The aim of surgical treatment of low- and high-grade gliomas is maximal tumor resection with preservation of neurological function. However, some patients experience new neurological deficits—transient or permanent—or worsening of neurological symptoms following tumor resection. Different risk factors for new postoperative neurological deficits have been identified, including older age, eloquent tumor location, and preoperative neurological deficits. The incidence rate for new permanent neurological deficits ranges from 4.5% to 19%. In patients with recurrent gliomas undergoing repeat craniotomy a higher incidence of new neurological deficits than after initial surgery has been reported, although reasons for this higher incidence remain vague and it might be attributable to a changed vascular pattern in patients with recurrent tumors.

Especially in lesions located close to or within so-called eloquent brain regions (areas of speech, motor function, and vision) the risk of postoperative deficits is high. Therefore, several different tools are used—notably intraoperative electrophysiological monitoring, neuronavigation, awake craniotomy with monitoring of neurologically...
cal function, and intraoperative MRI—to improve preservation of neurological function and to increase the extent of tumor resection.1,2,4,6,8,23

Reasons for new postoperative deficits can be either direct tissue damage from resection or secondary events, such as hemorrhage, venous congestive infarcts, or arterial ischemic events leading to tissue infarction. These secondary events are not necessarily detected by intraoperative monitoring, as has been recently shown.15 In most cases, secondary events are revealed by postoperative MRI, which is routinely performed to determine the extent of tumor resection and serves as a baseline for determination of postoperative treatment and possible tumor progression as well.21

So far, the use of early postoperative DWI has been evaluated by only a few authors, either for delineation of postoperative ischemic changes or as a baseline to evaluate further tumor progression during follow-up.18,20,25 However, this seems especially important for 2 reasons: 1) to detect vascular incidents that could explain new postoperative deficits and 2) to serve as baseline imaging for further follow-up (ischemic deficits convert to contrast-enhancing areas during the further course and might be interpreted as areas of tumor progression if initial postoperative DWI information is not taken into consideration). Therefore, in the present study the incidence of new postoperative infarctions following resection of newly diagnosed gliomas and recurrent gliomas and their relevance for new postoperative neurological deficits are assessed.

**Methods**

This study was approved by the medical ethics committee of the Technische Universität München.

The study population comprised 100 patients who underwent resection of an intracranial low- or high-grade glioma between June 2008 and June 2010 with preoperative and early postoperative (within 48 hours after surgery) MRI studies according to a protocol that included DWI. Patients were selected according to the presurgical availability of DWI. Neither the course of the operation nor the patient's clinical course was used as a criterion for selection. Cases involving newly diagnosed and recurrent tumors were assessed and compared. In addition to the immediate postoperative imaging, follow-up imaging was available for a subset of patients.

Clinical data were documented prospectively for each patient and included tumor entity, tumor grade, new postoperative neurological deficits, previous tumor resections, and previous chemo- or radiotherapy.

**Acquisition of MR Images**

Magnetic resonance imaging was performed with a whole-body 3-T imaging system (Achieva 3.0T, Philips Electronics N.V.) using an 8-channel head coil. The studies included DWI and ADC maps. The diffusion-weighted images were obtained using single-shot echo planar imaging with 2 b values of 0 and 1000 sec/mm². For sampling of the entire diffusion tensor, 3 or 6 different gradient directions were acquired. Isotropic diffusion-weighted images and ADC maps were calculated automatically.

Imaging parameters were a repetition time of 3388 or 8413 msec and echo time of 55 msec. The whole brain was covered, with an image resolution of $2 \times 2 \times 2$ mm³ or $1.6 \times 1.8 \times 5$ mm.

Additionally, the following sequences were acquired, with each resulting in 27 axial slices of 4-mm thickness with a gap of 1 mm and an in-plane resolution of $0.9 \times 0.9$ mm²: 1) T2-weighted FLAIR (TR 12000 msec, TE 140 msec, inversion time 2850 msec), 2) T2-weighted gradient echo (TR 813 msec, TE 16 msec), and 3) T1-weighted spin echo (TR 494 msec, TE 10 msec) prior to and after intravenous administration of 0.1 mmol/kg of gadopentetate dimeglumine.

**Analysis of MR Images**

Imaging studies were independently evaluated by a neuroradiologist and a neurosurgeon blinded to the individual patients’ clinical data. The tumor location and extension were classified. Involvement of the midline was document as was the involvement of different cerebral lobes (frontal, temporal, parietal, occipital) in cases of supratentorial lesions. Anatomical tumor location in relation to major arterial territories (anterior, middle, or posterior cerebral artery) or to central arterial territories (perforating artery territories) was assessed.

Early postoperative MR images were reviewed for areas of ischemic lesions as defined by a focal hyperintensity on DWI and a corresponding hypointensity on ADC maps (Figs. 1 and 2). Therefore definition of ischemic lesions was based on MRI standard morphological criteria only.15 Restricted diffusion areas related to methemoglobin (identified by T1 hyperintense blood products) were excluded as were slight rims of hyperintensity in DWI at the border of the tumor resection cavity (Fig. 2). Ischemic lesions were classified using 3 categories: 1) arterial territorial infarction (AT), 2) terminal branch infarction (TB), and 3) other infarction/venous infarction (V). Arterial territorial infarctions are defined as circumscribed areas of restricted diffusion matching a territory of the main branches of the ACA, MCA, or PCA.28 The respective arterial territory was documented for each arterial territorial infarction (Fig. 1). Smaller areas of restricted diffusion related to the tumor cavity and corresponding to a small or perforating artery were termed as terminal branch infarctions (Fig. 1). Areas of restricted diffusion that were not allocated to a certain arterial territory and did not represent a terminal branch infarction were termed as venous infarctions, as they presented characteristics of a venous congestive infarction, with a large and round area of restricted diffusion and partial bleeding, as well as slight perifocal edema (Fig. 2). An angiographic atlas28 was used for classification of vascular territories.

T2-weighted FLAIR and T1-weighted Gd-enhanced sequences of follow-up imaging were evaluated for visibility of the postoperative ischemic lesion, size, and contrast enhancement.

**Statistical Analysis**

Descriptive data analysis, logistic regressions, and Pearson chi-square tests were performed using PASW
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Statistics version 18.0 (SPSS Inc.). Differences with an error probability of less than 0.05 were considered statistically significant.

Results

One hundred patients who underwent resection of a newly diagnosed or recurrent supratentorial glioma and had early postoperative MRI according to the above protocol were included in the study. Sixty-three of the patients were male and 37 were female. The mean patient age was 55 years (range 15–86 years). Of these 100 patients, 84 underwent resection of a newly diagnosed glioma and 25 underwent resection of a recurrent glioma. Nine patients were included after their initial resection and were reassessed after resection of a recurrent tumor; therefore, 109 operations in 100 patients for newly diagnosed or recurrent gliomas were evaluated.

Newly Diagnosed Gliomas

Eighty-four patients underwent surgery for a newly diagnosed glioma (Fig. 3). Their mean age was 55 years (range 15–86 years). This group included 53 male patients and 31 female patients. According to histological examination of the surgical specimens, 24 patients had an LGG (WHO Grade I in 7 cases, WHO Grade II in 17), 60 patients an HGG (WHO Grade III in 11 cases, WHO Grade IV in 49). Four patients were treated for infratentorial lesions. Thirty-nine patients had left-side tumors. In 12 patients we observed midline involvement. In 49 patients 1 lobe was affected, in 19 patients 2, in 11 patients 3, and in 1 patient 4 lobes. Fifty-eight frontal, 24 parietal, 35 temporal, and 7 occipital lobes were affected by tumor.

Twenty-six (31%) of the 84 patients treated for newly diagnosed gliomas had areas of restricted diffusion resembling ischemia on postoperative MR images (9 AT, 13 TB and 4 V) (Figs. 4 and 5).

When the patients were considered in 2 groups based on glioma grade, 20 (33%) of 60 patients in the HGG group displayed ischemic lesions on postoperative MR images (7 AT, 10 TB, 3 V), while 6 (25%) of 24 patients in the LGG group were found to have new postoperative ischemic lesions (2 AT, 3 TB, 1 V) (Fig. 4).

Twenty (24%) of 84 patients had a transient or permanent worsening of neurological symptoms or new transient or permanent neurological deficits. In 14 of these 20 patients the deficits were transient: hemiparesis in 9, aphasia in 2, diencephalic dysfunction with central fever in 1, organic brain syndrome in 1, and visual field deficit in 1. The other 6 patients had permanent worsening of neurological symptoms or a new permanent neurological deficit: hemiparesis in 5 and visual field deficit in 1 (Fig. 6). Ten (50%) of these 20 patients had ischemic areas (6 AT, 3 TB, 1 V) on postoperative MR images (Fig. 7).

There was no correlation of the incidence of ischemic lesions with tumor location in certain lobes or the relation to the vascular territories of the ACA, MCA, and PCA. However, we observed a significantly higher incidence of ischemic lesions in patients with tumors affecting one or more territories of the central arteries (anteromedial, anterolateral or posterolateral central arteries) (p < 0.05).

Ischemic lesions were found in 16 (43%) of 37 patients with tumors close to or within the central arteries compared with 10 (21%) of 47 patients without involvement of the central arteries.

Further statistical evaluation of the patients treated for newly diagnosed tumors revealed no influence of age, tumor entity (LGG vs HGG), or number of affected lobes on the occurrence of ischemic lesions in logarithmic regression analysis. However, the occurrence of new neurological deficits was significantly higher in patients with ischemic lesions than in patients without ischemic lesions according to chi-square testing (p < 0.05) (Fig. 8).

Recurrent Gliomas

Sixteen male and 9 female patients underwent surgery for recurrent glioma. Their mean age was 55 years (range 30–75 years). Four patients suffered from LGG (WHO Grade II in all 4 cases) and 21 patients from HGG (WHO Grade III in 9 cases, WHO Grade IV in 12); 16 patients had left-side lesions. One infratentorial lesion was resected; there was no lesion with midline involvement. In 10 patients 1 lobe was affected, in 11 patients 2 lobes were affected, and in 3 patients 3 lobes were affected. Twenty-one patients had previously been treated with
brain irradiation, 14 had been treated with chemotherapy (temozolomide), and 4 had already undergone resective surgery for a recurrent glioma.

Twenty (80%) of 25 patients had new postoperative ischemic lesions (9 AT, 10 TB, 1 V) (Fig. 5) and 12 (48%) had a transient or permanent worsening of neurological symptoms or new transient or permanent neurological deficits (Fig. 6). A permanent worsening of neurological symptoms or new permanent neurological deficit occurred in 4 (16%) of 25 patients: hemiparesis in 3 cases
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2 and quadrantanopia in 1 case. Additionally, 8 patients (32%) experienced new transient deficits: hemiparesis in 2 cases, aphasia in 4, lateropulsion in 1, and organic brain syndrome in 1. Nine (75%) of the 12 patients with neurological worsening had new ischemic lesions on postoperative MRI (6 AT, 3 TB, 0 V) (Fig. 6).

Newly Diagnosed Versus Recurrent Gliomas

The statistical comparison of patients with newly diagnosed and patients with recurrent gliomas revealed a significantly higher incidence of ischemic lesions in patients with recurrent tumors (80% in recurrent vs 31% in newly diagnosed gliomas, p < 0.01) (Fig. 5).

Analysis of Follow-Up Imaging

Subsequent MR images were reviewed for the further imaging changes of the ischemic lesions. Follow-up imaging was available in 34 of the 46 patients in whom postoperative infarctions were identified (18 TB, 12 AT, 4 V). The mean time (± SD) from early postoperative imaging to follow-up MRI was 101 ± 38.09 days (range 38–214 days). Both T2-weighted FLAIR and T1-weighted Gd-enhanced sequences were available in all patients. In 12 (67%) of the 18 patients with terminal branch infarctions (TB), 9 (75%) of 12 with arterial territory infarctions (AT), and 2 (50%) of 4 with venous infarctions (V), the old infarction area was still visible. In 22 of the 34 infarction areas there was a clear regression of size; in 21 of the 34 image sets contrast enhancement was visible at the site of the previous ischemic lesion.

Discussion

The present study assessed the incidence of ischemic lesions as measured by DWI after resection of newly diagnosed in comparison with recurrent intracranial gliomas. We observed new postoperative ischemic lesions in 31% of patients after resection of newly diagnosed gliomas while the incidence of a new postoperative ischemic lesions after resection of recurrent gliomas was significantly higher (80%). Thus, a recurrent tumor or previous tumor resection is a significant risk factor for the postoperative development of new ischemic lesions. The proximity of a tumor to central arteries (that is, perforating arteries) was identified as a significant risk factor for ischemic lesions, whereas patient age, tumor entity, or number of involved lobes had no influence on the incidence of vascular events. The presence of a new postoperative lesion was associated with a higher probability of a new postoperative neurological deficit. A decline in neurological function occurred significantly more frequently in patients with new postoperative ischemic lesions than in patients without ischemic lesions.

The occurrence of new postoperative ischemic lesions in proximity to the resection cavity is well known to intracranial tumor surgeons and not completely preventable by meticulous subpial dissection avoiding vessel occlusion. Previous studies have assessed the incidence of postoperative DWI changes, and the incidence of postoperative new ischemic lesions in our series is well in accordance with the previously published data. Using DWI and ADC maps, Smith et al. evaluated 44 consecutive patients after resection of intracranial gliomas and found an incidence of new postoperative ischemic lesions of 64%. Areas of new ischemia were found in 50% of the included patients with Grade II gliomas, 100% of those with Grade III tumors, and 65% of those with Grade IV tumors. Using serial MRI, the authors described Gd enhancement and conversion to an encephalomalacia in 93% of patients with ischemic lesions during subsequent follow-up. In their series, clinical deficits were not linked to ischemic lesions. Ulmer et al. evaluated imaging studies in 50 consecutive patients who underwent surgery for glioblastomas and found new ischemic lesions in 70% of

Fig. 4. Bar graph showing the incidence of infarctions after resection of newly diagnosed HGG or LGG. There is no statistically significant difference in the incidence of ischemic lesions between the 2 groups. n.s. = not significant.

Fig. 5. Bar graph showing the incidence of infarctions following resection of newly diagnosed versus recurrent gliomas. The incidence is significantly higher in patients undergoing resection of recurrent tumors (occurring in 31% of patients with newly diagnosed gliomas and 80% of those with recurrent tumors).

Fig. 6. Bar graph showing the proportions of patients with transient or permanent new neurological deficits after resection of newly diagnosed or recurrent gliomas.
the early postoperative MR scans. In 6 cases the diffusion abnormality was associated with a new neurological deficit. The incidence in the series of 80 intracranial tumors reported by Khan et al.\textsuperscript{11} was lower, with DWI changes being detected in only 19% of cases. However, the authors assessed different tumor entities, with 41% of the lesions being metastatic and only 31% HGG. The 31% incidence of new ischemic lesions of the present series of cases of newly diagnosed glioma seems to be in accordance, albeit lower than the previously reported data.

Beyond the data of previous publications, we classified the observed lesions as arterial territorial infarctions (AT), terminal branch infarctions (TB), and venous infarctions (V) in an attempt to refer to the cause of the ischemic lesion. Since arterial territorial infarctions represent an area of restricted diffusion corresponding to at least one of the territories of direct branches of the ACA, MCA, or PCA, direct or indirect injury of these vessels has to be assumed. Possible mechanisms of injury are direct damage by bipolar coagulation and indirect injury by increased pressure on the vessel (for example, due to retraction by a brain spatula or due to vessel spasm).\textsuperscript{14} Terminal branch infarction refers to interruption of smaller cortical or subcortical vessels. These infarctions display imaging similarities to lacunar infarctions, although with different underlying cause.\textsuperscript{15} For infarctions that could not be classified as either arterial territory or terminal branch infarctions, we used the term "venous infarction." These lesions displayed qualities of venous infarction on MRI, such as slight perifocal edema, lack of restriction to arterial territories, and hemorrhage in the area of restricted diffusion.\textsuperscript{13} In these cases we assume that direct or indirect injury of cortical or subcortical veins has caused a congestive ischemic lesion.

To prevent ischemic damage and resulting neurological deterioration we believe an understanding of the underlying cause (of ischemic damage) is essential in improving the neurological outcome after resection of gliomas.

Furthermore, the present series is the first to assess the difference in the incidence of ischemic lesions between patients with newly diagnosed or recurrent gliomas. In the group of patients with recurrent tumors we recognized a rather high rate of postoperative ischemic lesions of 80%, significantly higher than in the group of patients with newly diagnosed glioma (31%). The reasons for this high rate of postoperative ischemic lesions in this group are unclear. We speculate that changes in the vascularization pattern and vessel structure due to postoperative scar tissue or previous irradiation might be a factor underlying this high incidence in recurrent tumors.\textsuperscript{14} Vascular reorganization or vessel obliteration by brain irradiation is well known and is even used as a therapeutic tool in neurosurgery as radiotherapy for vascular lesions such as arteriovenous malformations.\textsuperscript{26} This might explain the increased number of ischemic lesions after resection of recurrent gliomas.

Our rates of 7% for new postoperative permanent deficits or permanent worsening of neurological deficits after resection of newly diagnosed gliomas and 16% after resection of recurrent glioma resemble the deficit rates published by other authors for patients with malignant gliomas; with respect to surgery for recurrent gloma, postoperative neurological decline has been described as occurring in 36% of patients.\textsuperscript{3,14} Most of the studies dealing with recurrent gliomas and outcome after repeat craniotomies display a higher rate of morbidity or decline in patients' general status compared with results in patients with newly diagnosed gliomas, though detailed neurological outcome was not assessed.\textsuperscript{3,12}

In our study, we found rates of transient postoperative deficits of 17% and 32%, respectively, in our patients with newly diagnosed gliomas and recurrent gliomas. New postoperative neurological deficits or a worsening of neurological deficits are either generated by direct surgical structural damage of cortical or subcortical structures or by indirect damage due to hemorrhage, edema, or, most likely, cortical or subcortical ischemic events. Therefore, postoperative ischemic lesions could play an important role in the development of surgery-associated neurological deficits that are not caused by immediate surgical damage to eloquent regions.

Tools such as intraoperative neurophysiological mapping of language and motor functions (with or without awake craniotomy), preoperative functional MRI and intraoperative MRI are used to allocate a certain function to a certain cortical or subcortical structure that is locally
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preserved during tumor resection. However, use of these techniques does not prevent ischemic damage to spatially preserved eloquent regions.2,4,8,23

Regarding the occurrence of ischemic lesions, we initially hypothesized a relationship between age, tumor entity, and anatomy, as well. There is a general increase in vascular diseases and occurrence of common ischemic brain infarction with increased age and we expected this to influence the occurrence of ischemia in our patients as well. As for the tumor entity, we also assumed an impact due to the fact that HGGs show a much more aggressive and rapid growth pattern and therefore a disturbed vascular pattern. However, we did not find any significant influence of the 2 factors of age and tumor grade on the incidence of ischemic lesions in our patients. Regarding age and tumor entity we believe that the number of patients in our study is not sufficient to reveal any significant differences. Furthermore, we assume that a higher patient number would probably permit a more sophisticated and statistically relevant classification of ischemic lesions according to anatomical characteristics.

In the present study we found a statistically significant increase in ischemic lesions in patients with involvement of the central arterial territories. A cause might be the need for a deeper approach in these patients compared with those with a more peripheral tumor location, which could be accompanied by a higher risk of damage to the internal capsule and thalamus resulting in neurological deficits.

Given that early postoperative MRI serves as a baseline for evaluation of tumor progression, the assessment of postoperative DWI is of significant importance. Areas of contrast enhancement during follow-up might resemble previous ischemic areas; therefore correlation with postoperative DWI is important for differentiating recurrent tumor from post-ischemic tissue changes.25 Because postoperative ischemic lesions are frequent in patients undergoing glioma resection, DWI and ADC maps should be included in a postoperative MRI protocol for these patients.

Conclusions

The use of early postoperative DWI and ADC maps in patients undergoing glioma resection reveals postoperative ischemic lesions, particularly in patients with recurrent glioma. We found a correlation between ischemic lesions and new postoperative neurological deficits as well as an increase of both in patients undergoing surgery for recurrent glioma. In order to avoid new neurological deficits, attention should not only be paid to the allocation of cortical or subcortical areas harboring neurological functions, but also to the preservation of vascular structures and thereby prevention of new postoperative ischemic lesions.

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: Ringel, Gempt, Förschler. Acquisition of data: Gempt, Förschler, Buchmann, Pape, Krieg. Analysis and interpretation of data: Ringel, Gempt, Förschler, Buchmann, Pape, Ryang, Krieg. Drafting the article: Gempt, Förschler. 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: Ringel. Statistical analysis: Gempt, Förschler. Study supervision: Meyer.

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