

Optimizing the extent of resection in eloquently located gliomas by combining intraoperative MRI guidance with intraoperative neurophysiological monitoring

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Abstract Several methods have been introduced to improve the extent of resection in glioma surgery. Yet, radical tumor resections must not be attempted at the cost of neurological deterioration. We sought to assess whether the use of an intraoperative MRI (iMRI) in combination with multimodal neurophysiological monitoring is suitable to increase the extent of resection without endangering neurological function in patients with eloquently located gliomas. Fifty-four patients were included in this study. In 21 patients (38.9 %), iMRI led to additional tumor resection. A radiologically complete resection was achieved in 31 patients (57.4 %), while in 12 of these, iMRI had depicted residual tumor tissue before resection was continued. The mean extent of resection was 92.1 % according to volumetric analyses. Postoperatively, 13 patients (24.1 %) showed new or worsening of pre-existing sensory motor deficits. They were severe in 4 patients (7.4 %). There was no correlation between the occurrence of either any new ($P = 0.77$) or severe ($P = 1.0$) sensory motor deficit and continued resection after intraoperative image acquisition. Likewise, tumor location, histology, and tumor recurrence did not influence complication rate on uni- and

multivariate analysis. We conclude that the combination of iMRI guidance with multimodal neurophysiological monitoring allows for extended resections in glioma surgery without inducing higher rates of neurological deficits, even in patients with eloquently located tumors.

Keywords Extent of resection · Glioma surgery · Intraoperative MRI · Neurophysiological monitoring · Complications

Introduction

The extent of resection is one of the prognostic factors for patients with both low- and high-grade gliomas [1–5]. Intraoperative magnetic resonance imaging (iMRI) has been used as a surgical adjunct to improve resection of brain tumors for more than a decade [6]. Many groups have reported that iMRI guidance is beneficial in detecting unintentionally remaining tumor tissue intraoperatively leading to extended tumor resections, irrespective of the field strength of the magnet [7–10]. Some studies have even demonstrated benefits in terms of survival when looking at the extent of resection as a prognostic factor [11–13]. Recently, a randomized trial demonstrated superiority of iMRI guidance over conventional microsurgical techniques [14].

Undoubtedly, radical tumor resections must not be achieved at all costs: clinical patient status is one of the strongest prognostic factors [15, 16]. Neurophysiological monitoring methods, such as continuous motor- or sensory-evoked potentials, as well as direct cortical or subcortical stimulation, have been implemented into the neurosurgical routine to avoid neurological complications [17–20].

Having conducted a preliminary trial on the feasibility of the combined use of these two techniques, iMRI

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guidance on the one hand, and intraoperative neurophysiological monitoring (IOM) on the other [21], we now aim to assess whether the combined use of iMRI and IOM is of benefit in glioma surgery in terms of improving the extent of resection without inducing higher rates of neurological complications.

Patients and methods

Clinical patient data and treatment

We searched our prospectively collected database of glioma patients to identify procedures in which both IOM and iMRI were applied. All tumors were eloquently located, i.e. in close vicinity to cortical sensory motor areas (pre- and postcentral gyrus), subcortical sensory motor tracts, and/or major supplying vessels (middle cerebral or anterior cerebral arteries) according to preoperative diagnostic MRI. Patients with tumors in close proximity to speech areas (e.g., Broca's or Wernicke's area) were not included. We intended to perform tumor resection as extensively as possible without deliberate induction of neurological deficits. Therefore, complete tumor resection was not attempted in every case. All patients underwent thorough clinical neurological examinations preoperatively and postoperatively every day until discharge. Assessment of postoperative clinical status for analysis was done on day 7 after surgery. Routinely, patients had postoperative MRI exams within 72 h to determine the extent of resection and to rule out complications. A single neuroradiologist (A.B.) who was blinded to intraoperative findings and clinical outcome, assessed all pre- and postoperative imaging data to perform volumetric analyses. Independent neuropathologists examined tumor specimens. All patients received adjuvant treatment, if indicated, following histopathological diagnosis. All patients were followed up with clinical and MRI examinations every 3 months. This study was approved by the local ethics committee (approval no. 4/09, project SNO_NCH_01_11).

Intraoperative MRI

Surgeries were performed employing a mobile ultra-low-field strength iMRI device (PoleStar N-20; Odin Medical Technologies, Yokneam, Israel/Medtronic, Louisville, CO, USA) that was used for intraoperative navigation and resection control. Its setup and intraoperative use have been described previously [13, 22, 23]. When the surgeon was convinced the tumor had been either completely or to a maximum safe extent resected, surgery was interrupted for intraoperative scanning. Images were automatically transferred to the neuronavigation system (Stealth Station v6; Medtronic). Figure 1 gives an example of intraoperative

image quality. If residual tumor was detected that could be safely resected, surgery continued; if deemed impossible due to the anatomical location of residual tumor or due to the results of IOM, further resection was not undertaken.

Multimodal neurophysiological monitoring

IOM was performed with median and tibial nerve somatosensory potentials (SEPs) as well as motor-evoked potentials (MEPs) elicited transcranially and by direct cortical stimulation (DCS); additionally, subcortical stimulation was applied from within the resection cavity [20]. For the iMRI environment, single-use Pt–Ir electrodes (Care Fusion, Wi, USA) were used for SEP recording and transcranial MEP stimulation. The set-up followed a design tested and described previously [21]. A multipulse technique (train of five consecutive pulses, individual pulse width of 0.5 ms, interstimulus interval of 4 ms, train repetition rate of 0.5 Hz) was used to elicit MEPs. In tumors located within the vicinity of the motor cortex or subcortical part of the corticospinal tract, DCS following the above-mentioned protocol was performed for localization and continuous eliciting of MEPs. MEP or SEP amplitude decrement of >50 %, an increase in motor threshold (>20 mA for transcranial stimulation, >3 mA for DCS) or a loss of potentials was considered a warning sign, prompting to pause or alter the resection strategy. Motor thresholds to determine a safe resection border through subcortical stimulation were defined on empirical evidence.

Statistics

Statistical analyses were performed using commercially available software (BiAS for Windows 9.01; Epsilon, Frankfurt, Germany). Nominal dichotomized data were analyzed with Fisher's exact test or χ^2 test, when appropriate. Median and mean values between two groups were compared using Student's *t* test or Wilcoxon–Mann–Whitney *U* test, when appropriate. Differences between multiple groups were tested with analysis of variance (ANOVA) or Kruskal–Wallis test, when appropriate. To account for multiple testing after univariate analyses, we performed a logistic regression analysis of variables potentially influencing extent of resection or postsurgical sensory motor outcome. *P* values ≤ 0.05 were considered statistically significant.

Results

Patients

A total of 54 patients were included in this analysis. There were 29 and 25 female patients with a mean age of

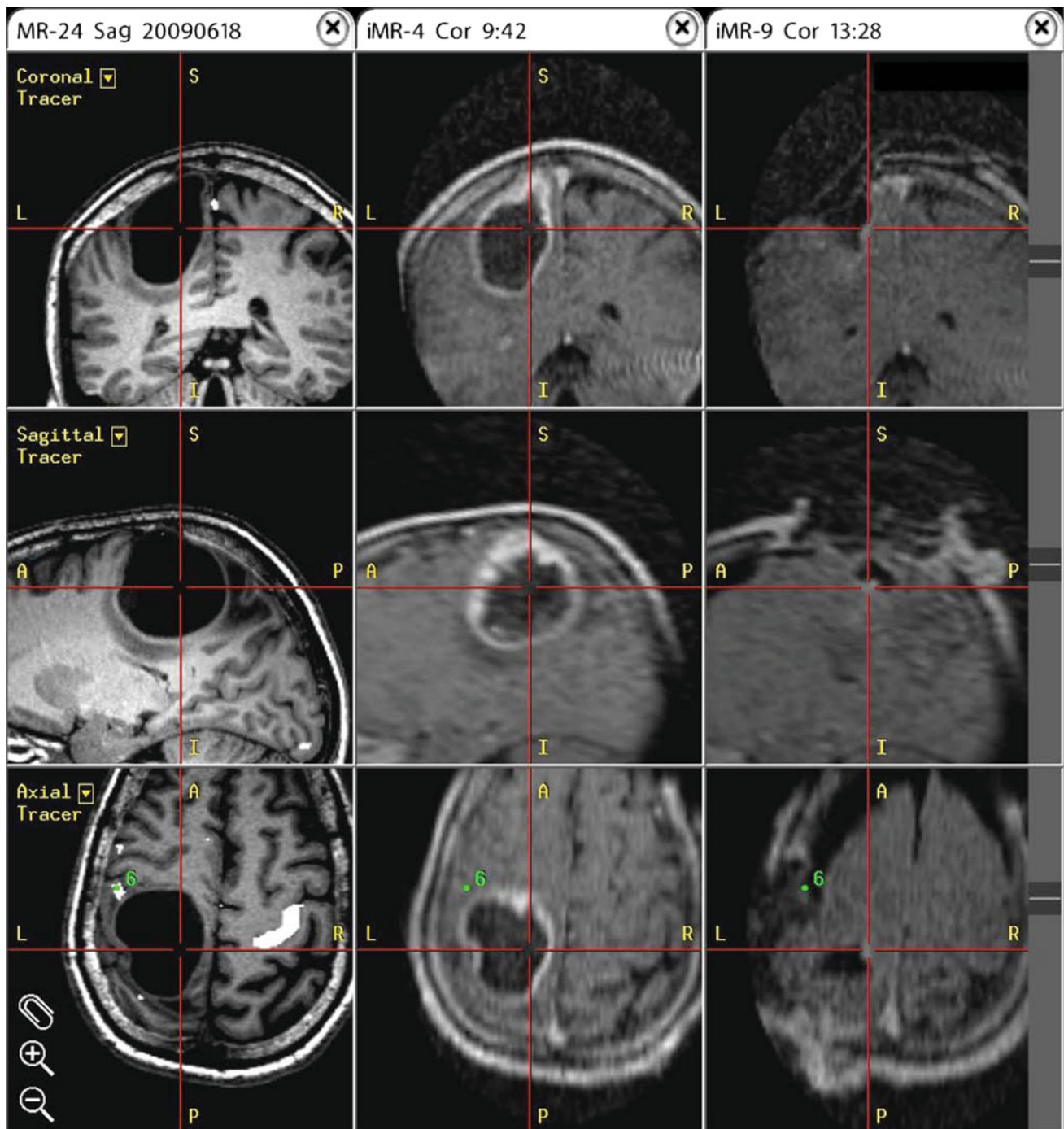


Fig. 1 Screenshot image from intraoperative neuronavigation displaying three different datasets of patient no. 48 with a left parietal glioblastoma in coronal, sagittal, and axial view (from top to bottom). *Left column* preoperative functional MRI obtained at 3 Tesla displaying motor hand activation in white. *Middle column* intraoperative pre-resection contrast enhanced T1-weighted scan delineating the tumor. *Right column* intraoperative post-resection scan showing

residual contrast enhancing tumor tissue. The *red crosshairs* point at the tumor remnant and its corresponding location on preoperative images—a brain-shift can be acknowledged. Tumor resection was not continued due to proximity of the corticospinal tract as indicated by neurophysiological monitoring findings. This patient suffered a mild hypesthesia of the contralateral leg postoperatively

47.7 ± 13.3 years (median age: 47.0 years), and 13 patients (24.1 %) were treated for recurrent tumors. On diagnostic imaging, 14 tumors did not display contrast

enhancement (CE). In 4 patients, CE of the tumor was only slight and focal. The remaining 36 tumors showed typical ring-enhancement. Table 1 summarizes histology and

Table 1 Distribution of glioma subtypes and location

Histology	Tumor location (no. of patients)				Σ
	Frontal	Temporal	Insular	Parietal	
Astrocytoma, WHO grade II	–	–	3	1	4
Oligodendroglioma, WHO grade II	2	–	1	–	3
Oligoastrocytoma, WHO grade II	–	–	–	1	1
Anaplastic astrocytoma, WHO grade III	4	1	–	2	7
Anaplastic oligodendroglioma, WHO grade III	–	–	–	–	0
Anaplastic oligoastrocytoma, WHO grade III	1	1	2	1	5
Glioblastoma, WHO grade IV	8	13	1	11	33
Gliosarcoma, WHO grade IV	1	–	–	–	1
Σ	16	15	7	16	54

tumor location. Table 2 specifies data on age and location. There were no differences in age between different tumor locations ($P > 0.9$ for all, ANOVA). We observed a statistical trend of patients bearing WHO grade IV tumors to be older than patients with WHO grade III tumors (51.5 vs. 41.0 years; $P = 0.053$, ANOVA), but there were no differences in age between patients with WHO grade II and WHO grades III or IV, respectively ($P = 0.99$, and $P = 0.15$; ANOVA).

Intraoperative MRI and extent of resection

Residual tumor was visible on intraoperative imaging in 12 out of 14 patients with non-enhancing tumors. In 7 of these (50 %), the surgeon decided to continue tumor resection intraoperatively. Finally, a gross total resection was achieved in 4 patients while resection was subtotal in 10 patients as determined by postoperative high-field MRI.

In all 4 patients with only focal contrast enhancement, intraoperative imaging depicted residual tumor, leading to continued resection in 2 patients (50 %). In one out of these 4 patients, postoperative MRI showed a gross total resection.

Out of 36 patients with ring-like contrast enhancement, iMRI demonstrated residual tumor in 19 cases. Tumor resection was continued after intraoperative imaging in 12 patients (33.3 %), 9 of which were without residual tumor on postoperative MRI. Thus, gross-total resection could be achieved in 26 patients with ring-like enhancing tumors.

All patients taken together, we continued tumor resection after intraoperative image acquisition in 21 out of 54 patients (38.9 %). In 12 out of these 21, postoperative MRI could later demonstrate radiological completeness of the resection. In summary, we achieved a gross total resection in 31 patients (57.4 %)—4 had non-enhancing, 1 had a focally enhancing, and 26 had ring-enhancing tumors. The median preoperative tumor volume was 24.6 cm³ (range:

0.3–167.0 cm³). Volumetric analysis of pre- and postoperative imaging data revealed that a mean extent of resection of 92.1 % could be achieved. The difference in the rates of radiologically complete resection before and after continued resection following intraoperative imaging (35.2 vs. 57.4 %) was statistically significant ($P < 0.05$, χ^2 test; Fig. 2).

With regard to tumor location, we achieved a complete resection more frequently in patients with temporal lobe tumors (14 out of 15, 93.3 %) than in other areas (17 out of 39, 43.6 %). This difference was statistically highly significant ($P < 0.005$, χ^2 test). We did not observe statistically significant differences comparing the extent of resection in frontally or parietally located tumors (8 out of 16, 50.0 %, for both; $P = 0.68$, χ^2 test). A complete resection was least frequently achieved in insular tumors (1 out of 7, 14.3 %; $P < 0.02$, Fisher's exact test). A logistic regression analysis confirmed the association of a higher rate of gross-total resections in temporally located tumors [$P < 0.01$, odds ratio (OR) 18.2, 95 % confidence interval (CI): 2.1–157.9].

IOM findings

Neurophysiological monitoring of sensory motor function could successfully be performed by means of transcranial elicited MEPs and SEPs recording in all patients. In 26 patients (48.1 %), direct cortical and subcortical stimulation was also used to establish resection boundaries. IOM remained unchanged during tumor resection in 44 patients (81.5 %). In ten patients (18.5 %), alterations in IOM findings occurred, which changed the surgical strategy (e.g., halt of resection, irrigation with warm saline solution). In eight of these ten patients, we could thereby prevent the occurrence of a permanent severe sensory motor deficit. Details of IOM findings in patients with sensory motor deficits are given in Table 3.

Table 2 Summary of tumor location, patient status and surgical outcome

Tumor location	Total No. of patients	Mean age Years	Pre-operative KPS score Median	Post-operative KPS score Median	Continued resection after iMRI No. of patients (%)	Complete resection achieved No. of patients (%)	Any new postop. deficit No. of patients (%)	Severe postop. deficit No. of patients (%)
Frontal	16	45.9*	95*	90*	7 (43.8)*	8 (50.0)*	6 (37.5)*	1 (6.3)*
Temporal	15	49.3*	80*	90*	4 (26.6)*	14 (93.3) ^a	1 (6.7) [#]	1 (6.7)*
Insular	7	45.6*	90*	90*	3 (42.9)*	1 (14.3) ^b	1 (14.3)*	1 (14.3)*
Parietal	16	48.9*	90*	90*	7 (43.8)*	8 (50.0)*	5 (31.2)*	1 (6.3)*
All	54	47.7	90	90	21 (38.9)	31 (57.4)	13 (24.5)	4 (7.4)

KPS Karnofsky performance score, CR complete resection

^a $P < 0.01$ χ^2 test with Yates-correction

^b $P < 0.05$ Fisher's exact test

* Statistically not significant

[#] Statistical trend

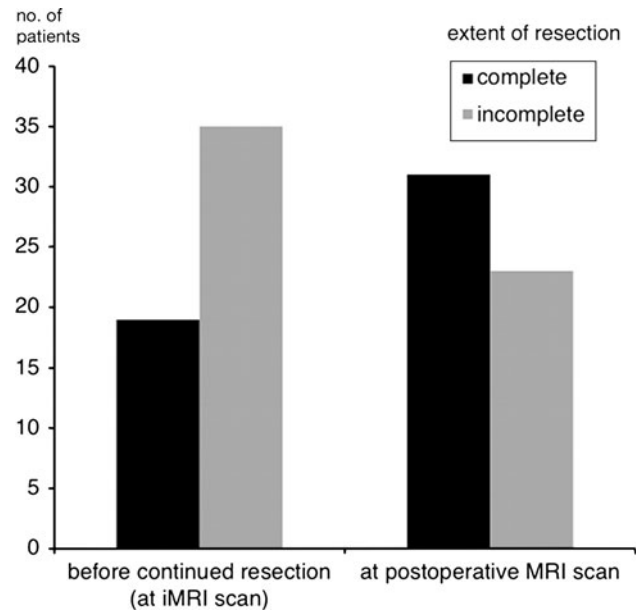


Fig. 2 Extent of resection as determined by MRI before continued resection and after surgery

Functional postsurgical outcome

Median preoperative KPS score was 90 (range: 100–60) and did not differ significantly between patients with frontal, temporal, insular, or parietal tumors ($P > 0.1$ for all, Kruskal–Wallis-test with Bonferroni–Holm correction). Median KPS score remained unchanged at 7 days post-surgery (range: 100–40; $P = 0.4$, Wilcoxon–Mann–Whitney U test). 13 patients (24.1 %) showed a new or a worsening of a pre-existing sensory motor deficit. In 4 of these (7.4 %), these deficits were severe. Two of these 4 patients suffered from postoperative hemorrhages resulting in hemiparesis. Neurological deficits improved until first follow-up (3 months postoperatively) in the majority of patients. Table 3 provides details on patients with surgically induced deficits.

Factors influencing functional outcome

Of 21 patients, in whom resection was continued based on intraoperative depiction of residual tumor and IOM findings, 5 (23.8 %) showed a new sensory motor deficit postoperatively as compared to 8 out of 33 patients (24.1 %), in which resection was terminated. This difference was not statistically significant ($P = 0.97$, χ^2 test). Severe deficits occurred in 1 patient with continued resection (4.8 %) as opposed to 3 patients (9.1 %) in which resection was terminated. Again, this difference was not statistically significant ($P = 1.0$, Fisher's exact test).

There were no statistically significant differences in the postoperative occurrence of either any (29.6 vs. 18.5 %) or

Table 3 Details of patients who developed sensory motor deficits

Age (years), sex	Histology, recurrent tumor	CE	Tumor localization	Continued resection after iMRI	Achieved resection	Preoperative KPS score	Postoperative KPS score	Sensory motor deficit	IOM findings	Neurological improvement	Clinical status at 3 months after surgery
40, m	O II, yes	No	Frontal, right	Yes	Subtotal	90	70	Mild hemiparesis	Stable SEP, MT increase in MEP	Yes	Independent, minor deficit
35, f	A II, no	No	Insular, right	Yes	Subtotal	100	60	Severe hemiparesis	Stable SEP, MEP loss	Yes	Ambulating
34, f	OA II, no	No	Parietal, right	No	Subtotal	100	70	Hemihyesthesia, mild ataxia	Stable SEP and MEP	Yes	Independent, minor deficit
24, f	O II, no	No	Frontal, right	No	Complete	100	90	Fine motor skill disturbance of the hand	Stable SEP and MEP	Yes	No deficit
41, f	A III, yes	Yes	Frontal, right	Yes	Complete	90	70	Hemihyesthesia	Stable SEP, fluctuation of MEP	Yes	No deficit
62, m	GSA, no	Yes	Frontal, right	No	Complete	80	40	Severe hemiparesis (hemorrhage)	Stable SEP and MEP	No	Hemiparesis
44, f	A III, no	No	Frontal, left	No	Complete	100	90	SMA-lesion	Stable SEP and MEP	Yes	No deficit
70, f	GBM, no	Focal	Parietal, left	No	Subtotal	100	60	Hemiparesis (hemorrhage)	Stable SEP and MEP	No	Hemiparesis
56, f	GBM, yes	Yes	Frontal, right	No	Subtotal	70	60	SMA-lesion	Stable SEP and MEP	Yes	No deficit
63, f	GBM, no	Yes	Parietal, right	No	Complete	80	80	Hemihyesthesia	Deterioration of SEP, stable MEP	No	Independent, minor deficit
42, m	GBM, no	Yes	Parietal, left	Yes	Subtotal	90	80	Hemihyesthesia	SEP loss, stable MEP	Yes	Independent, minor deficit
40, f	GBM, no	Yes	Parietal, right	Yes	Complete	100	90	Mild hyesthesia of the leg	SEP loss, stable MEP	Yes	No deficit
52, f	GBM, yes	Yes	Temporal, right	No	Complete	90	50	Hemiparesis (ischemia)	SEP loss, MT increase in MEP	No	Hemiparesis/tumor progression

CE contrast enhancement, KPS Karnofsky performance scale, iMRI intraoperative magnetic resonance imaging, IOM intraoperative neurophysiological monitoring, m male, f female, A II astrocytoma, A III anaplastic astrocytoma, A II oligoastrocytoma, GBM glioblastoma, GSA gliosarcoma, SMA supplemental motor area, SEP somatosensory evoked potentials, MEP motor-evoked potentials, MT motor threshold

severe (3.7 vs. 11.1 %) sensory motor deficits between patients below or above median age ($P = 0.53$ for any and $P = 0.61$ for severe deficits, Fisher's exact test). Likewise, preoperative KPS score was not associated with the occurrence of postoperative deficits. Out of 20 patients with a preoperative KPS score of 100, 6 patients (30 %; $P = 0.52$, Fisher's exact test) showed a new deficit that was severe in 2 patients (10 %; $P = 1.0$, Fisher's exact test). Out of 38 patients with a preoperative KPS score of ≥ 90 , 10 patients (26.8 %; $P = 0.73$, Fisher's exact test) showed a new deficit that was severe in 3 patients (7.9 %; $P = 1.0$, Fisher's exact test). Also, a preoperative KPS score of < 80 was not associated with a higher risk of neurological deterioration: 1 out of 4 patients (25 %; $P = 1.0$, Fisher's exact test) showed new postoperative deficits. None of these patients experienced a severe deficit ($P = 1.0$, Fisher's exact test).

There were no statistically significant differences in the occurrence of postoperative deficits between different tumor locations: while the rate of new deficits was highest in patients with precentral tumors (37.5 %), the difference compared to non-frontally located tumors (18.4 %) did not reach statistical significance ($P = 0.17$, Fisher's exact test). Yet, there was a statistical trend of having a lesser chance of developing new deficits when tumors were located in the temporal lobe (6.7 % compared to 30.8 % in other locations; $P = 0.083$, Fisher's exact test).

Patients with recurrent tumor showed sensory motor deficits more often than patients who had their first tumor resection [4 out of 14 (30.8 %) vs. 9 out of 41 (22.0 %)], but this difference was not statistically significant ($P = 0.71$, Fisher's exact test). There were no significant differences between patients with a purely astrocytic tumor and those with an oligodendroglial component ($P = 0.67$ for any, and $P = 0.60$ for severe deficits, Fisher's exact test). Also, there was no statistically significant association between WHO grades and sensory motor deficits. CE was also not a predictor of sensory motor outcome. 5 out of 14 patients (35.7 %) without CE showed new postoperative sensory motor deficits as opposed to 8 patients out of 40 (20.0 %), whose tumor exhibited CE ($P = 0.28$, Fisher's exact test).

Finally we performed a logistic regression analysis to determine an independent association between surgically induced deficits and the following variables: continued resection after intraoperative imaging, WHO grade, CE, recurrent tumor, and tumor location. None of these reached statistical significance.

Discussion

While extensive resection to the greatest feasible extent is the goal in the microsurgical treatment of gliomas,

concerns have been raised that “chasing tumor” by means of detecting minute tumor remnants with iMRI or 5-ALA might not be of benefit, but rather harm patients by causing neurological deficits. Use of 5-ALA was reported to be associated with a higher rate of temporary early neurological worsening than conventional microsurgery [24]. Comparable data for intraoperative imaging-guided procedures are not available. With this analysis, we could show that the combination of iMRI guidance with neurophysiological monitoring assists in achieving most extensive resections without inducing higher rates of sensory motor deficits in eloquently located gliomas. Complication rates were acceptable and did not differ between patients in whom intraoperative imaging detected residual tumor that was subsequently resected, and patients in whom tumor resection was terminated on both uni- and multivariate analysis.

IOM techniques, e.g., continuous motor-evoked potentials or direct subcortical stimulation, have evolved as reliable means to avoid surgical complications in glioma surgery [18, 25, 26]. Complication rates of up to 30 % overall, with permanent morbidity occurring in more than 10 % of the cases, are not uncommon [27]. Complication rates in the surgical treatment of eloquently located gliomas are usually higher than in non-eloquently located tumors [28–30]. IOM is used to identify or rule-out the vicinity of eloquent structures that must not be damaged during surgery. IOM provides a safety margin to eloquent cortical or subcortical structures and thus helps to avoid or minimize postoperative deficits. On the one hand, IOM may limit the extent of resection, but on the other, a safety margin based on anatomical imaging alone might be larger than the one established with IOM. Therefore, the potential benefit of IOM use is to enhance the extent of resection within functional boundaries [31], especially in combination with intraoperative MR imaging, which is able to detect unintentional residual tumor. In our series, the rate of (permanent and severe) deficits was acceptably low compared to other reports.

In our series, iMRI led to continued resection in about every second patient with a non-enhancing tumor and in about every third patient with an enhancing tumor. Had resection not been continued after intraoperative scanning, the gross total resection rate in this series would have been merely 35.2 % (19 out of 54 patients) as opposed to 57.4 %, which we finally achieved. Even in the group of temporal lobe tumors, in which a very high rate of complete resection was achieved, iMRI led to continued resection in about every fourth patient.

When performing brain tumor surgery in eloquent areas, neurophysiological monitoring techniques are generally considered indispensable. The gold standard to monitor neurological function is to have the patient awake and

perform tasks during electric stimulation of cortical or subcortical areas [32]. This technique can also be combined with iMRI guidance [33, 34]. Yet, complications are unavoidable even in awake craniotomy [35]. Multimodal IOM techniques have shown to be reliable means to identify sensory motor cortex and the corticospinal tract even under general anesthesia, thereby minimizing surgically induced disturbances of sensory motor pathways [25, 36–38]. In a group of 37 patients, Gupta et al. [39] reported an even lower incidence of sensory motor deficits in patients undergoing tumor resection with IOM guidance under general anesthesia when compared with patients undergoing awake craniotomies. Another option to avoid damage to the pyramidal tract is to integrate functional MRI data and diffusion-tensor imaging-based fibertracking (DTI-ft) into the neuronavigation system [40]. This type of imaging, however, should not be relied upon unless updated intraoperatively, since anatomical alterations and movement of the brain during surgery will cause neuro-navigation that is solely based on preoperative imaging to be inaccurate [41]. Using IOM and iMRI in conjunction, we achieved a higher rate of complete tumor resection with fewer neurological complications than was reported in a series relying on preoperative DTI-ft and intraoperative use of ultrasound [42].

We analyzed factors potentially affecting sensory motor complication rates in the resection of gliomas located in proximity to the central sulcus and sensory motor fiber tracts, and we could not find a statistically significant predictor of poor neurological outcome. Previously, repeat craniotomy for recurrent tumor has been reported as a clinical prognosticator of worse outcome [43]. Although observing a higher rate of deficits in this group of patients, this difference was not statistically significant, possibly owing to the small proportion of patients with recurrent tumors. Yet, we recently reported that the incidence of postoperative infarction does not differ significantly between first and repeat surgery in a larger series [44]. In the current series, we did not find tumor location to be predictive of neurological deficits, which might be explained by the fact that, however heterogeneous in histology or contrast behavior on diagnostic imaging, all tumors were eloquently located. We observed a statistical trend for a lower risk of complications for patients with temporal tumor location. This may be explained by the fact that the middle cerebral artery and its branches are spared using meticulous subpial resection techniques. None of the other factors, including patient status or histological features, was associated with sensory motor complications in this series. It is conceivable that our series may not have been large enough to identify predictors of poor neurologic outcome, and the ideal set-up to identify or definitely rule out potential factors would certainly be a large-scale randomized study.

The main limitation of our study is its retrospective design without a reference group. It could be argued that iMRI might not always have been performed when the surgeon believed the initially intended amount of tumor to have been resected. A prospective randomized trial would be necessary to rule out any bias regarding the acquisition of intraoperative images and to prove the benefit of iMRI in terms of extent of resection. Our results concerning the detection rate of residual tumor are, however, in line with previous, equally retrospective reports on iMRI [10–12, 45–47]. In a recently published prospective randomized trial, iMRI led to continued resection in every third patient [14], but comparable data are lacking for patients with eloquently located tumors. Here, we did not perform a controlled study, so we cannot rule out for certain that, in some instances, iMRI was used to show the amount of expected residual tumor. Yet, we would undoubtedly not have achieved a mean resection of >90 % of the initial tumor volume without iMRI guidance in this series.

In addition to its exact location, iMRI gives the surgeon information about the volume and extension of any remnant, which is different to, e.g., fluorescence-guided surgery with 5-ALA. Therefore, iMRI gives the surgeon a good idea as to what risk or benefit there may be in resecting further tumor tissue, especially when eloquent structures are involved. It will be interesting to see in the future whether a combination of iMRI, IOM, and use of 5-ALA might result in even more extensive resections without increasing complication rates.

Despite the limitations mentioned above, our data indicate that continued resection after intraoperative image acquisition in patients with eloquently located tumors, analogous to patients with non-eloquently located tumors [14], does not inevitably lead to an increased rate of patients suffering from new deficits if surgery is performed under continuous IOM, but rather results in an increased rate of gross total resections.

Two of our patients developed a delayed postoperative hemorrhage at the site of tumor resection, causing hemiparesis. IOM techniques and intraoperative imaging are unable to prevent this type of complication that can only be minimized by thorough surgery, meticulous hemostasis, and correction of coagulation disorders, if present. Three patients with precentrally located tumors had stable IOM findings during resection, but presented with a severe hemiparesis postoperatively, that resolved completely within a few weeks. The most likely cause was direct lesioning of the supplementary motor area, resulting in an initiation difficulty; since the corticospinal tract is unaffected here, motor-evoked potentials will remain unchanged, and patients will show only a temporary weakness.

Conclusion

Close to functional motor areas, tumor resections should not be performed without multimodal monitoring techniques, since there is a high risk of neurological deterioration in these cases. Intraoperative MRI is a helpful tool to increase the extent of resection in *these patients* also. Intraoperative MRI guidance along with neurophysiological monitoring allows a maximum safe resection of brain tumors, even if eloquently located. The combined use of these techniques does not appear to be associated with an additional risk of neurological deficits.

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Conflict of interest All other authors declare that they have no potential conflicts of interest.

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