus.

### SAMPLE TASKS FOR LANGUAGE MAPPING BASED ON THE CORTICAL AREA

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<th>Anatomic Area</th>
<th>Language Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-sylvian region (IFG, STG, anterior IPL)</td>
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</tr>
<tr>
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</tr>
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<td><strong>Posterior language area:</strong></td>
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<tr>
<td>Posterior (±middle) STG, posterior MTG, angular gyrus, supramarginal gyrus (posterior limb)</td>
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<td>Basal temporal language area</td>
<td>Visual naming (most common ESM induced disruption), auditory verbal comprehension “token test” (second most common impairment), auditory naming, reading</td>
</tr>
<tr>
<td>Anterior temporal lobe</td>
<td>Auditory naming</td>
</tr>
</tbody>
</table>

### SAMPLE SHEET FOR RECORDING RESPONSES

<table>
<thead>
<tr>
<th>Behavioral State</th>
<th>Pulse Frequency (Hz)</th>
<th>Pulse Duration (μs)</th>
<th>Train Duration (s)</th>
<th>Polarity (reference in case of monopolar)</th>
<th>Task</th>
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<td></td>
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Note: All the tasks are not required. A selection should be made based on cortical areas to be stimulated, functional anatomy of planned resection, patient-specific factors such as ability to cooperate, post-operative vocational goals, and time constraints. The task selection is better planned in consultation with a neuropsychologist. See text for abbreviations.

Note: *document if habitual aura or elements of the semiology were reproduced during stimulation

---

*ADs* = Activating Directions, *EIS* = Electrode Insertion System