Intraoperative MR Imaging Increases the Extent of Tumor Resection in Patients with High-Grade Gliomas

Michael Knauth, Christian R. Wirtz, Volker M. Tronnier, Nurdagül Aras, Stefan Kunze, and Klaus Sartor

BACKGROUND AND PURPOSE: MR is being used increasingly as an intraoperative imaging technique. The purpose of this study was to test the hypothesis that intraoperative MR imaging increases the extent of tumor resection, thus improving surgical results in patients with high-grade gliomas.

METHODS: Thirty-eight patients with intracranial high-grade gliomas underwent 41 operations. Using a neuronavigation system, tumors were resected in all patients to the point at which the neurosurgeon would have terminated the operation because he thought that all enhancing tumor had been removed. Intraoperative MR imaging (0.2 T) was performed, and surgery, if necessary and feasible, was continued. All patients underwent early postoperative MR imaging (1.5 T). By comparing the proportions of patients in whom complete resection of all enhancing tumor was shown by intraoperative and early postoperative MR imaging, respectively, the impact of intraoperative MR imaging on surgery was determined.

RESULTS: Intraoperative MR imaging showed residual enhancing tumor in 22 cases (53.7%). In 15 patients (36.6%), no residual tumor was seen, whereas the results of the remaining four intraoperative MR examinations (9.7%) were inconclusive. In 17 of the 22 cases in which residual tumor was seen, surgery was continued. Early postoperative MR imaging showed residual tumor in eight patients (19.5%) and no residual tumor in 31 cases (75.6%); findings were uncertain in two patients (4.9%). The difference in the proportion of “complete removals” was statistically highly significant ($P = .0004$).

CONCLUSION: Intraoperative MR imaging significantly increases the rate of complete tumor removal. The rate of complete removal of all enhancing tumor parts was only 36.6% when neuronavigation alone was used, which suggests the benefits of intraoperative imaging.
Acid). The imaging parameters of the T1-weighted images of contrast agent (gadolinium diethylenetriamine penta-acetic acid) were 532/15/3 (TR/TE/excitations); section thickness, 1.4 mm; field of view, 250 × 250 mm; and matrix size, 192 × 256. This 3D MR dataset was used to “update” the neuronavigation system if surgery was to be continued. The total duration of the intraoperative MR examination was approximately 1 hour, consisting of 25 to 30 minutes of imaging time and approximately 30 to 35 minutes of set-up time.

Each patient underwent an early (day 1 to day 3 after surgery) postoperative MR examination using a high-field scanner (1.5 T). The examination protocol included T1-weighted sequences obtained before and after the IV administration of a single dose (0.1 mmol/kg of body weight) of a paramagnetic contrast agent (gadolinium diethylenetriamine penta-acetic acid). The imaging parameters of the T1-weighted images of the early postoperative MR examinations were 674/20/2; section thickness, 6 mm; field of view, 230 mm; and matrix size, 192 × 256.

The study was approved by the local ethics committee. Informed consent was obtained from all patients before the intraoperative examinations were performed.

**Statistical Evaluation**

With our approach, the impact of intraoperative MR imaging on the extent of tumor resection in patients with high-grade gliomas can be assessed. Using a neuronavigation system, the surgeon operated to the point at which he would otherwise have terminated surgery. Therefore, the results of the intraoperative MR examination represent the surgical outcome achievable using neuronavigation alone. If necessary and feasible, surgery was continued after the intraoperative MR examination. By comparing the proportions of patients in whom a complete resection of all enhancing tumor was shown by intraoperative and early postoperative MR imaging, respectively, the impact of intraoperative MR imaging on the extent of tumor resection can be determined. Fisher exact tests were used for this purpose.

**Results**

The intraoperative MR examinations showed residual enhancing tumor in 22 cases (53.7%). In 15 patients (36.6%), no residual tumor was seen, whereas the results of the remaining four intraoperative MR examinations (9.7%) were inconclusive (ie, it was not possible to confidently diagnose or exclude residual enhancing tumor tissue). Uncertain findings were due to “surgically induced enhancement”; ie, contrast enhancement that was caused by the surgical manipulation itself (eg, electrocoagulation, tissue ablation) and not residual tumor (9, 10). In one of the four uncertain cases, a small biopsy was obtained that did not show residual tumor (Fig 1).
Summary of the findings of intraoperative MR and early postoperative MR

<table>
<thead>
<tr>
<th></th>
<th>Residual Enhancing Tumor</th>
<th>No Residual Enhancing Tumor</th>
<th>Uncertain Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of Patients (%)</td>
<td>22 (53.7)</td>
<td>15 (36.6)</td>
<td>4 (9.7)</td>
</tr>
<tr>
<td>Intraoperative MR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early postoperative MR</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note.—By comparing the proportions of patients in whom a complete resection of all enhancing tumor was seen at intraoperative MR and early postoperative MR, respectively, the impact of intraoperative MR on the radicality of surgery can be determined. The difference in the proportion of “complete removals” was statistically significant (Fisher exact test; \( P = .0004 \)).

In 17 of the 22 cases in which residual enhancing tumor was shown by intraoperative MR imaging, surgery was continued using a neuronavigation device. No further intraoperative MR examination was performed. The tissue removed during the second surgical pass was sent separately for neuropathologic analysis and proved to be tumor tissue in all cases.

Early postoperative MR imaging showed residual enhancing tumor in eight patients (19.5%), and no residual enhancing tumor in 31 patients (75.6%); findings were uncertain in two patients (4.9%). In all eight patients in whom early postoperative MR imaging showed residual enhancing tumor, intraoperative MR imaging also had shown residual tumor. The results are summarized in Table 1. Figures 2 through 4 show examples of residual tumor seen at the intraoperative MR examination.

The proportion of patients in whom complete removal of all enhancing tumor tissue was diagnosed by the intraoperative MR examinations (36.6%) was compared with the rate of complete removals seen on early postoperative MR images (75.6%). This difference in the proportion of “complete removals” was statistically highly significant (Fisher exact test, \( P = .0004 \)) and reflects the impact of the intraoperative MR examinations on the extent of tumor resection in patients with high-grade gliomas (see above).

This analysis compares the proportions of patients in whom the goal of surgery, which is the removal of all enhancing tumor, has been achieved. By doing so, “uncertain” cases are counted implicitly as failures. If the analysis is conducted from the opposite perspective (ie, if the proportions of patients in whom residual enhancing tumor was definitely seen are compared), only the definite failures are compared. Intraoperative and postoperative MR imaging definitely showed residual enhancing tumor in 22 of 41 cases and eight of 41 cases, respectively. This difference was also statistically significant (Fisher exact test, \( P = .0026 \)).

Discussion

Intraoperative MR imaging is being used increasingly during neurosurgical interventions (6, 11–14); however, it has not yet been proved that its use leads to better surgical results. Our data show a highly significant increase in the proportion of patients in whom complete removal of all enhancing tumor tissue can be achieved when intraoperative MR examinations are performed. To the best of our knowledge, this is the first proof of the effectiveness of intraoperative MR examinations during neurosurgical operations. The total duration of the intraoperative MR examination of approximately 1 hour is quite long, but with increasing experience in the interpretation of intraoperative MR images, the examination protocol probably can be shortened. Other intraoperative MR groups work with an MR scanner with a different configuration.

Fig 2. A 41-year-old woman with a recurrent glioblastoma multiforme.
Left, Preoperative T1-weighted image shows a left-hemispheric lesion (674/20/2).
Middle, Intraoperative MR image (632/15/3) shows residual enhancing tumor (arrowhead).
Right, Surgery was continued, and the residual tumor was removed, as shown in this early postoperative MR image (674/20/2).
(10, 14), which allows a much shorter setup time than the one used in our study.

Of course, the complete removal of all enhancing tumor tissue in patients with high-grade gliomas must not be confused with the removal of all tumor cells. It has been shown that isolated tumor cell infiltration extended at least as far as the hyperintense area on T2-weighted images (15) (ie, far beyond the contrast-enhancing tumor tissue). Nevertheless, many studies have found a beneficial effect of the removal of all enhancing tumor (1, 16–20) on patient survival and/or progression-free intervals in patients with high-grade gliomas, whereas some other studies were not able to confirm these findings (21, 22).

Because the follow-up period in our own patient group is not yet long enough, we cannot at this time reliably answer the question of whether the improved surgical results in our patients undergoing intraoperative MR imaging translate into longer survival times, longer progression-free intervals, and improved quality of life. The rate of complete removal of all enhancing tumor parts was only 36.6% when neuronavigation alone was used to assist the neurosurgeon. It is disappointing that by using neuronavigation alone, a complete removal of all enhancing tumor parts could be achieved in only approximately one third of the patients, although this is approximately twice as much as in a series of patients who had been operated on in the
same institution without the use of neuronavigation (1). This relatively low rate of complete removal probably occurs because neuronavigation systems work with MR datasets that are acquired preoperatively. These datasets grow “old” during the course of the operation; this is known as the “brain shift problem” of neuronavigation. Brain shifts of 5 to 10 mm and more during the course of neurosurgery have been reported (23–25), explaining the limited usefulness of neuronavigation for the assessment of the completeness of tumor resection. This also emphasizes the need of an intraoperative imaging technique to correct for these distortions.

Conclusion

Intraoperative MR examinations improved the surgical results in a series of patients with high-grade gliomas. Although in a strict scientific sense an improvement in surgical results has been proved only for patients with high-grade gliomas in this study, we are confident that these findings can be applied to other enhancing intra-axial tumor entities in which the overall prognosis is better than in cases of high-grade gliomas.

Acknowledgments

We thank the radiology technologists, Bettina Bittmann, Tina Kerby, Andreas Krupp, Cora Sauer, and Sabine Unterwaldt, for their collaboration.

References