



Introduction of a novel connection clip for the ultrasonic aspirator for subcortical continuous motor mapping



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Introduction: A connection clip to the ultrasonic aspirator handpiece was introduced for simultaneous resection and mapping of corticospinal motor tract (CST) (Kombos et al., 2001).

Research question: To report retrospectively the use of this clip in cerebral surgery with CST mapping.

Material and methods: Eight women and four men were included (mean: 55.8 years, SD 17.3 years). The ultrasonic aspirator handpiece was stimulated every second (5 biphasic pulses, 0.4 ms per phase, max 14 mA). Motor evoked potentials (MEPs) (Taniguchi et al., 1993), with transcranial and direct cortical stimulation, were alternated with CST mapping. The distances between the stimulus locations to the CST (diffusion tensor imaging based fibre tractography) were determined postoperatively. Muscle strength was evaluated pre-operatively, at discharge and 3 months.

Results: Motor mapping thresholds ranged between 2 and 13 mA, in 12 consecutive patients (7 post-central, 5 insular). The distance of the stimulation site to the CST was fitted ($y = 0.63x + 2.33$, $R^2 = 0.33$; x, mA; y, mm), approximating the rule of thumb of 1 mA indicating 1 mm ($R^2 = 0.22$). One patient presented with a deterioration of motor function (wrist, M4+). No intraoperative seizures were observed.

Discussion: The concept that 1 mA corresponds to 1 mm from the CST, was roughly observed within this low current range. This rule must be applied, integrating the confidence limits, when getting close to the CST, in conjunction with MEPs.

Conclusion: The standardization of this clip, for continuous stimulation of the ultrasonic aspirator with simultaneous tissue resection, made the guided surgical flow smoother, more refined and very natural.

1. Introduction

1.1. Background

Surgical resection of brain lesions located in proximity to the primary motor cortex or to subcortical motor corticospinal tracts (CST),¹ performed under general anesthesia, benefit from techniques of intraoperative neuromonitoring (Kombos et al., 2001; Taniguchi et al., 1993). Neuromonitoring aims at detecting early changes due to reversible alterations of the nervous system, and serves as a warning signal to the operator in order to adapt the operative strategy to prevent irreversible

neurological deficits. Besides monitoring per se, the domain of neuro-monitoring also encompasses the functional allocation of cortical areas and subcortical white matter tracts - so-called mapping.

Multiple techniques are employed in order to monitor the primary motor cortex and the CST. An important surgical step for tumor resections in supratentorial central regions is the localization of the central sulcus, which separates the precentral primary motor cortex from the postcentral somatosensory cortex. This is done by determining the so-called "phase reversal," which serves today as the gold standard method (Cedzich et al., 1996; Neuloh and Schramm, 2004). Besides the localization of the central sulcus and motor evoked potentials (MEPs)²

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¹ CST: corticospinal tract.

² MEP: motor evoked potential.

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(Kombos et al., 2001; Boex et al., 2016a; Neuloh et al., 2007), direct and continuous stimulation of motor CST has been shown to be of major importance, especially during the resection of infiltrating lesions around the motor CST (Raabe et al., 2014; Sala and Lanteri, 2003; Nossek et al., 2011; Seidel et al., 2020). Nowadays, it is accepted that the distance from the surgical site to the CST (Nossek et al., 2011; Kamada et al., 2009; Ohue et al., 2012) can be estimated by the so called *rule of thumb* of 1 mA indicating 1 mm distance (Raabe et al., 2014). That rule has been established by dynamic continuous subcortical motor mapping combined with suction stimulation (Raabe et al., 2014).

Ergonomics play an important role during surgery. Frequently changing instruments, i.e. by swapping the ultrasonic aspirator with i.e. a stimulating probe interrupts the natural flow of the surgical procedure. That is why the advantage of combined tools, either a suction-stimulator (Raabe et al., 2014) or an ultrasonic aspirator-stimulator (Boex et al., 2016b) seems useful. Depending on the handedness and the habits of the surgeon, one technique may appeal more than the other. The principal advantage of integrating the stimulator to the resection device is to receive continuous neurophysiological feedback through the same device, which per se, is the potential source of damage. Thanks to the current source stimulators of present neuromonitoring systems (Boex et al., 2016b), (Shiban et al., 2015) dynamic continuous stimulation of the ultrasonic aspirator handpiece has been performed in our center since 2014. Actually, while scarcely reported in the literature, surgeons do stimulate the ultrasonic aspirator handpiece in order to estimate the distance of the resection site to the motor CST (Shiban et al., 2015; Roth et al., 2017).

1.2. Objectives

The present study aims to introduce an add-on component to the ultrasonic-aspirator handpiece (Söring GmbH, Germany) with the objective to improve ergonomics and to simplify the intraoperative flow. With a specifically designed connector clip, the ultrasonic aspirator becomes a simultaneous resection and stimulating device for continuous dynamic motor mapping. Whenever it was deemed useful to the surgery, augmented reality (AR)³ display with CST was used in conjunction to the resection device. The *rule of thumb* of 1 mA indicating 1 mm distance rule was analyzed again for the continuous dynamic stimulation of the ultrasonic aspirator handpiece, simultaneous with tissue resection. We report here the results of a retrospective case series of 12 patients.

2. Methods

The analysis was performed in a consecutive series of patients, according to the ethical guidelines of the declaration of Helsinki and was approved by our local Ethical Committee (CE n°2020-00686). All patients gave their consent to participate retrospectively through the use of our University Medical Center's general research consent.

2.1. Patients

Twelve consecutive patients who underwent resection of brain lesions located in proximity to the CST participated (Table 1). The series included 8 women and 4 men with a mean age of 55.8 years (SD 17.3 years).

Muscle strength was assessed preoperatively, 1 or 2 days after surgery, at discharge, and at 3 months postoperatively, based on the British Medical Research Council Scale (2000).

All surgeries were performed with intraoperative sensorimotor neuromonitoring, with sensory evoked potentials, MEPs obtained by transcranial and direct cortical stimulation, with central sulcus verification by the technique of phase reversal (Boex et al., 2016a).

2.2. Motor mapping

Dynamic continuous motor mapping during resections was performed by applying the connection clip for the Söring ultrasonic aspirator (Stimulation clip set 520049, Inomed Medizintechnik GmbH, Germany; Fig. 1). This clip is made of a connector (1.2 cm in length) located distally, clipped on the dorsal part of the Söring handpiece (Söring GmbH, Germany). It allows simultaneous stimulation during tissue resection without interfering with the ergonomic particularities of the ultrasonic aspirator handpiece. It comes with a sterile cable (1.5m in length) for direct connection to the stimulator of the neuromonitoring system, as done for any other monopolar stimulation probe or aspirator (Raabe et al., 2014).

Stimulation was monopolar (Szelenyi et al., 2011), using one contralateral corkscrew subdermal electrode as the return electrode (usually C3 or C4, as determined by the international 10/20 EEG system, according to the side of the lesion). The parameters of stimulation were train-of-five biphasic charge balanced pulses (0.4 ms per phase, inter-pulse interval of 2 ms). Stimulation trains were delivered up to every second from the connector clip according to the stage of the surgery. The initial stimulation intensity was set to 12 mA. Once muscular responses were observed, the amplitude of stimulation was decreased by 1 mA increments, with the aim to detect motor thresholds.

Muscular responses were recorded by pairs of subdermal needle electrodes inserted in standardized target muscles of the contralateral hemi body, as described previously (Boex et al., 2016a), i.e. for the upper limb, the thenar, hypothenar, brachio-radialis and biceps; for the lower limb, the abductor hallucis, tibialis anterior, gastrocnemius and vastus medialis; for the hemiface, the orbicularis oris muscle or mentalis. The muscular responses (100 ms, filtered: 20–1500 Hz) were retained if their amplitudes were at least of 15 μ V peak to peak. The intraoperative neuromonitoring systems used were either the ISIS IOM system (Inomed Medizintechnik GmbH) or the NimEclipse system (Medtronic, USA).

Standard MEPs were performed with direct cortical and transcranial and stimulation (5 biphasic pulses, 350 Hz, 0.4 ms phase duration, maximum 160 mA for transcranial stimulation and 14 mA for direct cortical stimulation, no averaging). The same muscles were monitored for all motor monitoring, i.e. mapping, direct cortical and transcranial stimulation.

2.3. Anesthesia protocol

All surgeries were performed under standard general anesthesia as for cases done with intraoperative neuromonitoring (Boex et al., 2016a). Anesthesia was induced by target-controlled infusion of propofol (Schnider et al., 1998, 1999) and sufentanil (Gepts et al., 1995). The initial concentration of propofol was 4.5–5.0 mg/mL and that for sufentanil was 0.3–0.4 ng/mL. During maintenance, these concentrations were adjusted according to the patients' needs (3.0–4.5 mg/mL propofol and 0.15–0.25 ng/mL sufentanil).

2.4. Imaging

Volumetric computations of the tumors were performed from pre- and early postoperative (<48 h) MRIs (Siemens Trio 3.0 T scanner) with a semi-automated volumetric tool (Smart Brush Tool, BrainLAB Elements Cranial, BrainLAB, Germany). For non-enhancing lesions, the post-operative residual tumor volume was computed on 3D T2/FLAIR sequences, by segmenting the area of residual tissue abnormality in all planes and excluding the resection cavity, excluding post-operative blood products from volume calculations. For enhancing lesions, the extent of resection was calculated (Smith et al., 2008) computing the residual tumor volume on post-contrast 3D T1-weighted MPRAGE gadolinium-enhanced slices.

Relevant anatomical structures (lesion, white matter tracts, and vessels) including DTI based fiber tractography were integrated for AR

³ AR: augmented reality.

Table 1
Characteristics of patients, lesions, stimulations, and motor responses.

Patients	Lesion location	Side	Pathology Recurrence of surgery	Volume Pre/ post (cm ³)	Neuro- navigation with AR (if not N)	Stimulation (mA)	Distance to the corticospinal tract (mm)	Site of response	Amplitude of muscle response (μ V)	Changes in MEPs >50 % in amplitude	Changes in muscle strength at 3 months
P1	Postcentral	L	Glioblastoma 1st surgery	8.8/0.0	N	4.0	7.6	Anterior tibialis	300	None	None
P2	Postcentral	R	Glioblastoma 1st surgery	6.0/0.1	N	9.2	7.9	Abductor hallucis	15	None	None
P3	Temporo- insular	L	Glioblastoma 2nd surgery	15.0/ 1.5	AR	5.0	1.9	Thenar	1600	None (transcranial only)	None
P4	Postcentral	L	Metastasis	16.2/ 0.0	AR	4.0	4.1	Abductor hallucis	120	None	None
P5	Postcentral	R	Glioblastoma 1st surgery	3.2/0.0	AR	7.1	4.1	Abductor hallucis	15	None	M2 (ischemia)
P6	Postcentral	L	Dysplasia	3.2/0.0	AR	12.5	13.0	Thenar	40	None (transcranial only)	None
P7	Postcentral	L	Metastasis	3.2/0.0	N	4.7	6.0	Anterior tibialis	60	None	None
P8	Insula	L	PCNSL*	3.2/0.0	AR	6.4	5.0	Thenar	30	Not contributive (strip displacement)	None
P9	Postcentral	L	Metastasis	3.2/0.0	N	4.8	9.0	Abductor hallucis	20	None (transcranial only)	None
P10	Temporo- insular	R	Astrocytoma 3rd surgery	41.7/ 0.0	AR	10.8	5.0	Vastus lateralis	35	None (transcranial only)	None
P11	Temporo- insular	R	Astrocytoma 4th surgery	35.7/ 6.23	AR	6.3	4.5	Thenar	25	None	Full recovery post VPS
P12	Temporo- insular	R	Glioblastoma 1st surgery	26.7/ 1.5	AR	2.0	1.5	Thenar	20	None	M4+ face and wrist

Are indicated: location, side (L: left, R: right), pathology (*confused with high grade glioma before surgery), preoperative and postoperative volumes of the lesions, implementation of augmented reality (AR) or not (N); stimulation applied (mA) and distance of the stimulation site at the margins of the resection cavity to the motor corticospinal motor tract (mm); site of motor responses and amplitude of responses μ V); Possible changes in motor evoked potentials (MEPs) (if more than 50 % of the initial MEP amplitude) and possible changes in motor strength at 3 months. VPS: ventriculo-peritoneal shunt. Shaded cells: NimEclipse monitoring system, and not shaded cells: ISIS IOM system.

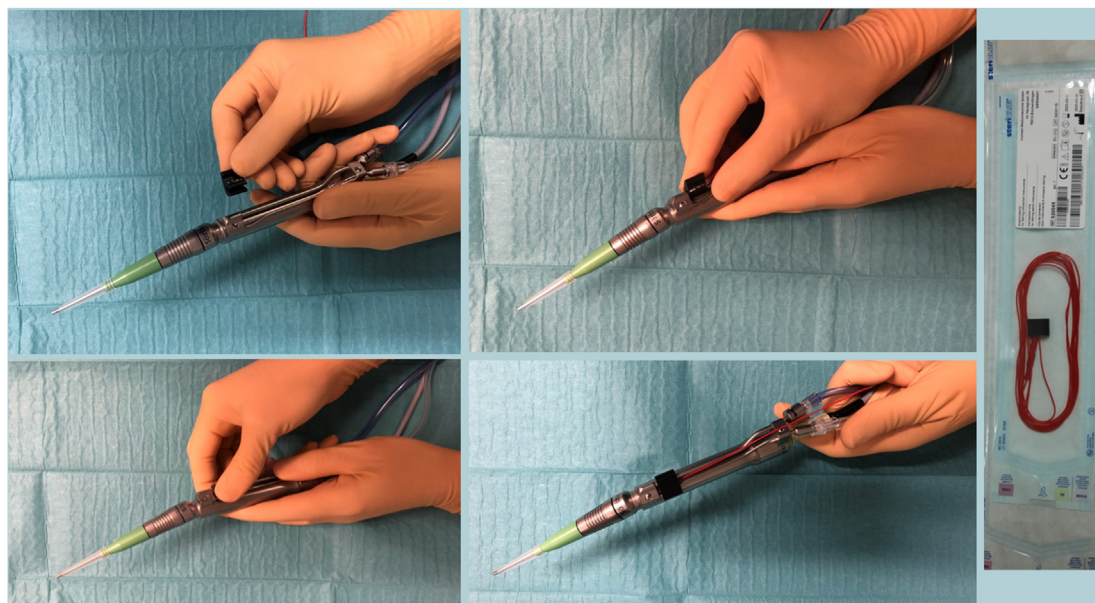


Fig. 1. Connector clip for the ultrasonic aspirator. Connector clip positioned on the dorsal tube of the Söring handpiece (Söring GmbH, Germany), thus becoming a concomitant stimulation and resection device during tissue removal (Stimulation clip set 520 049, Inomed Medizintechnik GmbH, Germany). The sterile cable (1.5m in length) is directly clipped connected to the stimulator of the neuromonitoring system, as done for any other monopolar stimulation probe or aspirator.

display and injected for guidance into the surgical microscope (Leica M530 OHX; Leica Microsystems)

and on the neuronavigation system (BrainLab, Germany) intraoperatively. Shift of brain structures due to cerebrospinal fluid loss and tissue resection were corrected by up-dating

the navigation registration with the use of signature vessel structures, both recognizable on preoperative imaging and within the operative field (Bijlenga, 2020).

Postoperative DTI sequences, obtained by single-shot spin echo planar imaging, were transferred to a BrainLAB Elements Work Station and fused with postoperative 3D slices. The CST was computed using the Fibertracking tool (BrainLab Elements Cranial). The DICOM “Viewer” tool of the BrainLab Elements Cranial was used to visualize the reconstructed CST overlaid on the anatomical images. The minimal distance from the CST to the resection cavity was identified, visualized on triplanar slices and estimated by calculating the mean of the minimal distances between the CST, across axial, coronal and sagittal slices and the closest margin of the resection cavity.

2.5. Theory/calculation

With this connector clip, the stimulated ultrasonic aspirator becoming a simultaneous resection and stimulating device, the linear regression of the stimulation intensity with the distance from the CST was finally performed (SigmaPlot, Systat Software Inc, Richmond, CA, USA). Also 95 % confidence bands of this linear regression of the stimulation intensity with the distance from the CST, were computed.

3. Results

Motor thresholds were obtained in 12 consecutive patients who underwent neurosurgical procedures for post-central (7 patients) or insular (5 patients) tumor resections (2 astrocytomas, 5 glioblastomas, 3 metastases, 1 primary central nervous system lymphoma (PCNSL initially suspected as a high grade glioma before surgery), and 1 extended lesionectomy of a cortical dysplasia. Table 1 describes the characteristics of patients with preoperative and postoperative volumes of the lesions.

3.1. Illustrative cases

Fig. 2 illustrates the application of the connector clip to the ultrasonic aspirator which becomes a simultaneous resection and stimulating device, in patient P11, who underwent surgery for temporo-insular

astrocytoma WHO grade II. AR included the motor CST (blue to green). These images were injected into the visual field of the operating microscope during the tumour resection. In all cases, the initial stimulation intensity was set to 12 mA. Once responses of the contralateral tibialis anterior (“Tib”) were observed at 12 mA, the amplitude of stimulation was decreased by 1 mA increments, as long as one muscular response could be observed (i.e. at least of 15 μ V) and in this case reduced to 6.3 mA. No change was observed in the amplitudes of MEPs conducted with direct cortical stimulation. At 3 months postoperatively, a contralateral motor hemi syndrome (M4) was present and then resolved following a new surgical procedure for ventriculo-peritoneal shunt positioning.

Another application of the direct stimulation of the ultrasonic aspirator handpiece is illustrated in video 1, in patient P5, who underwent surgery for a postcentral glioblastoma. In this video, AR segmentations were performed for the CST (green to blue), the lesion (orange) and the skull and were injected intraoperatively into the eyepieces of the operating microscope (Leica M530 OHX; Leica Microsystems). During tissue resection, initial responses of the contralateral abductor hallucis (“Foot”) were observed with 11 mA stimulation and were maintained when stimulation was reduced up to 4 mA. Post-surgery, the distance of the CST to the resection border was found of 7.1 mm. In this patient, MEPs were not obtained by transcranial stimulation during the whole surgery. These difficulties motivated the suspicion of air embolism, confirmed by the anesthesia team. Ischemia of the primary motor cortex was suspected (sensory evoked potentials were normal). Postoperatively the ischemia was found in one subregion of the precentral gyrus. MEPs were obtained with direct cortical stimulation, for high amplitudes, 17 mA, i.e. above the usual amplitude of stimulation in our Centre, which is typically 8 mA. The stimulation of the CST suggested that the air embolism did not affect the CST. The patient suffered from a left sided hemiplegia which improved to M2 at 3 months postoperatively.

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.bas.2021.100002>

In another case of insular glioblastoma resection with muscular responses to subcortical motor mapping found with 2 mA stimulation amplitude, patient P12 observed a discrete deterioration, half grade M4+, immediately postoperatively. These parameters were in agreement

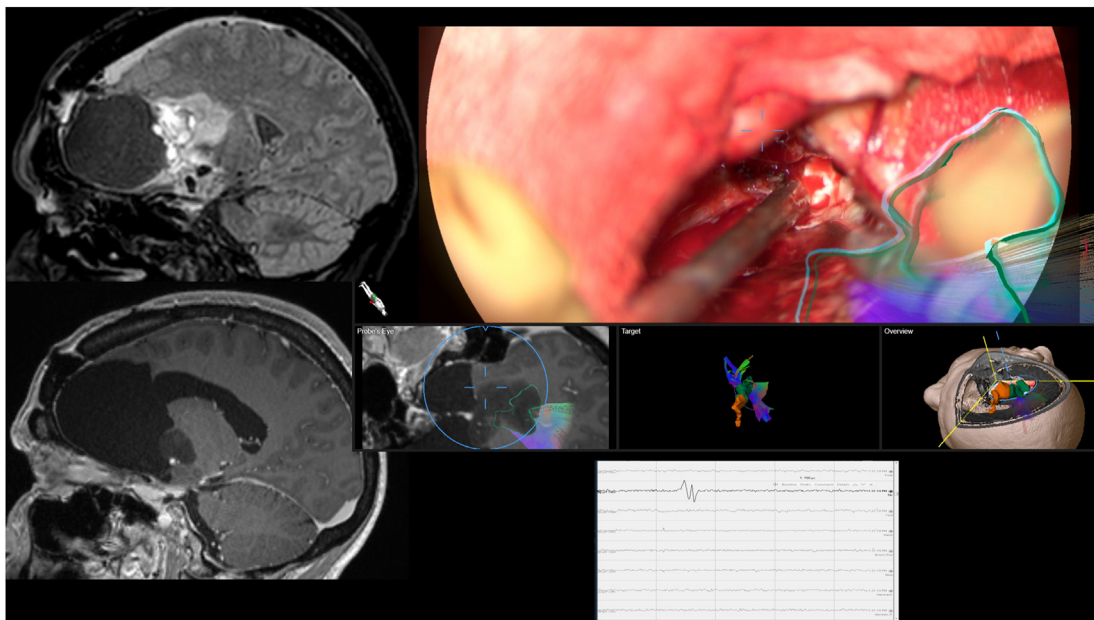


Fig. 2. Application of concomitant stimulation and resection device in the case of a temporo-insular astrocytoma. Pre- and post-operative MRIs, at the time of her 4th resective surgery of temporo-insular astrocytoma. DTI for the cortico-spinal tract (blue to green) was injected intraoperatively into the eyepiece of the operating microscope (Leica M530 OHX; Leica Microsystems) and during tissue resection. Initial responses of the contralateral anterior tibialis (“Tib”) were observed for the stimulation of CST for finally 6.3mA in patient P11.

with a close location of the CST to the resection cavity.

The other 9 patients did not exhibit any new motor deficits 3 months post-surgery, and gross total resections were performed for all patients in whom the distance to the motor CST was found superior to 2 mm post-operatively on MRI. Table 1 illustrates the stimulation amplitudes with the distances to the CST, together with the amplitude of the muscular responses and their location. Motor thresholds were identified for stimulation intensities ranging between 2 and 13 mA. Muscular responses were observed for the thenar, abductor hallucis, tibialis anterior and vastus medialis for amplitudes ranging between 15 and 1600 μ V. Muscle MEPs did not change in all other patients except in patient P8, in whom MEPs were not contributive due to intraoperative displacements of the cortically placed strip electrode.

3.2. Distance to the cortico-spinal tract (CST)

Fig. 3 shows the distances between the location of the stimulus, determined as the margin of the resection cavity, to the CST [mm, ordinate] with the amplitude of stimulation [mA, abscissa]. With each patient's code (e.g. P1), symbols indicate the amplitudes of the muscular responses (e.g. 300). The linear regression ($y = 0.63x + 2.33$; $R^2 = 0.33$; blue line), drawn with a 95 % confidence interval of the regression (dashed blue lines), models slightly better the data than the *rule of thumb* 1 mA indicating 1 mm for stimulation amplitude ($R^2 = 0.22$; dotted line).

For 9 of the 11 patients in whom tumor volume was determined, gross total tumor resection was achieved. That includes all patients in whom the distance to the motor CST was found superior to 2 mm. In patient P2, a remnant <5 % of the initial volume of the tumor was observed post-operatively. In this patient, the resection was stopped while the stimulation amplitude was 9.6 mA. Postoperatively the distance of the resection cavity to the motor CST was determined to be indeed of 7 mm which would have allowed further resection in retrospect. Another

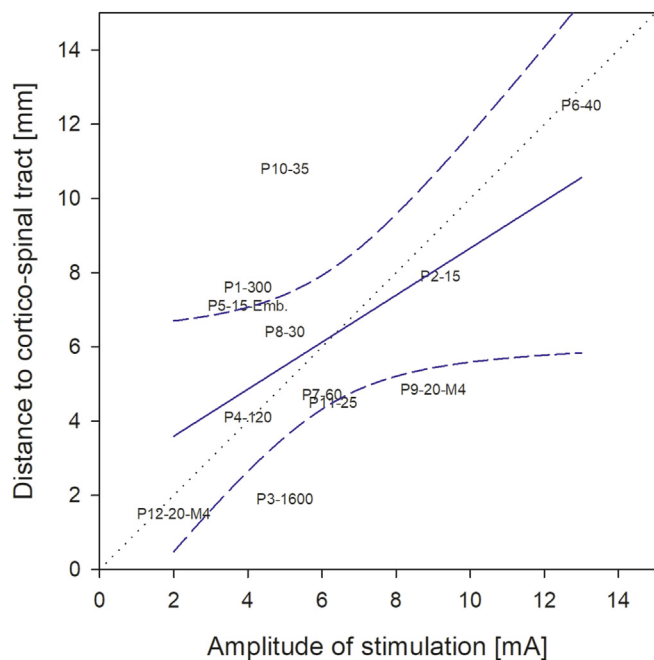


Fig. 3. Relation between stimulation location and CST distance [mm, ordinate] and the stimulation amplitude [mA, abscissa]. The distance between the location of the stimulation, determined as the closest border of the resection cavity to the corticospinal tract [mm] is documented in ordinate; the amplitude of stimulation in documented in abscissa [mA]; the amplitude of the responses (μ Vpp, e.g. 300) is given as symbols with the identification of patients (e.g. P1 in P1-300). The linear regression ($y = 0.63x + 2.33$; $R^2 = 0.33$; blue line) is drawn with the 95 % confidence intervals of the regression (dashed blue lines). The rule of thumb 1 mA indicating 1 mm is drawn ($y = x$; $R^2 = 0.22$, dotted line).

patient, P3, in whom the resection was not complete and with a post-operative residual tumor volume of 10 %, presented the largest amplitude in muscular responses (1600 μ V) for 5 mA stimulation. Postoperatively, this distance was measured to be of 1.9 mm. This high voltage response (1.6 mV) suggested yet the CST was certainly closer than 5 mm, and that the resection was stopped at the right time thus avoiding neurological damage.

No seizures or any other intra- or extra-operative complications related to the applied mapping was observed.

4. Discussion

4.1. Ergonomics

Ideally, for surgery adjacent the CST, the surgeon is continuously informed about the immediate effect of the ongoing resection. Direct stimulation of the ultrasonic aspirator simplified the intraoperative ergonomics by abolishing the need to alternate between the resection device and a dedicated i.e. monopolar stimulation tool. That allowed for integrated, dynamic and continuous motor mapping, simultaneous with the tumor resection. Delayed ischemic damage on the other hand may not be avoided by subcortical mapping, but the latter may directly guide resection and prevent from immediate mechanical damage. With the standardization of this clip the stimulation of the ultrasonic aspirator brings subcortical stimulation into one straightforward setup, facilitating the use of mapping techniques. That direct feedback from the combined resection and mapping device should increase surgical safety, because it allows for immediate change of the surgical strategy, depending on the present stimulation parameters. Currently it is adapted and approved for one commercially available ultrasonic aspirator only (Söring GmbH, Germany).

Moreover, the full integration of fiber tract overlay by intraocular AR injection, in conjunction with ultrasonic aspirator-connected continuous and dynamic mapping improves the surgical flow by becoming smoother than in the past and was intuitive.

In line with Roth et al. (2017), we did not find any evidence of inhibition of the CST with the connector clip to the ultrasonic aspirator as suggested by Carraba et al. (Carrabba et al., 2008) In that latter report, suspicion of inhibition may have been confounded with a technical issue, such as saturation of the electrophysiological amplifier, that may have been caused by a grounding issue (some electromyographic –EMG– traces became flatter during the stimulation whether the ultrasonic aspirator was ON or OFF).

4.2. Rule of thumb

The *rule of thumb* of 1 mA indicating 1 mm distance (Raabe et al., 2014) between motor thresholds and distance from the resection border to the CST could be only roughly observed in the present patient series.

Previous reports of this *rule of thumb* appears more precise. This difference can be first explained by the shorter range of stimulation amplitude applied in the present patient series [1.9–12.5 mA], focusing on a subpart of measurements reported earlier. Indeed, the regression was here computed for one range about twice narrower than reported before: Kadama et al. (Kamada et al., 2009) [1.8–25], Nossek et al. (2011) [2–22 mA], Ohue et al. (2012) [2; 20 mA].

As mentioned below in the limitations of the study, the variance of the relationship between motor thresholds and distance from the resection border to the CST can be also explained by the fact that the motor threshold was not always sought beyond the first observation of muscular response to the stimulation and by the fact that the measurements of the stimulus site to the motor CST were not performed intraoperatively but postoperatively in this initial series.

Moreover, different parameters of electrical stimulation have been applied. Previous measurements of this *rule of thumb* were performed for train of 5 pulses usually and for 2 different arrangements of parameters:

Kadama et al. (Kamada et al., 2009) and Ohue et al. (2012) (cathodic waveform, bipolar configuration, 0.2 ms pulse duration); Nossek et al. (2011) (anodic waveform, monopolar configuration, 0.5 ms pulse duration). The use of a biphasic waveform in the present patient series is motivated by its potential to excite fibers whatever are their spatial orientation (Holsheimer et al., 2007). The biphasic pulse waveform can also contribute to decrease the risk of seizures compared to monophasic stimulation (anodic or cathodic), notable in this series which documents the absence of seizures as already observed (Boex et al., 2016a).

4.3. Safety margin

Besides the use of this *rule of thumb*, the identification of one stop-threshold, i.e. the minimum stimulation amplitude beyond which it becomes too risky for the motor CST to continue resection has been a subject of debate. The confidence limit of the linear regression computed in the present patient series indicates that at 2 mA, the distance can be as low as 0.5 mm. So, this rule should not be applied below 2 mA, in agreement with previous report of this rule that has always been reported for stimulation higher than 2 mA. (Kamada et al., 2009), (Nossek et al., 2011), (Ohue et al., 2012) The study of one stop-threshold was conducted in regard to the patient's motor outcome. First, Sala and Lanteri (2003) applied stop-threshold ranging between 5 and 7 mA as their cutoff point to stop resection (anodal, 5 pulses, 0.5 ms). Prabhu et al. (2011) found persistent motor deficits in cases where muscular responses were observed for stimulation amplitude of 5 mA or less, and none for stimulation threshold of at least 11 mA (anodal, 5 pulses, 0.3–0.5 ms). Nossek et al. (2011) utilized a stimulation stop-threshold of 6.8 mA (cathodal, 5 to 7 pulses, 0.5 ms). Seidel et al. (2012) recommended a stimulation stop-threshold of 5 mA (cathodal, 5 pulses; 0.5 ms), which may be furthered to 3 mA with continuous mapping, according to the operator decision and with careful observation of MEP from direct cortical stimulation (Seidel et al., 2020). Plans et al. (2017) confirmed this stimulation stop-threshold of 5 mA (cathodal, 5 pulses, 0.5 ms). In the present series and in view of the single case of new moderate motor deficits (2 mA, M4+), besides 2 cases due to either embolism or ischemia, we cannot recommend any stop-threshold in amplitude of stimulation for subcortical resection during continuous mapping at this point. Continuation of resection may be achieved according to the surgeon's decision, aware of the patient's situation, with careful observation of the MEP's from direct cortical stimulation and fine tuning the ultrasonic aspirator power and suction. So far, conducting MEPs with direct cortical stimulation remains the most reliable prognostic tool (Kombos et al., 2001; Boex et al., 2016a). Corticospinal motor mapping should be applied keeping in mind the *rule of thumb* does not integrate confidence intervals. Still, neuromonitoring with MEPs from direct cortical stimulation remains so far the gold standard for such surgeries with prognostic validity, while subcortical mapping remains a localization tool in the intraoperative setting along with intraoperative imaging techniques and knowledge of anatomical landmarks.

4.4. Limitations

This observational study is retrospective and was conducted in a small group of patients.

The variance of the relationship between motor thresholds and distance from the resection border to the CST could be attributed was largely due to the fact that the motor threshold was not always sought beyond the first observation of muscular response to the stimulation, i.e. the resection was not systematically suspended to take the time to measure the motor threshold per se. This fact contributed to the variance of the relationship between motor thresholds and distance from the resection border to the CST. Indeed, motor threshold is defined as the amplitude of stimulation that evokes a reference muscular response of minimal amplitude (15 μ V in the present series). Stimulation amplitude, at the time of first observation of a muscular response, is not a motor

threshold if the response is well beyond the reference muscular response amplitude. This is illustrated by patient P3, in whom large amplitude muscular responses were associated with underestimated proximity of the tumor to the CST (1600 μ V, 5 mA, and 1.9 mm). Note that the low amplitude, 15 μ V, reference response amplitude requires adequate filtering of motor responses in order to be reproducible. This was obtained by applying adequate filtering, and by attenuating the low frequency part of the muscular responses (e.g. band-pass: 20–1200 Hz).

The variance of the relationship between motor thresholds and distance from the resection border to the CST could be partly attributed to was also large in consequence of the fact that the measurements of the stimulus site to the motor CST were not performed intraoperatively but postoperatively in this initial series.

5. Conclusions

The use of this novel connection clip for the ultrasonic aspirator allows for an integrated and continuous motor mapping simultaneously to the resection process. Simultaneous tissue resection and subcortical continuous motor mapping has the potential to advance glioma surgery, simplifying the intraoperative ergonomics by decreasing tool manipulations. The use of this stimulation-resection device, in conjunction with AR, enables the surgeon to maintain a natural surgical workflow when resecting nearby the visualized concerned fiber tract. Further advances in language, visual, or executive tract mapping could also be imagined with this tool.

The *rule of thumb* of 1 mA indicating 1 mm distance was only roughly observed here for low stimulation amplitudes. The enrollment of a larger patient cohort with surgery performed with intraoperative distance measurements of the stimulation site to the CST and precise motor threshold measurements would be necessary to verify the relationship between motor thresholds and distance from the resection border to the CST at low stimulation amplitudes. Corticospinal motor mapping should be applied keeping in mind the existence of confidence intervals illustrated here and that MEPs from direct cortical stimulation remains the gold standard to predict motor outcome.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bas.2021.100002>.

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