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Intra-operative Acquisition of Electrophysiological Data in Human Motor Eloquent Neurosurgery

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We use this protocol and it's working

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Keywords: Direct Electrical Stimulation, Subcortical Mapping, Neurosurgery, Corticospinal Tract, distance between the subcortical stimulation point, subcortical stimulation point, human motor eloquent neurosurgery problem, spatial shifts of the brain, electrophysiological data, neurosurgery, data set of electrophysiological data, corticospinal tract, location of the brain, motor eloquent pathology, surgery of motor, evoked potential, phenomena such as brain shift, brain shift, spatial shift, stimulation, other procedure, standard operating procedure

Abstract

Problem: When acquiring intra-operative subcortical stimulation data, it is important to account for the spatial inaccuracies that may be introduced due to a spatial mismatch between pre-operative imaging and the location of the brain after resection. Phenomena such as brain shift contribute to the discrepancy between where the intra-operative stimulation points lie on pre-operative MR images and where the stimulations points lie on intra-operative MR images. This protocol aims to correct for this discrepancy when acquiring intra-operative stimulation data without the need for time-expensive intra-operative MRI. Furthermore, this protocols aims to increase transparency in the employed methods to encourage replication studies.

Aim: If followed correctly, the protocol will result in a data set of electrophysiological data, based on motor evoked potentials, obtained during surgery of motor eloquent lesions. Specifically, the data can be used to assess the distance between the subcortical stimulation point and the corticospinal tract. This distance is corrected for brain shift. Suitable patients are adult patients (≥ 18 years) with a motor eloquent pathology.

Innovation: This protocol stands apart from other procedures because it employs intra-operative ultrasound to correct for spatial shifts of the brain that occur during or after resection. Furthermore, this protocol is designed to pose minimal interference with the standard operating procedures in neurosurgery.

Pre-requisites: This protocol assumes familiarity with conducting intra-operative neuromonitoring.



Guidelines

Limitations: This protocol is designed for mapping the corticospinal tract in surgeries of motor eloquent areas. It is not suitable to replace standard intra-operative neuromonitoring procedures for motor-, speech-, or other eloquent surgery cases.

Assumptions: The protocol assumes that the materials and software listed in the "*Materials*" section are used. Parts of the protocol may need be to adjusted if other materials or software are used.

Required expertise: Implementation of the protocol requires practical experience with intra-operative neuromonitoring, including how to place electrodes and how to interpret the motor evoked potentials. Further, the user must be familiar with standard operating procedures in neurosurgery to minimise disruption to the standard care of the patient. Lastly, the protocol assumes good communication between operating surgeon and user to ensure that the location of the stimulation points is saved concurrently with the application of the direct electrical stimulation.

Materials

Motor-evoked potential monitoring

- *IONM system*: ISIS Xpert plus 32-channel system for neurosurgery, item no.: 504004-32CH; <https://shop.inomed.com/en/Systems/Systems-IONM/ISIS-IOM-Systems/ISIS-Xpert-plus-32-channel-system-for-neurosurgery.html>
- *MEP needles*: Spes Medica S.r.l.; Twisted Pair Subdermal needle electrodes 0,40×18mm, 150cm cable, DIN42802, item no.: MN4018D15A/S; <https://www.spesmedica.com/en/iom/subdermal-needle-electrodes/>
- *Handbook*: inomed Medizintechnik GmbH; Application Notes for ISIS Systems Ring Binder with Applications Notes DE, item no.: 504800; <https://shop.inomed.com/en/Systems/Literature/Application-notes-for-ISIS-systems-Ring-binder-with-applications-notes-DE.html>
- *Stimulation probe*: inomed Medizintechnik GmbH; Mapping Suction Probe 3/90, monopolar, item no.: 525650; <https://shop.inomed.com/en/Accessories/Accessories-IONM/Other-accessories-IONM/Mapping-suction-probe-120-mm-by-Raabe-monopolar.html>

Microscope video

- *Intraoperative microscope*: Carl Zeiss Meditec AG; OPMI PENTERO 900, item no.: 302582-9902-000
- *Video cable*: Sommer Cable Germany; Vector, 0.8 / 3.7, 75 Ohm, HDTV/SDI
- *HD-SDI splitter*: Superbat; BNC Splitter Adapter, 75 Ohm, BNC Male to Dual BNC Female Splitter, SDI HD-SDI

Software

- *Neuronavigation*: Brainlab AG; Image Fusion - 4.0.2.8 release; SmartBrush - 2.6.0.121 release; Viewer - 5.1.1.98 release; Backbone - 1.6.2.54 release; Backbone Viewer - 1.6.2.578 release; Brainlab NodeMaster - 1.6.0.48 release; Brainlab TrackingService - 4.1.0.9 release; BrainwashExportPerformer - 2.0.0.24 release
- *Intraoperative neuromonitoring*: inomed Medizintechnik GmbH; ISIS IOM System; System für intraoperatives neurophysiologisches Monitoring; item no.: 504 004

Neuronavigation system

- *Navigation software*: Elements, Brainlab, Munich, Germany
- *Navigational camera*: Brainlab, Munich, Germany
- *Double monitor mounted on the ceiling*: Curve, Brainlab, Munich, Germany
- *Two screens fixed to the wall*: Buzz, Brainlab, Munich, Germany



Safety warnings

! **Safety warnings:** Direct (sub)cortical stimulation may induce seizure events. Ensure that measures to detect and terminate seizures are readily available. Said measures may include intra-operative electroencephalography (e.g., surface electrodes or strip electrode on the motor cortex) and cold Ringer's solution.

Ethics statement

Ethics and regulation statement: Informed consent from each patient must be obtained prior to surgery, and ethical clearance by the local hospital/university ethics committee must be granted.

Before start

Before starting the protocol, ensure all the materials listed in the "*Materials*" section are available in the operating room and ethical approval and patient consent is obtained.

Preparation

- 1 Abbreviations
 - m. = musculus
 - MEP = motor evoked potential
 - IONM = intra-operative neuromonitoring
 - MRI = magnetic resonance imaging
 - DES = direct electrical stimulation
- 2 Ensure all the necessary **material** is available to you in the operating room. See the "*Materials*" section for the list of required materials.
- 3 For increased efficiency of section 2 ("Motor evoked potential (MEP) monitoring"), **label and colour-code** the IONM needles before use with printed paper labels.
 - 3.1 Colour-code IONM needles by muscle, e.g., a red cables for shoulder muscles, green cables for arm muscles, etc.
 - 3.2 Label each IONM needle with the muscle and the side, e.g., "deltoideus, left". Attach the label at the end of the cable opposite the end with the needle.
 - 3.3 Example image of a labelled IONM needle.



Motor evoked potential (MEP) monitoring

- 4 This section is to be completed in the **anaesthesia bay**, outside the operating room if possible. After the patient is put under general anaesthesia, each muscle (see below) will be monitored bilaterally. Bilateral monitoring allows comparison of the ipsi-lateral to the contra-lateral muscle to judge whether a change in MEP response is due to technical faults or a true stimulation effect.

Note**Beware: Effects of anaesthesia on MEP amplitudes**

- Inhalation anaesthetics may reduce MEP amplitudes, or even completely suppress MEP amplitudes --> avoid if possible, or use low dosage
- Nitrous oxide may reduce MEP amplitudes by 30-70% --> avoid if possible, or use low dosage
- Propofol may increase latencies depending on dosage --> recommended anaesthetic for IONM, use low dosages
- Ketamine may increase MEP amplitudes --> always used in combination with another anaesthetic
- Opioids may reduce MEP amplitudes if used above standard dosage --> do not exceed standard dosage if possible
- Muscle relaxants suppress MEP amplitudes --> avoid if possible, or only use short-lasting boluses

(Source: "Application Notes for ISIS Systems Ring Binder with Applications Notes DE", see "Materials")

- 5 Insert the **MEP needles** into the target muscle belly. Each needle pair should have a distance of approx. 1-4cm between each needle, depending on the size of the muscle. After insertion, fixate the needle placement with plasters or tape at the site of insertion, to avoid dislocation of needles when positioning the patient. The monitored muscles are listed below.

**Note**

Always arrange the cables, so that the IONM cables run below those used for anaesthesia. In case of emergency, immediate anaesthetic access is vital.

Other electronic cables or equipment that is used may introduce artefacts in the MEP signal that must be considered when interpreting MEPs. For example, if a monopolar cautery pencil is used, the corresponding return electrode is often placed on the thigh of the patient which may add signal noise to nearby electrodes.

- 5.1 **Face: m. orbicularis oris** - insert needles above and below the lip with a distance of approx. 0.5-1cm between electrodes
Caveat: a stimulation of the left m. orbicularis oris, may also elicit a positive stimulation response in the right m. orbicularis oris - and vice versa - because it is a *ring* muscle
- 5.2 **Back: m. trapezius** - 1) palpate lateral border of the acromion, 2) palpate medial, upper part of the m. trapezius one hand's width from the acromion, 3) insert needles with a distance of approx. 1-3cm
- 5.3 **Shoulder: m. deltoideus** - insert needles in the midpoint between acromion and tuberositas deltoidea humeri with a distance of approx. 1-3cm

- 5.4 **Arm: m. triceps brachii** - 1) palpate the m. triceps brachii at the dorsal humerus when the arm is extended or lightly in flexion, 2) insert needles at approx. four fingers' width below the shoulder with a distance of approx. 1-3cm
- 5.5 **Arm: m. brachioradialis** - 1) bring arm in supination with flexion in the elbow, 2) palpate the muscle belly just below the elbow on the radial side, 3) insert needles at approx. two fingers' width from the elbow
Caveat: too medial an insertion may target the m. flexor carpi radialis; too deep an insertion may target the m. flexor digitorum superficialis
- 5.6 **Hand: thenar muscle** (e.g., m. abductor policis brevis) - 1) palpate first metacarpophalangeal joint and carpometacarpal joint, 2) insert needles at the midpoint between these two joints
- 5.7 **Leg: m. rectus femoris** - insert needles at the midpoint between an imaginary line between spina iliaca anterior superior and patella with a distance of approx. 1-3cm
Caveat: the lateral and medial parts of the m. quadriceps femoris may be targeted
- 5.8 **Leg: m. tibialis anterior** - 1) palpate the tuberositas tibiae, 2) m. tibialis anterior lies laterally to the tuberositas tibiae, 3) insert the needles at approx. four fingers' width from the tuberositas tibiae
Caveat: insertion too laterally and too deep may target the m. extensor digitorum longus
- 5.9 **Foot: m. abductor hallucis** - 1) palpate the medial malleolus, 2) distally at approx. two fingers' width lies the os naviculare, below which lies the m. abductor hallucis, 3) insert needles in the muscle body below the os naviculare
Caveat: too deep insertion of the needle may target the m. flexor digitorum brevis; too distal insertion of the needle may target the m. flexor hallucis brevis
- 5.10 (The description of how to target each muscle is translated from "Application Notes for ISIS Systems Ring Binder with Applications Notes DE", see "*Materials*")
- 6 Immediately after applying MEP needles, connect the **video splitter** to the intra-operative microscope video output.



Note

- Connect the video splitter before the neuronavigation of the patient is loaded. Connecting the video splitter after the neuronavigation is loaded may require a re-loading of the neuronavigation, which introduces delays.
- Do not yet connect the video cable from the microscope output to the IONM computer to reduce the risk of tripping as staff are still moving in and out the operating room.
- Connect the video cable from the microscope output to the IONM computer once the patient is draped. Thereby, the MEPs alongside a view of the surgical field can be displayed.

6.1 Example image of the video splitter being inserted in the microscope output.



Microscope HD-SDI output after video splitter insertion.



Microscope HD-SDI output after video splitter insertion with connecting cables attached.

- 7 After connecting the electrodes to the IONM computer, **start a screen recording** of the IONM computer screen. (Note: If you use the ISIS IOM System, as listed in the materials, the MEPs and corresponding stimulation parameters are automatically recorded). For later analysis, take particular care that the following is recorded:
- Record the MEPs induced by the stimulation probe
 - Record the microscope video
 - Record the stimulation settings of the stimulation probe

Direct Electrical Stimulation (DES)

- 8 In case of a **seizure**, terminate the seizure and assess whether a continuation of the protocol is feasible. Whether to proceed with the protocol is decided by the surgeon in charge of the operation.

Note

If **propofol or barbiturates** are administered to terminate the seizure, the subsequent suppression of cortical excitability may lead to a shift in the DES stimulation threshold.

1. Determine the new stimulation threshold
2. Continue the protocol with the new stimulation intensity
3. The stimulation parameters will automatically be saved in the IONM computer

- 9 Perform intra-operative **ultrasound** via the *ultrasound* option in Brainlab and save it. Caveat: Bleeding may introduce artefacts in the ultrasound and should be stopped before performing the ultrasound scan.
- 10 **Fuse** the **ultrasound** image with **pre-operative MRI** image using the automated steps within the Brainlab neuronavigation software.
- 11 While the pre-operative MRI image is being spatially corrected, **navigate** the **stimulation probe** via the *instrument options* in Brainlab.

Direct Electrical Stimulation (DES)

11.1



Navigated stimulation probe. The tip of the probe is in the tool for registering the probe with the navigation system.

Direct Electrical Stimulation (DES)

- 12 Assess the **accuracy** of your instrument navigation by calculating the tip deviation using *instrument options* in Brainlab.

Note

Troubleshooting in case of inaccurate instrument navigation.

- The long arm of the navigation star should be in line with the instrument axis (see image in 11.1)
- When reading in the tool but also *during* resection, hold the star directly into the navigation camera
- Elevate the microscope above the resection cavity, so the navigation camera has an unobstructed view of the navigation star
- Repeatedly check probe tip deviation using a reference point, e.g., after every 10 stimulations. In case of large tip deviations, navigate the instrument again.

- 13 Apply **DES** on the resection wall closest to the cortico-spinal tract in a grid-like manner. Maintain a consistent distance between stimulation points that is proportional to the stimulation intensity (for a stimulation intensity of 15mA, maintain a 1.5cm distance between two successive stimulation points, 10mA - 1cm, 5mA - 0.5cm, etc.). All subcortical stimulation should occur at least 10mm below the cortical surface to avoid activation of the corticospinal tract via cortical neurons.

Stimulate the resection cavity with 15mA. If the stimulation does not elicit an MEP, the next point will be stimulated. If the stimulation does elicit an MEP, the *same* point will be stimulated again with reduced stimulation intensity (the stimulation intensity is to be reduced in steps of 1mA). A gradual reduction in stimulation intensity is performed until no MEPs are induced. Thereafter, the next point will be stimulated.

Wait at least **2 seconds** between two stimulations of the same point. Remove the stimulation probe from the tissue during these 2 seconds until the next stimulation to account for any facilitation effects.

Manually record each stimulation point in the Brainlab neuronavigation software concurrently with each stimulation. In Brainlab, the stimulation points will automatically be numbered and fitted with a time tag (hours:min:sec) upon recording the stimulation points.

Note

Stimulation parameters

- High-frequency stimulation (1.7Hz)
- Train-of-five stimulation
- 500µs pulse width
- 4ms interstimulus interval
- 0.5Hz high-pass filter (on IONM display)
- 2000Hz low-pass filter (on IONM display)
- 300V voltage
- 15mA default stimulation intensity (the default intensity may be adjusted case-dependently, e.g., for highly eloquent located lesions, the default stimulation intensity may be <15mA)

- 14 Throughout stimulation, track occurrence of events that may affect the **volume of stimulated tissue** (e.g., bleeding, changes in contact pressure, seizure) and enter comments on the timeline of the IONM computer screen video. These stimulation points may require special consideration during analysis.

Log the patient's blood pressure, body and room temperature, use of a heating blanket, anaesthetic protocol throughout surgery, as changes in these parameters affect the conductivity of tissue and therefore, affect MEP amplitudes and/or latencies.

Note

Time-synchronisation of recordings

All recordings - namely, subcortical stimulation points and motor evoked potentials - are time-locked. Upon recording a stimulation point, the stimulation point is automatically fitted with a time tag in Brainlab (hours:minutes:seconds). Likewise, the monitor of the IONM computer displays a timeline allowing identification of the time (hours:minutes:seconds) at which an MEP was recorded. The time tags of the subcortical stimulation and the corresponding MEPs, therefore, allow time-synchronisation of all recordings.

Moreover, the microscope video is saved onto the IONM computer, allowing the user to see when the stimulation probe made contact with the brain tissue and when the corresponding MEP occurred.

Saving data

- 15 After the surgery, save the **stimulation points** in your navigation software and export their coordinates for analysis.



- 16 Save and export the **IONM screen video** from the IONM computer for analysis.