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Continuous dynamic mapping of the corticospinal tract during surgery of motor eloquent brain tumors: evaluation of a new method

Clinical article

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Object. The authors developed a new mapping technique to overcome the temporal and spatial limitations of classic subcortical mapping of the corticospinal tract (CST). The feasibility and safety of continuous (0.4–2 Hz) and dynamic (at the site of and synchronized with tissue resection) subcortical motor mapping was evaluated.

Methods. The authors prospectively studied 69 patients who underwent tumor surgery adjacent to the CST (< 1 cm using diffusion tensor imaging and fiber tracking) with simultaneous subcortical monopolar motor mapping (short train, interstimulus interval 4 msec, pulse duration 500 µsec) and a new acoustic motor evoked potential alarm. Continuous (temporal coverage) and dynamic (spatial coverage) mapping was technically realized by integrating the mapping probe at the tip of a new suction device, with the concept that this device will be in contact with the tissue where the resection is performed. Motor function was assessed 1 day after surgery, at discharge, and at 3 months.

Results. All procedures were technically successful. There was a 1:1 correlation of motor thresholds for stimulation sites simultaneously mapped with the new suction mapping device and the classic fingerstick probe (24 patients, 74 stimulation points; $r^2 = 0.98$, $p < 0.001$). The lowest individual motor thresholds were as follows: > 20 mA, 7 patients; 11–20 mA, 13 patients; 6–10 mA, 8 patients; 4–5 mA, 17 patients; and 1–3 mA, 24 patients. At 3 months, 2 patients (3%) had a persistent postoperative motor deficit, both of which were caused by a vascular injury. No patient had a permanent motor deficit caused by a mechanical injury of the CST.

Conclusions. Continuous dynamic mapping was found to be a feasible and ergonomic technique for localizing the exact site of the CST and distance to the motor fibers. The acoustic feedback and the ability to stimulate the tissue continuously and exactly at the site of tissue removal improves the accuracy of mapping, especially at low (< 5 mA) stimulation intensities. This new technique may increase the safety of motor eloquent tumor surgery.
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Key Words • **brain mapping** • **corticospinal tract** • **electrical stimulation** • **intraoperative neuromonitoring** • **motor evoked potential** • **tumor surgery** • **functional neurosurgery**

Electrical stimulation is a validated intraoperative technique for identifying the motor fibers in deep white matter tracts.[1,3,15,38] Intermittent subcortical mapping with a handheld probe is used intraoperatively to localize the corticospinal tract (CST) and to reduce the risk of motor deficits, especially when operating on nearby infiltrating tumors.[2,14] There is growing evidence that maximizing the extent of resection (EOR) improves survival, both in low-grade gliomas[7,21,30,47,48] and in glioblastomas.[28,41,50,57] In the latter, achieving gross-total resection (GTR) or complete resection of enhancing tumor (CRET); that is, removal of the final 1%–2% of the tumor, seems to provide the most benefit in terms of survival.[28,41,50]

Although mapping is the gold standard for localizing the CST during surgery, it is far from being standardized or ideal. Different techniques, stimulation intensities, concepts, and warning signs are used.[2,14,25,40,55] Besides methodological limitations,[55] the temporal and spatial information provided by contemporary mapping techniques are only punctiform. During tumor removal the surgeon does not know exactly where and how critically the CST is approached, unless the resection is stopped and the mapping probe is used to explore the resection cavity point by point.

Abbreviations used in this paper: CRET = complete resection of enhancing tumor; CST = corticospinal tract; CUSA = Cavitron ultrasonic surgical aspirator; DCS = direct cortical stimulation; EEG = electroencephalography; EOR = extent of resection; GTR = gross-total resection; MEP = motor evoked potential; MRC = Medical Research Council; MT = motor threshold; TES = transcranial electrical stimulation; TOF = train of five.

Using the monopolar train-of-five (TOF) technique, a motor threshold (MT)-to-distance relationship exists for the subcortical mapping of the CST.[22,25,36,37,39] We recently showed that a safe mapping corridor for mechanical injury of the CST exists between high and low MTs, and that both significant signal changes in motor evoked potential (MEP) monitoring and permanent motor deficits do not occur before very low MTs of < 1–2 mA.[45] We also provided data supporting the hypothesis that the interruptive and punctiform technique of mapping with insufficient spatial and temporal coverage of the surgical site may be a cause of motor deficits despite higher and apparently safe MTs (3–6 mA).[45]

The objective of this prospective study was to evaluate a new mapping technique that allows continuous stimulation of the white matter in the surgical cavity without interrupting the procedure of tumor removal. This can be achieved using an electrically isolated suction and mapping device (Fig. 1) instead of the classic monopolar fingerstick probe. The device is equipped with additional acoustic feedback for the surgeon when an MEP is elicited.

We specifically investigated the following areas: 1) whether we could get reliable and robust MEP signals during the surgical manipulation; 2) the correlation between the motor thresholds for the dynamic device and the classic monopolar fingerstick probe; and 3) the safety of the method with regard to postoperative neurological deficits or intra- and postoperative seizures.

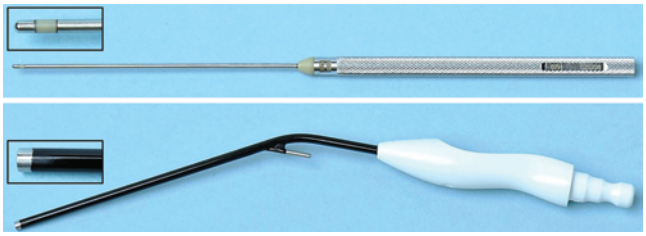

Fig. 1. Photographs showing the combined mapping and suction device. Continuous stimulation current can be delivered via the connector beneath the handle.

Methods

Patient Population

A series of 69 patients with intraaxial tumors close (≤ 10 mm) to the CST who underwent tumor surgery between August 2010 and December 2012 were included. Detailed information about the preoperative preparation and imaging can be found elsewhere.[45] Six of these patients were included in a previous mapping study.[45] Preoperative clinical evaluation was done according to the Medical Research Council (MRC) Scale score (M1–M5), National Institutes of Health Stroke Scale score, and Karnofsky Performance Scale score. All patients signed an informed consent for the surgery and the procedure. This analysis was approved by the local institutional ethics review board (Cantonal Ethics Commission [Kantonale Ethikkommission—KEK], Bern University Hospital, Bern, Switzerland).

Preoperative Data

There were 38 male and 31 female patients; the mean age of the patients was 49 years (SD 16 years). Forty-nine patients presented with a newly diagnosed cerebral tumor and 20 suffered from tumor recurrence. The chief complaint leading to diagnosis was epileptic seizure in 27 patients, progressive motor weakness in 14, mental status changes in 8, and headache in 6. In 14 patients tumor progression was diagnosed in the MRI follow-up evaluation. The preoperative Karnofsky Performance Scale score was 100% in 5 patients, 90% in 49, 80% in 12, and 70% in 3 patients. Forty-one patients had normal preoperative motor status and 16 presented with slight motor impairment (M5− or M4+). Ten patients had a preoperative motor impairment ranging from M4 to M3, and 2 patients presented with Grade M2–M1 motor impairment.

Intraoperative MEP Monitoring and Mapping

All operations were performed after induction of general anesthesia, which was induced with a bolus of propofol (1–2 mg/kg body weight), fentanyl (1–2 μg/kg body weight), and remifentanil (1–2 μg/kg body weight), and was maintained with propofol (100–200 μg/kg/min) and remifentanil (0.5 μg/kg/hr). A short-acting relaxant (Esmeron, 0.6 mg/kg body weight) was administered for intubation purposes only. Recovery from muscle relaxation was tested by use of the "train-of-four" technique involving percutaneous stimulation of the right median nerve (40 mA, 0.2-msec pulse duration).[56]

For intraoperative neurophysiological monitoring and mapping, the ISIS system equipped with a constant current stimulator (OSIRIS, maximal stimulator output 220 mA; both from Inomed Co.) was used. Muscle MEPs were recorded by pairs of needle electrodes inserted in standardized contralateral target muscles for the face as well as the distal and proximal upper and lower limbs. Details about the direct cortical stimulation (DCS)-MEP monitoring performed using a strip electrode can be found elsewhere.[45,54] The DCS-MEPs were considered as stable, allowing ranges of (relative) thresholds ± 4 mA from baseline values. A sudden threshold increase > 4 mA in motor stimulation intensity that could not be explained by technical or anesthetic confounders[5,26] was interpreted as a specific MEP warning sign. Loss of MEP was defined as no motor response even when using DCS intensity up to 20 mA.[34] The surgeon was notified when motor stimulation intensity had to be increased > 4 mA, or when a loss in MEPs occurred.

Transcranial electrical stimulation (TES) was performed if the placement of a grid electrode was impossible, for example due to dural adhesions. For TES, corkscrew electrodes were placed at C1, C2, C3, C4, and CZ according to the 10–20 electroencephalography (EEG) system.[9,54] The same stimulation parameters as for DCS were applied and are described elsewhere.[44] Monitoring for seizures was done using the corkscrew scalp electrodes that had been placed for the purpose of somatosensory evoked potential recordings. Different derivations of recordings were applied simultaneously, for example C3′/Fz, C4′/Fz, C3′/C4′, C3′/Cz′, and C4′/Cz′. The surgeon was informed when spikes occurred, and irrigation with cold Ringer solution was performed.

Standard Mapping Using a Fingerstick Probe

We used the standard fingerstick probe for systematic verification of the MTs that were obtained with the dynamic device in the first 24 patients. In the remaining 45 patients, mapping was performed only with the new dynamic device.

For standard mapping, a monopolar probe with a 1.6-mm electrode was used to deliver a monophasic current up to 22 mA.[25,52] The reference electrode was placed at Fzp.[10] Identical stimulation parameters as described above for DCS were applied (TOF stimuli, interstimulus interval 4 msec, pulse duration 500 μsec).[10,22,25,36] Cathodal (negative current) stimulation was used for subcortical mapping.[20,22,25,33,36,40]

Dynamic Continuous Mapping Device

The device can be regarded either as a monopolar probe with suction capabilities or, as we would prefer, a suction device with monopolar mapping capabilities (Fig. 1). The term "dynamic" refers to the quickly changing location of the tip of the suction according to the "flow" of the tissue removal or operation. It provides continuous stimulation (mostly we used 2 Hz) of the tissue where the tip of the suction device is actually placed. The electrophysiological parameters are identical to the parameters used with the fingerstick probe. Stimulation is activated by connecting the cable for the standard monopolar fingerstick probe directly to a connection site at the suction device. The surface of the suction probe is isolated to limit the electrical contact to the tip of the device.

Software Adaptations

To allow a continuous stimulation while avoiding concurrent induction of seizures, a low repetition rate of the trains was chosen (0.4–2 Hz). Otherwise the identical stimulation parameters as for the classic monopolar TOF, described above, were selected. Furthermore, two sounds were used for acoustic feedback to guide the surgeon. Both sounds were easy to differentiate even in a noisy environment. The first sound (high pitch) was delivered with every single train of stimulation as a feedback signifying that adequate current was delivered to the tissue. The second sound (low pitch) was only delivered if the amplitude of a MEP response in the recorded muscles reached a value > 30 μV. At the same time, the responses could be observed in both the free-running and triggered electromyography screens.

Use of Continuous Dynamic Quantitative Mapping During Tumor Removal

Manual use of the new mapping probe is identical to the standard suction device; it is manipulated in one hand while the Cavitron ultrasonic surgical aspirator (CUSA) or the bipolar forceps is manipulated in the other hand. During tumor resections, the surgeon moves the suction tip automatically to the same place where the resection is performed, with micromovements around the tip of the resecting instrument to provide a clean surgical field and a direct view to the site of the tumor-removing instrument. Thus, the tip of the mapping suction device can deliver the stimulation current directly at the place where the CUSA or bipolar forceps actually destroys and removes the tumor tissue. Because the suction probe usually works at the same site as the resection instrument, it provides a dynamic mapping with changing locations.

When getting used to the dynamic device, it is more deliberately used as "CST radar"—that is, testing whether a MEP can be elicited with a chosen stimulation intensity around the current site of tissue removal. Attention must be paid to keep in contact with the tissue at the site of resection. We activated the mapping suction device when we were approximately 10 mm from the CST, as indicated by neuronavigation with fiber tracking or according to the anatomical orientation of the surgeon. The stimulation intensity was initially set at 10–15 mA, which corresponds to a distance of approximately 10–15 mm from the CST in our experience and as reported by others.[22,25,36,37,39,45] The "high pitch" sound indicates that the current is applied correctly to the tissue. When an MEP is elicited, the surgeon immediately hears the "low pitch" sound and observes where the mapping device is working (Video 1).

Video 1. During this removal of a glioma in the median-dorsal frontal lobe the stimulation current of the suction-mapping device is 3 mA. The tumor is slowly removed with CUSA at low power settings. The high-pitch sound indicates that stimulation is being performed, but there is no response from the CST. The low-pitch sound indicates the site where resection approaches the CST. Copyright Andreas Raabe. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

The stimulation intensity is then reduced in 2-mA steps. Then the surgeon continues tumor removal until again a "low pitch" sound indicates that resection is getting closer to the CST. The lowering of the stimulation intensity corresponding to reduction of the distance when approaching the CST is reflected in the term "quantitative" mapping.[45]

In cases in which the surgeon judged from the intraoperative setting that he or she would not be able to remove the tumor completely, we usually stopped resection when an MT of 3 mA was reached. However, when the surgeon believed that a GTR or CRET could be achieved, and provided that DCS-MEPs remained stable, resection was continued slowly, delivering 1- or 2-mA stimulation during dynamic mapping. Resection was stopped when the 1- or 2-mA stimulation intensity triggered an MEP, indicating the close distance to the CST. If alterations in DCS-MEP (defined above) were noticed, resection was immediately paused. In an attempt to avoid permanent postoperative motor deficit, removal of further tumor tissue was stopped when these DCS-MEP alterations persisted for > 15 minutes despite pausing, and despite removing the retractor (which was rarely used), increasing cerebral perfusion pressure to normal, irrigating with warm saline, local application of nimodipine, normalizing anesthesia, and ruling out technical confounders.[34]

Postoperative Imaging

Postoperative MRI, performed within 48 hours after surgery, was evaluated by independent senior radiologists from the neuroradiology department. The primary goal of surgery was GTR, defined as resection of all areas with FLAIR signal in WHO Grade II gliomas; or CRET,[58] defined as any T1 contrast–enhancing tissue in gliomas (WHO Grade III) and glioblastomas (Grade IV). Additionally, every early postoperative MRI perfusion- and diffusion-weighted sequence included a routine search for perforator injury and infarction.

Clinical Examination and Data Analysis

Postoperative clinical evaluations were performed with the same scales used preoperatively. The evaluation was repeated 1 day after surgery, at day of discharge, and at the 3-month follow-up visit. Descriptive statistical analyses were performed (mean, SD, and percentage) for selected parameters, including patient characteristics and MTs of MEP responses. For analysis of neurophysiological acquired data, NeuroExplorer of the ISIS (Inomed Co.) was used.[44]

Results

Final Histopathological Findings

The tumor entities according to final histopathological findings after surgery were distributed as follows: low-grade glioma (n = 10 patients: 3 astrocytoma, 2 oligodendroglioma, 3 oligoastrocytoma, 2 pilocytic astrocytoma); anaplastic glioma (n = 17 patients: 5 anaplastic astrocytoma, 8 anaplastic oligodendroglioma, 4 anaplastic oligoastrocytoma); glioblastoma (n = 26); ependymoma (n = 1); primitive neuroectodermal tumor (n = 3); metastasis (n = 7); and cavernoma (n = 5). Thus, 83% of patients (n = 57) had intraaxial brain tumors and 17% (n = 12) had metastatic or vascular lesions.

Technical and Handling Analysis

There were no technical problems. The dynamic mapping device was connected via the same cable for monopolar stimulation as the fingerstick probe. The MTs that were found during the stimulation were stable and the method robust; that is, it was always reproducible at the same site, and surgical manipulation did not lead to any instability of the MEP stimulation or recording. The surgeons using the device found it more helpful and more ergonomic than the classic fingerstick probe. They reported a higher confidence in knowing the exact location and safe distance from the CST during resection compared with the classic fingerstick probe.

Extent of Resection and Reasons to Abort Further Removal

Postoperative MRI, performed within 48 hours after surgery, showed radiologically complete resection in 75% (n = 9) of the metastatic or vascular lesions and GTR/CRET in 68% (n = 39) of the intrinsic brain tumors. Subtotal resection was achieved in the remaining 21 patients. In 14 of these patients, the surgeons stopped tumor removal at mapping MTs between 2 and 5 mA when they recognized that complete resection would not be possible. In the remaining 7 of the 21 patients, debulking only was planned and performed according to the preoperative MR images (infiltration of other eloquent systems like basal ganglia, thalamus, optic radiation, or corpus callosum).

Motor Thresholds With Continuous Dynamic Quantitative Mapping

In the first 24 patients, both stimulation probes were used. A virtually 1:1 correlation of motor MTs for stimulation sites simultaneously mapped with the suction device and the fingerstick probe was found (74 stimulation points, $r^2 = 0.98$, $p < 0.001$; Fig. 2). Starting with Case 25, the fingerstick probe was no longer used and mapping was performed using only the continuous dynamic technique.

All procedures were technically successful. The lowest individual MTs were as follows: > 20 mA, 7 patients; 11–20 mA, 13 patients; 6–10 mA, 8 patients; 4–5 mA, 17 patients; and 1–3 mA, 24 patients (Fig. 3). The MEP monitoring (DCS, TES, or combined method) showed stable signals in 51 patients, unspecific changes in 12, and sudden and irreversible alterations in 6. No patient showed an irreversible loss of MEPs.

Adverse Events

Postoperative Motor Deficits. New postoperative worsening in motor status on the day after surgery was observed in 33% of cases (n = 23): 19 patients with intrinsic tumors and 4 with metastatic or vascular lesions. Of these, 12 presented with a motor worsening of 1 point and 11 patients presented with a motor worsening of ≥ 2 points on the MRC Scale. At the day of discharge, the deficit had already reversed in 16 patients, and was still present in 7 (10% of all cases). Of these 7 patients, 2 had a relative worsening of motor status of ≥ 2 points on the MRC Scale (Fig. 3). At the 3-month visit, 2 patients (3%) presented with a persistent motor deficit. One patient had a vascular injury of a major artery (Case 4, A_2 segment of the anterior cerebral artery), and the other had a micro-

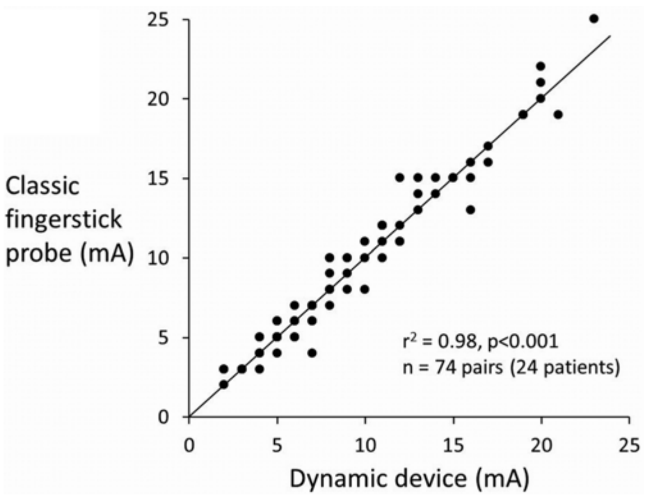

Fig. 2. Scatterplot showing motor mapping thresholds measured with the classic fingerstick probe and the dynamic mapping device at the topographically identical site (24 patients, 74 stimulation sites).

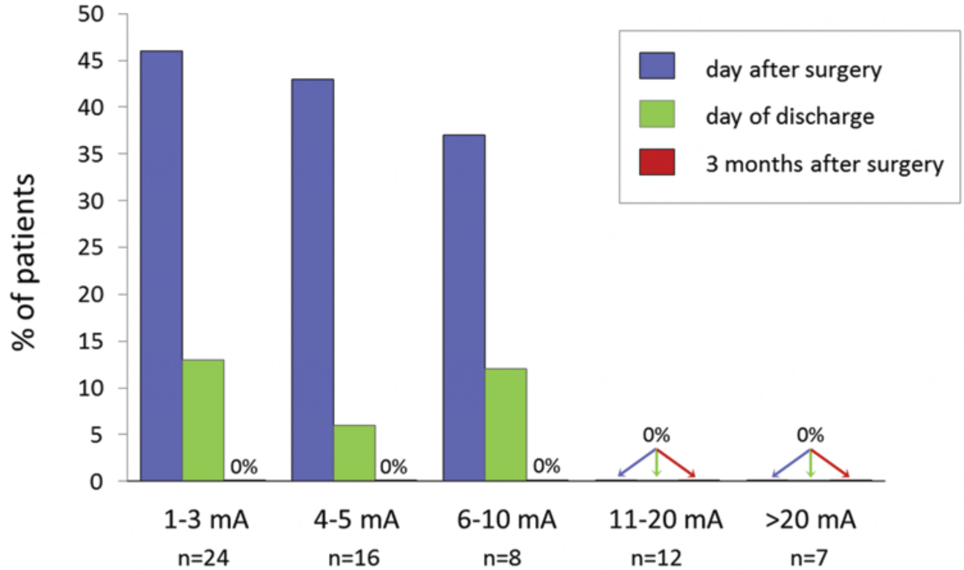

Fig. 3. Bar graph showing the rate of new postoperative motor deficits attributable to mechanical CST injury in the different lowest mapping motor threshold groups on the day after surgery, at discharge, and at the 3-month visit. At the 3-month visit, no patient had a motor deficit caused by mechanical injury of the CST (nil third bars; 0%). The 2 patients with vascular injury were excluded; they would have appeared in the "4–5 mA" and the "11–20 mA" mapping groups, and both showed a permanent motor deficit.

vascular injury at the cortical level of the precentral gyrus (Case 57, Fig. 4). The patient in Case 4 showed a relative worsening of motor status, from M5 to M3 (lowest mapping MT 20 mA; sudden, irreversible threshold increase > 4 mA in DCS-MEP stimulation). The patient in Case 57 had a permanent motor worsening from M5 to M4+ (lowest mapping MT 4 mA; sudden, irreversible threshold increase > 4 mA in DCS-MEP stimulation intensity). No patient had a direct mechanical injury of the CST.

Seizures. A single intraoperative seizure related to continuous dynamic mapping occurred in 3 patients (4%). All intraoperative seizures were detected early in the simultaneously performed EEG recordings. They were terminated by application of standby cold Ringer solution and intravenous bolus injection of clonazepam or thiopental, without further consequences.

Discussion

In patients with low-grade gliomas or glioblastomas, presumed motor eloquence of the tumor according to the preoperative MR images is a risk factor for both incomplete resection and postoperative motor deficit.[1,7,30] The latter is also a risk for a decreased quality of life, disease progression, and death.[7,30] However, preoperatively presumed motor eloquence is regarded to be modifiable by intraoperative neuromonitoring such as MEP monitoring and mapping.[7,8] Whereas monitoring provides information about the electrical and structural integrity of the tract,[9,11,12,34] mapping is aimed at localizing the position of and indicating the safe distance from the CST.[1,2,14] With the use of mapping techniques, many tumors that were presumed to be motor eloquent based on preoperative assessment were shown via intraoperative monitoring to be located outside the fibers of the CST and could be removed without permanent deficits.[1,2,4,7,8,10,13,15,34,43,45] However, the motor threshold below which the tumor may no longer be safely removed remains unclear, and there is

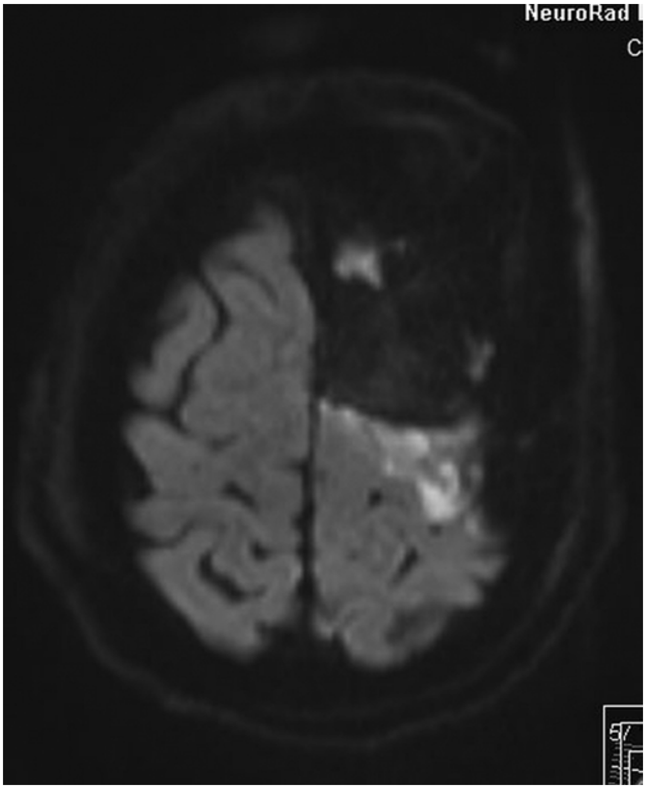

Fig. 4. Early (24 hours) postoperative diffusion-weighted imaging showing microvascular injury within the hand notch of the precentral gyrus as the cause of permanent motor deficit in the patient in Case 57.

also doubt as to whether a reliable threshold exists, both for monopolar and bipolar stimulation techniques.

Is There a Safe Lower MT?

We have recently confirmed that in monopolar high-frequency TOF mapping there is a safe corridor between 20 mA, which is usually the highest stimulation intensity to start with, and 5 mA at the lower range.[45] An MT within this range excludes mechanical damage of the CST and permanent motor deficit, provided that the measured MT is indeed the lowest in the resection cavity, the surgeon does not continue resection after mapping, and no vascular injury has occurred. This MT corridor has been reported by several authors.[22,25,32,36,37,55] However, we also found that the critically low mapping MTs associated with motor deficit are probably lower than previously thought. In our experience, of the patients with a very low mapping MT of 1 mA, 75% showed stable DCS-MEP or only unspecific reversible changes, and none of them had a permanent motor worsening at 3 months.[45] Still, it should be noted that nonvascular motor deficits occurred at MTs of 6, 3, and 1 mA.[45]

The Cause of Deficits Despite Reliable Low MTs

Apart from the vascular injuries, how can we explain these deficits? From our investigation of these cases we conclude that it is unlikely that variability of the electrophysiological parameters or MTs were the cause of these deficits. Assuming that the CST was within a very short distance (MTs of 1, 3, and 6 mA) and after analyzing the videos from the operations, we believe that the continuing resection was the cause of the CST injury, because it was not interrupted appropriately for repeated 1-mm stepwise mapping. This problem is methodologically inherent to the sequential-in-time and punctiform-in-space method of mapping with the fingerstick probe.

The present study also supports the concept of reliably low MTs. Tumors in a total of 24 (35%) of 69 patients were resected until an MT of 1–3 mA was reached, and none of the patients showed a permanent motor deficit. As illustrated in Fig. 3, temporary motor deficits occurred in this study only when an MT of < 11 mA was reached; these were slightly higher in the lower MT groups (temporary motor deficit rate at 1–3 mA, 46%; 4–5 mA, 43%; 6–10 mA, 37%) but improved in all MT categories until the patients were discharged (temporary motor deficit rate at 1–3 mA, 13%; 4–5 mA, 6%; 6–10 mA, 12%) and had completely recovered at the 3-month visit (no permanent deficit in any MT group). These are preliminary findings; whether continuous dynamic mapping indeed increases the safety of the operation should be investigated in a randomized study in which a comparison with classic subcortical monopolar mapping using the fingerstick probe is performed.

The Concept Behind Continuous Dynamic Quantitative Mapping

In our view, the concept of resecting tumor tissue down to very low MTs (1–2 mA) calls for a refinement of the mapping technique. The information about the topographical localization of the CST with respect to the tumor resection cavity or the actual dissection plane should not be obtained by interrupting the tumor resection and mapping punctiform in space. Optimally, CST localization should be available continuously during the surgical manipulation to prevent inadvertent injury to the CST (Fig. 5). This is especially important when a surgeon attempts to complete tumor tissue resection in areas of already low MTs. Continuous (temporal coverage) and dynamic (spatial coverage) mapping can be technically realized by integrating the mapping probe at the tip of a suction device with the stimulating tip; that is, the mapping probe is in contact with the tissue where the resection is performed.

When using this device, the surgeon should start with a stimulation intensity of approximately 10–15 mA when the image guidance indicates a distance of approximately 10–15 mm from the CST. When the resection approaches the CST, the first positive MEP can be found, which we have coupled with an acoustic low-pitch sound. The surgeon then usually continues the resection at the tumor site more distant from the CST; that is, where no MEP is triggered. When returning to the MEP-positive site, the stimulation intensity is lowered in 2-mA steps and the resection is continued, and so on.

The important principle is to keep working only on MEP-negative sites. With this technique, the tumor is always removed first at areas more distant from the CST. If tumor is only left at MEP-positive sites, the stimulation intensity is then slowly decreased. Working on MEP-positive sites risks resection into areas where the MT is actually lower than the applied stimulation intensity, and motor deficits may occur even though an apparently CST safe-distance stimulation intensity was applied.

When a subtotal resection is planned, we still adhere to the principle to stop tumor removal at 3-mA positive MEP sites. However, if GTR/CRET can potentially be achieved, resection may be continued slowly while 2-mA stimulation current is applied, and the resection site remains MEP negative with 2 mA. Naturally, removing the tumor at these low MTs—not more than 0.5- to 1-mm layers of tissue—should be done with the lowest CUSA settings or only suction. After using 2 mA as the critical MT during most of the study time and gaining more confidence, we now stop resection definitively when we reach an MT of 1 mA. We set the stimulation intensity to 1 mA and continue very slowly and carefully, but stop definitely at a 1-mA MEP-positive site, even when the DCS-MEP monitoring remains very stable. Using the dynamic mapping device and this approach, we had no cases in which a loss of MEP monitoring signal occurred that was attributable to mechanical CST damage.

Technical Considerations of Electrical Stimulation

In addition to the monopolar 200- to 300-Hz TOF or "short train" stimulation used in this study, the classic Penfield bipolar 50- to 60-Hz mapping is a reliable technique for localizing the CST.[24] However, the monopolar TOF stimulation allows a more quantitative evaluation of MEP changes regarding amplitude, latency, and duration.[10,24,44,56] In contrast to the bipolar Penfield method, the

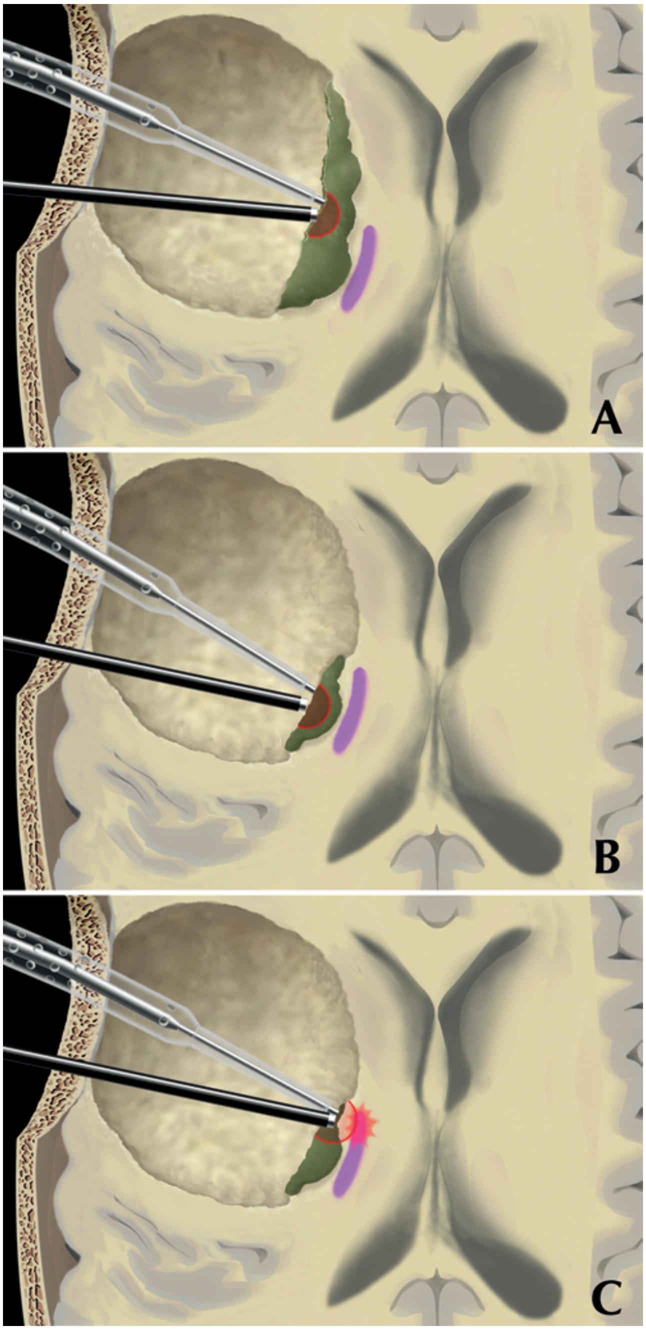

Fig. 5. Illustration of the surgical technique. The suction-mapping device applies the stimulation current at the site of tumor removal **(A)**. The depth of tissue penetration of the stimulation current is proportional to the applied stimulation intensity (rule of thumb: 1 mA = 1 mm). In this illustration, the stimulation intensity is set at 7 mA. Resection proceeds toward the CST, but the continuous stimulation generates a "warning" zone around the suction-mapping device during tumor removal **(B)**. At a distance < 7 mm from the CST, the suction-mapping device stimulates the CST and triggers MEPs **(C)**. Copyright Andreas Raabe. Published with permission.

monopolar TOF stimulation triggers a single MEP rather than a tonic muscle response.[24] Moreover, radial spreading of the electrical field of the monopolar TOF probe allows the electrical current to enter perpendicularly into the axon, resulting in a more effective stimulation.[55] The field of a bipolar stimulation probe is more heterogeneous with regard to the lines of equal potential, with the exception of the space between the two tips. So if the region of interest is not directly located between the two tips and farther away from the stimulation site, the electrical field is not homogeneous. All of these aspects, taken together, may explain why monopolar TOF stimulation might be more reliable for working with quantitative thresholds and trying to predict the distance from the CST by absolute stimulation current values.[17,22,36,37,39,45,55]

Significance of Completing a Resection (GTR/CRET)

The contemporary dogma of surgery for gliomas can be summarized by the term "maximum safe resection."[16,19] However, the attempt to increase survival by extending the resection toward eloquent areas has a Janus face. The EOR directly influences the prognosis of glioma patients.[28,50] Therefore, maximizing the EOR has become the goal that has driven development of new resection-enhancing imaging technologies such as intraoperative MRI, ultrasound, 5-aminolevulinic acid fluorescence imaging, and in vivo confocal microscopy.[42,46,49,50] This strategy of a more extensive resection, however, increases the risk of permanent neurological deficits, which have been shown to decrease quality of life, limit further adjuvant therapies, and reduce overall survival time.[31,51]

There is accumulating evidence that CRET or GTR is disproportionately beneficial in terms of survival. In a recent analysis of the influence of EOR in glioblastomas, the highest impact on survival was found for removal of the final 2% (that is, between 98% and 100% tumor removal).[28,41] Likewise, the analysis of 5-aminolevulinic acid study data showed a significant survival difference only between patients with GTR and patients with residual tumor, and not between patients with varying volumes of residual tumor. Long-term survivors (> 24 months) were almost exclusively in the group of patients with GTR.[50] Thus, the target in terms of maximizing the EOR—that is, complete resection, GTR, or CRET—is well defined for the neurosurgeon. Mapping techniques that help to better delineate the CST may therefore have the potential not only to prevent deficits, but also to maximize resection and to improve long-term survival.

Critical Discussion

Our results confirm the findings of our previous study on safe subcortical low-threshold (< 3–5 mA) motor mapping.[45] However, the absence of patients with mechanical injury remains surprising given that we were working below the 3–5 mA that is usually considered a critically low mapping MT in the literature.[22,25,36] Our permanent motor deficit rate of 3%–5%[45] compares favorably with the 3.5%,[29] 7%,[6,15,23] 9%,[35] 10%, 12%,[25,27,36] and 17%[18,39,59] of other reports. However, a comparison between the different published studies remains problematic for various reasons. Not all tumors were very close to or within the CST, the deficit rates were often given at different time points, corresponding MTs were not always reported, and surgeries used different techniques (TOF vs Penfield vs only MEP monitoring) or were not reported separately for different eloquent areas (motor, language, visual, memory, and so on).[8] That the tumors in our study were indeed close to the CST is illustrated by the mapping findings. Of our 69 patients, motor tracts were identified by mapping in 90% of patients (n = 62), and 59% had low MTs of either 1–3 mA (24 patients) or 4–5 mA (17 patients).

The 3- to 5-mA MT as the classic stop sign of monopolar short-train mapping was established by experience. It might therefore include a safety margin of a few millimeters that the surgeon requires due to the temporal and spatial variability intrinsic to the classic interruptive and punctiform fingerstick probe mapping.

The findings supporting the concept of safe low MTs and continuous dynamic mapping include the high correlation between the MTs obtained with the fingerstick probe and the dynamic device, and the observation that during tumor resection performed using dynamic mapping, no cases of MEP monitoring signal loss occurred. These results may be explained by a 1- to 2-mm safety margin that was respected for all areas of the surgical cavity critically close to the CST, which may be difficult to achieve without simultaneous stimulation of the site where the tumor is resected.

The incidence of 3% for vascular causes of a permanent motor deficit corresponds with the 2% reported in our previous study.[45] In the literature, injury of major vessels or perforating arteries is a well-known cause of motor deficits,[34,35] but the numbers were rarely reported separately from mechanical injury of the CST. In a study investigating the early postoperative MRI findings in patients with intraoperative MEP deterioration or loss, 22% of patients had an ischemic and 4% had a hemorrhagic lesion in the CST or motor cortex as the presumable cause of MEP abnormality.[53]

Continuous dynamic mapping is more relevant for the resection of infiltrative tumors. Although the majority of patients in our study had gliomas (83%), metastases comprised 10% (n = 7) and cavernomas 7% (n = 5) of all cases. The latter entities are usually more amenable to complete resection. There were several reasons for including them in our study. In our daily clinical routine, we also use mapping and monitoring for metastases and cavernomas. Although they are usually better delineated than gliomas, the distance to the CST remains an important risk factor for a new motor deficit after resection. Also, not all metastases are easily removable. Some are cystic with a thin wall, which folds irregularly into the white matter after collapse of the cyst during surgery. These are "pseudoinfiltrative" rather than infiltrative, and deserve the same mapping precautions as gliomas, for which it may be preferable to leave a remnant behind for radiosurgery rather than to risk causing a deficit that might impair motor function in these patients, with an often reduced life expectancy. In our current study, metastases comprised 10% of cases. Of the patients with metastases, 3 (43%) of 7 had tumors with intraoperatively poorly defined margins, and we stopped resection when we reached electrophysiological warning criterion (MT = 2 mA, MT = 3 mA with significant MEP change, and MT = 5 mA). Despite stopping resection, all 3 had a temporary postoperative motor deficit, which fortunately resolved completely.

Using the general electrophysiological concept as described in this and our previous study,[45] the surgeon can still decide—depending on the histological type of the lesion, the border of the tumor, and the patient's situation—whether the resection at a particular MT should be continued. The advantages of mapping techniques are more obvious in intrinsic tumors, but knowing the proximity of the CST may influence the resection strategy, the tissue manipulation, the speed of dissection, the power of electrocoagulation, and the technique of hemostasis in metastases and cavernomas as well.

Conclusions

Continuous dynamic mapping was found to be a feasible and ergonomic technique for localizing the exact site and distance from the operational site to the CST. The acoustic feedback and the ability to stimulate the tissue continuously and exactly at the site of tissue removal improved the accuracy of mapping, especially at low (< 5 mA) stimulation intensities. This new technique may increase the safety of motor eloquent tumor surgery.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Raabe, Beck, Seidel. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Raabe.

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