The relevance of the corticographic median nerve somatosensory evoked potentials (SEPs) phase reversal in the surgical treatment of brain tumors in central cortex*

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Tumors of the central brain cortex change the original anatomy of this important area and so an intraoperative localization of the perirolandic structures is crucial in decision concerning the way and the extent of tumor resection. The phase reversal of median nerve SEPs is an essential tool for neurosurgical procedures in and around the perirolandic gyri. This study examines the relevance of the method in a group of 62 patients having surgery of tumors in and around the central region. A success rate in obtaining the SEP phase reversal was 94%. In all groups of patients the complete resection of tumor was achieved in 58% , subtotal resection in 19% and partial or biopsy only in 23%. The long term impairment of neurological status was observed in 6% of patients. Compared to the recently published studies our results are acceptable both in completeness of tumor resection and relatively low ratio of impaired postoperative neurological deficit despite the fact, that in the majority of patients the phase reversal mapping was the only method guiding the surgical procedure. Our study supports the crucial role of the central cortex mapping using the SEP phase reversal method in the surgery for the tumors of the primary sensorimotor cortex.

Key words: somatosensory evoked potentials, phase reversal, parietal tumors, intraoperative monitoring

Surgery for intracranial tumors harbors a significant risk for new neurological deficit if these lesions are located close to the motor cortex or motor tracts or other important fiber systems. Reasons include direct injury or ischemia from inadvertent occlusion of neighboring vessels, sometimes brain retraction or vasospasm induced by tumor resection [1,2]. Accurate intraoperative localization of sensorimotor cortex is an essential adjunct to successful surgical excision of tumors involving the precentral and postcentral gyri. During the past decade the use of anatomical landmarks usually displayed by computed tomography (CT) or magnetic resonance imaging (MRI) has been further developed by advanced functional neuroimaging techniques, which include functional MRI (fMRI), magnetic source imaging (MSI) and PET. These non-invasive diagnostic tools not only provide excellent information for presurgical planning, but their integration into neuronavigational systems allows safer and more radical surgery in and around the sensorimotor cortex [3]. The rapid development of navigational devices has provided the neurosurgeon with an unprecedented degree of surgical accuracy and precision for the planning as well as performance of a large variety of neurosurgical procedures. The original concept of intraoperative MRI and functional neuronavigation has been expanded by including Proton-spectroscopy and diffusion weighted images (DTI). Proton-spectroscopy data are helpful to expand the tumor resection from anatomical to metabolic mapping in gliomas. Meanwhile DTI allows visualization of pathways, especially the pyramidal tract, which can be integrated into neuronavigation and intraoperatively revisualized [4]. Fluorescence-guided resections using 5-aminolevulinic acid (5-ALA) allow a larger number of complete resections of gliomas [5]. Traditionally, intraoperative identification of the perirolandic gyri has been accomplished using electrophysiological techniques: either electrical stimulation mapping of exposed motor cortex [1, 3, 6, 7] or recording the phase reversal of SEPs across the central sulcus [1, 7–11]. The recording of phase reversal is still considered a reliable tool for localisation of central sulcus, which is crucial for intraoperative planning of tumor resection. The method is

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simple, reliable and not time consuming. We retrospectively summed the results of our group of 62 patients operated on brain tumor in or adjacent to the primary sensorimotor cortex, in which the phase reversal was the only electrophysiological guidance during the neurosurgical procedure. We focused on the relationship of the tumor location toward the central sulcus and the extent of resection and postoperative neurological deficit in patients.

Table 1. Diagnoses in the group of patients

Diagnosis	n	%
Glioma	33	51
Meningioma	21	33
Cavernoma	5	8
Metastasis	3	5

Material and methods

In 66 consecutive patients undergoing open surgery between 1997 and 2004 for tumors (n=61) and cavernomas (n=5) involving or abutting brain primary sensorimotor cortex, the localization of the central sulcus was performed by median SEP recordings from the exposed cortex. We included in the study 62 patients (n=62), in whom the intraoperative SEP phase reversal was recorded. In four patients (6%) phase reversal was not obtained and we excluded them from the study.

The patients ranged in age from 26 to 79 years (mean 55.1 years, SD = ±14.4). There were 30 men and 32 women. In all patients the brain tumors (glioma, meningioma or metastasis) or cavernoma in or around the sensorimotor cortex were diagnosed by preoperative MRI or CT. Glioma was the most frequent diagnosis (Tab. 1). Forty two patients (68%) showed focal sensorimotor deficit preoperatively, 20 patients (32%) were without any neurological deficit and they were diagnosed after epileptic seizures, headache or other less specific symptoms.

All patients were operated on under general anaestesia using midazolam, nitrous oxide and isofluran, sufentanil and a short acting muscle relaxant for introduction.

The SEPs were recorded in a four channel montage using Dantec Counterpoint 2 device. The median nerve contralateral to the lesion was stimulated at the wrist with 6 pulses/second and a current intensity 25 mA. A strip electrode with 10 mm interelectrode spacing was placed over the putative central sulcus. A subdermal needle electrode at the forehead served as the reference. All recordings were performed using a filter band pass of 3–3000 Hz and a time base of 50 ms (Fig. 1) Two hundred responses were averaged in each run [1, 3].

After intraoperative localization of central sulcus, the neurosurgeon has been asked to determine the position of pathological lesion in relation to the central sulcus. The patients were divided into 4 groups: a. patients with a tumor before the central sulcus, b. patients with a tumor behind the central sulcus, c. patients with a tumor directly involving the central sulcus and d. patients with a tumor in white matter below the central sulcus. Patients with meningiomas were assigned to a group according to that area on the brain surface, where the maximum of compression has been found. In 6 cases tumor mass was not recognizable on the brain surface and the ultrasound or stereonavigation was used.

Immediately after the resection of a tumor the surgeon was asked to give his estimation of the completeness of tumor removal (complete, subtotal or partial). The accuracy of the surgeon's estimation of the tumor resection extent was checked on postoperative CT with contrast medium. The extent of the resection was qualified as "complete" when a sur-

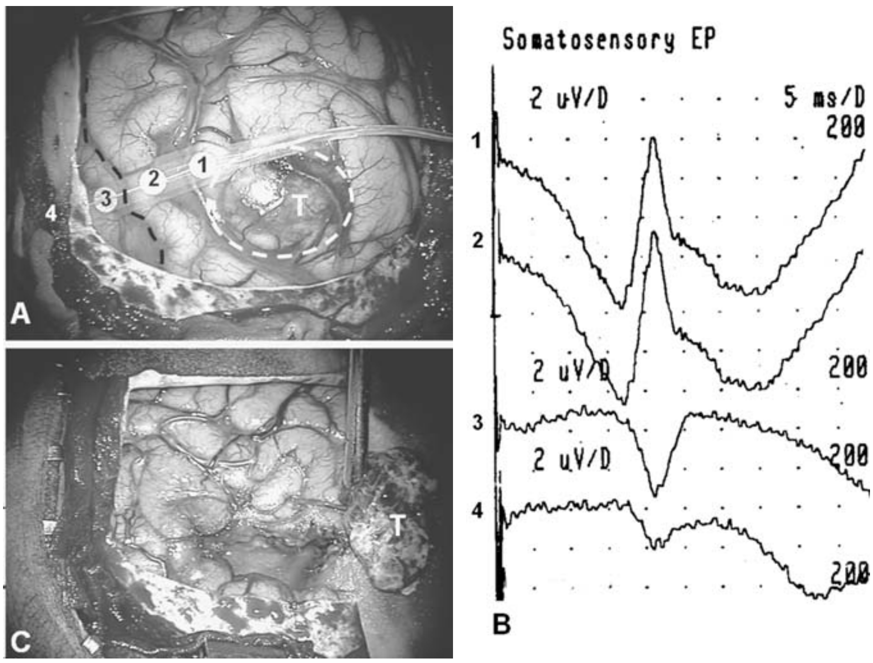

Figure 1. Intraoperative localization of the central sulcus by SEP phase reversal. 63-year old woman with metastasis of the thyroid papillocarcinoma behind the postcentral gyrus. 1A. Strip electrode crossing the anatomically changed central sulcus (black broken line), tumor circumscribed with white broken line (T). 1B. Change in polarity of the response between the 2nd and 3rd element of the strip electrode (the 4th element is under the dural edge). This is the place, where the electrode crosses the central sulcus. 1C. The situation after complete removal of the tumor.

geon determined the resection as complete and no residuum of tumor was visible on the postoperative contrast CT scans, as "subtotal" when a small rest of tumor was left in parenchyma even if no clear residuum was seen on CT and "partial" when the rest of tumor was seen on the contrast CT scans. In cases with glioma the term "complete" means "macroscopically complete". The extent of surgical tumor removal in the patients with meningioma was evaluated using SIMPSON grading system [12]. Complete removal of a tumor corresponded with Simpson grade I, subtotal removal with Simpson grades II and III and partial removal with Simpson grade IV.

The postoperative CT with contrast medium has been performed in all patients up to three days after the surgery (in the vast majority of patients on the first postoperative day). All patients were examined by MRI between 3 and 6 months after the surgical procedures. Neurological status of patients was compared with the preoperative finding 7 days and 3 months after the operation.

Groups were statistically analyzed using column statistics analysis that described the distribution of values in a column and tested whether the distribution differed significantly from a Gaussian distribution. Nonparametric variables were analyzed by Chi-squared test and Fisher exact test. Significance was assumed at $p<0.05$. Statistical analysis was performed using Statistica 6.0 Software, StatSoft.

Results

The intraoperative localization of central sulcus by median SEP phase reversal was possible in 62 patients. The average time for the phase reversal determination was 15 minutes. Despite various changes in the waveform of cortically recorded median SEPs we were able to identify the initial N20/P20 component of median SEPs in the presented group of patients. The latency of N20 varied between 19.7 and 24 ms (mean 21.3 ms) and amplitude N20/P25 varied between 2.4 and 18 uV (mean 12.6 uV). The central sulcus was clearly identified between the electrodes, where the phase reversal was obtained in all cases.

Knowing the position of the central sulcus, the resection of the tumor followed. Without considering tumor size, location, and histological diagnosis the surgeon's assessment of the extent of tumor removal was "complete" in 36 patients, "subtotal" in 12 patients and "partial" or "biopsy only" in 14 patients. The completeness of resection for each type of tumor is shown in Figure 2. In the groups of metastases and cavernomas we achieved complete resection in all cases. On the other hand, in the group of gliomas the macroscopical completeness of removal was possible in 31% of cases and subtotal resection in 27% of cases. The reason of subtotal resection in two patients with meningioma was spreading of the tumor into the sagittal sinus, where resection of an invaded dura mater was impossible. Without considering the type of tumor the best results in completeness of resection was accomplished in the group of patients with tumor localized behind the central sulcus (Fig. 3). The differences, however, were not statistically significant ($p=0.2$).

Neurological status of patients stayed normal or has improved in 41 patients, has remained unchanged in 10 patients and has impaired in 11 patients on the 7-th day follow up. On the 3-month follow up neurological status was normal or improved in 48 patients, unchanged in 10 patients and impaired in 4 patients (Tab. 2). Transient aphasia was observed in 3 patients and in all of them disappeared within several days. There was a relationship between the localization of tumor and neurological deficit (Fig. 4). The majority of patients with impaired neurological deficit were in groups of tumor infiltrating the central sulcus and below the central sulcus. The best results in terms of neurological deficit were in the group of tumor location behind the central sulcus ($p=0.007$).

Discussion

The normal anatomy of primary sensorimotor brain cortex is usually significantly changed by tumors localized in close proximity to the central cortex. The neurosurgeon must, therefore, identify the most important structures of the brain

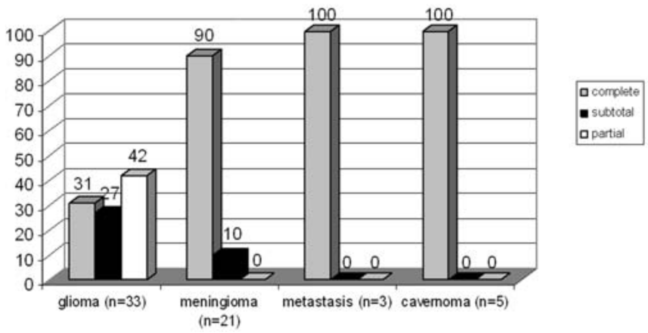

Figure 2. Completeness of the tumor resection in different types of tumor.

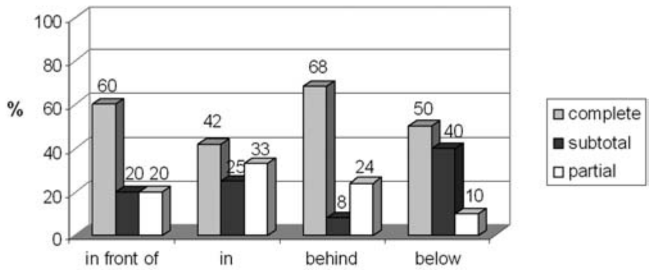

Figure 3. Completeness of the tumor resection without considering the type of tumor in different location to the central sulcus. The group of patients with tumor localized in front of the central sulcus is signed "in front of", infiltrating the central sulcus is signed "in", localized below the central sulcus is signed "below".

Table 2. Postoperative neurological status in all patients

Neurological status	7 days follow-up	3-month follow-up
Normal or improved	41 (66%)	48 (78%)
Unchanged	10 (16%)	10 (16%)
Impaired	11 (18%)	4 (6%)

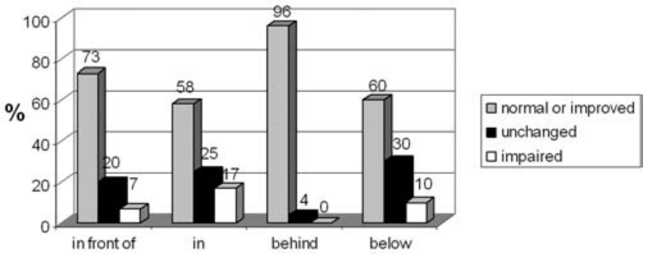

Figure 4. Postoperative neurological status in reliance on the location of the tumor to the central sulcus (follow-up 3 months).

central region (central sulcus, precentral and postcentral gyri). First experimental identification of the motor cortex by direct cortical stimulation was done by FRITSCH and HITZIG in 1870 [13]. PENFIELD and BOLDREY [6] introduced the method of direct cortical stimulation to assess motor function in the clinical routine. At that time, the brain surgery was performed frequently or solely in awake patients under the local anesthesia. With the introduction of general anesthesia this method was more reluctantly used because the motor evoked responses were only visible with a reduced anesthesia and/or with a high charge density to the motor cortex [1]. The problem was solved during the last few years in two ways: a modified anesthesia procedure and modified stimulation technique [14]. The stimulation technique was changed to a short train of rectangular pulses at high frequency (300–500 Hz) and the consistence of motor evoked response increased.

Awake craniotomy with brain mapping and tumor resection under local anesthesia is still advocated by some authors [15–18], especially in patients, where the localization of the brain speech centers is needed. They see the advantages of awake craniotomy over the standard craniotomy in general anesthesia in the optimal opportunity for brain mapping, avoiding general anesthesia, and a low complication rate. Permanent neurological deficit has been described in 4% of patients after awake craniotomy [16, 18]. Patients who undergo awake craniotomy are conscious at the end of the procedure, reducing their need for postoperative intensive care monitoring. One of the disadvantages is the fact, that thorough cooperation of the patient is inevitable and it was possible only in 66% of patients in the large study of TAYLOR and BERNSTEIN [18].

Functional MRI is a very helpful tool in preoperative determination of brain eloquent area and importing of fMRI imaging data into the neuronavigation system allows neurosurgeon easy orientation on the brain surface [19]. However, the problem is a shift of the brain after durotomy and during resection of the tumor and so the correlation with some type of electrophysiological method and/or intraoperative imaging is usually needed.

In the 1970s the somatosensory evoked potential (SEP) phase reversal method was developed for localization of the central sulcus. In most cases it is possible to obtain a SEP phase reversal and to localize the rolandic fissure within a few minutes [1, 3, 7–11, 20–22]. This method was based on the fact that the dipole of the afferent volley changes from the postcentral sulcus to the precentral sulcus, that is, a somatosensory evoked potential can be recorded from the sensory cortex and its mirror image can be recorded from the motor cortex [1, 7, 11]. SEPs are more consistent under general anesthesia and the technique of phase reversal is considered reliable in localization of the central sulcus. The success rate of phase reversal has been described between 91% [1] and 94% [11] in the literature and we accomplished 94% success rate in our patients. The failure rate of phase reversal elucidation (6–9%) can be explained by the fact, that the central sulcus forms a bend in the hand area so that sensory and motor hand areas are not exactly opposite on pre- and postcentral gyri. Hence, an "on-axis" line passing through the maxima of the N_{20}-P_{30} responses of SEPs forms an acute angle of 70 degrees with the approximate overall direction of the central sulcus. Therefore, if the recording electrodes are placed in an "on-axis" line, a typical phase reversal will be obtainable, but if they are placed in an "off-axis" fashion, a loss of only N_{20} or P_{20} can be seen [1, 11]. Although the surgery in the area of sensorimotor cortex has always meant a high risk of new or increased motor deficits, no exact rates of morbidity were available before 1990s. CEDZICH et al [1] found a permanent impairment of motor function in 17% of patients operated on central region tumors with neurophysiological monitoring. GANSLANDT et al [23] used functional neuronavigation with magnetoencephalography in combination with neurophysiological monitoring and observed a deterioration of neurological function in only 4% of patients. REITHMEIER et al [24] described deterioration of neurological status in 14% of patients, where combination of neuronavigation and electrophysiological monitoring was used. In the control group of patients, where no or only some of an electrophysiological technique was used, impairment of neurological status was described in 29%. Tumor rest was presented on postoperative MRI in 27% of monitored patients compared to 52% of non-monitored patients [24]. ROMSTÖCK et al [3] presented the results of their group of 230 patients operated on space occupying mass lesions in or around the primary sensorimotor cortex. Without considering tumor size, location, histological diagnosis and grading, complete removal of a tumor was possible in 40% of patients, subtotal removal in 53% of patients and partial removal or biopsy only in 7% of patients. The postoperative sensorimotor function was unchanged or improved in 83.5% of patients, transiently worsened neurological status was observed in 12% of patients and permanent new deficit in 3% of patients. In our group of patients the complete resection of pathological lesion was possible in 58% of patients, subtotal resection in 19% and partial or biopsy in 23% of patients. We achieved the best results in completeness of resection in patients with circumscribed tumors (meningioma, metastasis) and cavernomas. Considering the location of tumor the most cases where complete resection was possible, were in the subgroup of tumor location behind and in front of the central sulcus (p=0.2). The permanent impairment of neurological status was observed in 6% of patients.

When compared with recently published studies [1, 3, 23, 24] we achieved acceptable results in the treatment of tumors of brain central cortex despite the fact that we used the median nerve SEP phase reversal for mapping of central sulcus as the only electrophysiological guidance of surgical procedures in our group of patients. Our results showed that knowing the relationship between the central sulcus and pathological lesion is crucial for making the decision about the way and extent of the tumor resection. Direct electrical stimulation used for mapping of the motor cortex gives us some additional information but is time consuming. Furthermore, some authors [25] consider MEP monitoring more useful than mapping of the motor cortex, because the change in MEP response is (unlike the mapping of the motor cortex) the parameter which can allow a neurosurgeon to operate even in the motor cortex area or make a neurosurgeon to stop the resection of tumor and save the patient from impairment of neurological status. They use mapping of motor cortex by direct stimulation only in some cases.

The problem of neuronavigation still could be the source of a mistake due to preoperative imaging, and/or brain shift during the operation. Intraoperative imaging methods (sonography, intraoperative MRI) give the neurosurgeon “on-line” morphological information during the operation and in combination with electrophysiological mapping and monitoring methods make the operation procedure more accurate, safe and allow larger extent of resection of brain tumor. We accomplished good results in maintainance or improvement of neurological status in our group of patients, but we believe that combination with other new methods of intraoperative imaging will allow us to safely enlarge the extent of tumor resections especially in patients with infiltrative tumors of the perirolandic area.

In conclusion we consider the localization of central sulcus by median nerve corticographic SEP phase reversal technique crucial for acceptable clinical results in the open brain tumor surgery in sensorimotor cortex both in terms of completeness of tumor resection and maintenance or improvement of neurological status. The development and introduction of new methods to clinical practice brings more effective and safer neurosurgical procedures.

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