Determining the utility of intraoperative magnetic resonance imaging for transsphenoidal surgery: a retrospective study

Clinical article

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Object. Intraoperative MRI (iMRI) provides updated information for neuronavigational purposes and assessments on the status of resection during transsphenoidal surgery (TSS). The high-field technique additionally provides information about vascular structures at risk and precise information about extrasellar residual tumor, making it readily available during the procedure. The imaging, however, extends the duration of surgery. To evaluate the benefit of this technique, the authors conducted a retrospective study to compare postoperative outcome and residual tumor in patients who underwent conventional microsurgical TSS with and without iMRI.

Methods. A total of 143 patients were assessed. A cohort of 67 patients who had undergone surgery before introduction of iMRI was compared with 76 patients who had undergone surgery since iMRI became routine in TSS at the authors’ institution. Residual tumor, complications, hormone dependency, biochemical remission rates, and improvement of vision were assessed at 6-month follow-up. A volumetric evaluation of residual tumor was performed in cases of parasellar tumor extension.

Results. The majority of patients in both groups suffered from nonfunctioning pituitary adenomas. At the 6-month follow-up assessment, vision improved in 31% of patients who underwent iMRI-assisted surgery versus 23% in the conventional group. One instance of postoperative intrasellar bleeding was found in the conventional group. No major complications were found in the iMRI group. Minor complications were seen in 9% of patients in the iMRI group and in 5% of those in the conventional group. No differences between groups were found for hormone dependency and biochemical remission rates. Time of surgery was significantly lower in the conventional treatment group. Overall a residual tumor was found after surgery in 35% of the iMRI group, and 41% of the conventional surgery group harbored a residual tumor. Total resection was achieved as intended significantly more often in the iMRI group (91%) than in the conventional group (73%) (p < 0.034). Patients with a planned subtotal resection showed higher mean volumes of residual tumor in the conventional group. Progression-free survival after 30 months was higher according to Kaplan-Meier analysis with the use of iMRI, but a statistically significant difference could not be shown.

Conclusions. The use of high-field iMRI leads to a significantly higher rate of complete resection. In paraseellar tumors a lower residual volume and a significantly lower rate of intrasellar tumor remnants were shown with the technique. So far, long-term follow-up is limited for iMRI. However, after 2 years Kaplan-Meier analyses show a distinctly higher progression-free survival in the iMRI group. No significant benefit of iMRI was found for biochemical remission rates and improvement of vision. Even though the surgical time was longer with the adjunct use of iMRI, it did not increase the complication rate significantly. The authors therefore recommend routine use of high-field iMRI for pituitary surgery, if this technique is available at the particular center.

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Key Words • pituitary surgery • transsphenoidal approach • intraoperative magnetic resonance imaging • residual tumor • resection rate

Abbreviations used in this paper: iMRI = intraoperative MRI; OR = operating room; TSS = transsphenoidal surgery.
Intraoperative MRI for transsphenoidal pituitary surgery

(iCT) and MRI (iMRI)\(^{10}\) seems to have improved resection rates, not only in gliomas but also in transsphenoidal pituitary surgery.\(^{2,6}\) First introduced as a low-field technique\(^{11}\) improving resection, especially in suprasellar tumors,\(^{4}\) its sensitivity in detecting intra- and parasellar tumor remnants was significantly lower compared with postoperative 1.5-T MRI.\(^{4,22}\) With application of high-field iMRI, the sensitivity in detecting tumor remnants in TSS was similar to a 3-month conventional follow-up MRI, and the rate of complete removal was higher in comparison with previously published literature.\(^{5,13,21,22,25}\) The hitherto published data seem very favorable for the application of iMRI, yet the main drawback (beyond the considerable equipment cost) is a substantial increase in duration of surgery.\(^{28}\) On the other hand, the increase of safety and resection rates would justify a prolonged operating room (OR) time for most surgeons.

At the time of this writing no study existed comparing microsurgical TSS with and without use of iMRI. We therefore conducted a retrospective comparative study with the aim of investigating the routine use of iMRI in TSS.

Methods

Our center has used a dedicated intraoperative 1.5-T MRI scanner (Espree, Siemens AG) as a one-room solution since October 2008. In the beginning we treated mostly complex pituitary cases with the aid of iMRI and prospectively analyzed its impact as a resection control tool and as a means of updating the neuronavigation route.\(^{14}\) Encouraged by the results, we changed our surgical technique and now use iMRI for all TSSs. To evaluate the impact of the introduction of iMRI we compared the outcome of patients after conventional microsurgical transsphenoidal tumor resection between 2007 and 2008 in the “pre-iMRI era” with the outcome of patients treated between 2009 and 2011 with the aid of high-field iMRI.

Patient Population

A total of 143 patients who had undergone surgery via a transsphenoidal approach were assessed. A cohort of 67 patients who had surgery in 2007 and 2008 without the use of iMRI was compared with a cohort of 76 patients who had surgery between 2009 and 2011 with routine use of iMRI. Ninety percent of surgeries were performed by the senior authors (K.S., C.R.W.), who had at least 15 years of experience with TSS. Patient characteristics are summarized in Table 1.

Table 1: Characteristics in 143 patients treated using TSS with or without iMRI

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Conventional Op</th>
<th>Op w/ iMRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>67</td>
<td>76</td>
</tr>
<tr>
<td>age in yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median</td>
<td>58</td>
<td>55</td>
</tr>
<tr>
<td>range</td>
<td>16–85</td>
<td>14–77</td>
</tr>
<tr>
<td>sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>44%</td>
<td>38%</td>
</tr>
<tr>
<td>extent of tumor invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>intrasellar</td>
<td>15%</td>
<td>11%</td>
</tr>
<tr>
<td>suprasellar</td>
<td>60%</td>
<td>50%</td>
</tr>
<tr>
<td>parasellar</td>
<td>25%</td>
<td>38%</td>
</tr>
<tr>
<td>previous ops</td>
<td>13%</td>
<td>33%</td>
</tr>
<tr>
<td>intended complete resection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>76%</td>
<td>62%</td>
<td></td>
</tr>
</tbody>
</table>

Pituitary function was assessed before and 6 weeks after surgery. Ophthalmological assessment including visual fields was performed before admission and 6 months after surgery. Follow-up was performed 6 months after surgery. A clinical examination and a contrast-enhanced MRI study were conducted at this point.

Surgical Technique

A standard direct perinasal paraseptal transsphenoidal route was used in all cases. In the conventional group, fluoroscopic imaging was used for the approach and intrasellar orientation. The microsurgical technique was used for opening the sellar floor and for tumor dissection. A fibrin-coated sponge was used for reconstruction of the sellar opening. The nasal septum was repositioned and fixed with nasal packing. In cases of intraoperative CSF leakage, a lumbar drain was inserted for 3–5 days.

In patients in whom iMRI was used, the head was fixed in a dedicated head holder with integrated MRI coil (NORAS MRI Products GmbH). Registration of the navigation system (VectorVision Sky, BrainLab AG) was performed either by surface matching or automated registration after acquisition of T1-weighted MPRAGE (magnetization-prepared rapid acquisition with gradient echo) images by using an integrated registration matrix.

Intraoperative MRI

Intraoperative MRI was performed at the surgeon’s discretion. For imaging, the nasal speculum was removed and the upper part of the MRI coil was reattached. The sterile operating field was covered with drapes and the patient was transferred into the MRI scanner as described by Hlavac et al.\(^{13}\) Intraoperative imaging started with T2-weighted turbo spin echo sequences in the coronal and sagittal planes. When no obvious tumor remnant was identified, imaging continued with T1-weighted spin echo sequences with and without contrast enhancement in identical planes. In large tumors with parasellar extension, MR angiography was added to the imaging protocol. In cases of intraoperative tumor remnant, the navigation route was updated with the newly acquired intraoperative data set after segmentation of the remnant. Further resection was performed if the tumor was accessible at reinspection. In cases of extended resection after iMRI, repeat imaging was performed prior to closure. If a contrast agent had been applied in the previous imaging session, administration of contrast was not repeated.

Data Acquisition and Statistical Analysis

The data obtained in the 143 patients were analyzed retrospectively. As a first step, the 6-month follow-up records of all eligible patients were examined for hormone
substitution, requirement of hormone therapy, state of vision, and visual field in comparison with the preoperative findings. The MRI scans for the outpatient clinic at our center are performed by independent radiologists. The radiologist’s judgment concerning residual tumor was used as the basis for a final decision by the senior neurosurgeon at the outpatient clinic. In our retrospective analysis we evaluated both interpretations. In case of conflicting assessments at the 6-month follow-up, the 12-month or the latest available follow-up was used to reassess the case. If 12-month follow-up was not available, residual tumor at 6-month follow-up was assumed. The assessment was done as a categorical judgment for all items in this step of the evaluation. Presence of residual tumor was only based on the first follow-up assessment after surgery. A later tumor recurrence, except for the above-mentioned situation, or a loss to follow-up did not affect the calculation. If no follow-up existed at 6 months, patients were not included in the calculation for residual tumor. Patient records were searched for peri- or postoperative complications. In cases in which there was an intradural extension of the lesion, opening of the CSF space and placement of a lumbar drain were planned as part of the surgical approach. These procedures were not classified as a complication.

The groups were split by date of surgery and use of iMRI into a conventional group and an iMRI group. Descriptive statistics tests were performed. The distribution of values of the above-mentioned items was analyzed using the Fisher exact test. A p value below 0.05 was considered statistically significant.

Concerning the assessment of residual tumor, we analyzed all surgeries in which gross-total resection was intended by using categorical judgment again. In all other patients with parasellar extension of tumor in whom a complete resection was not intended, a volumetric assessment of the residual tumor was performed. There were no patients in any cohort in whom the aim was a transsphenoidal biopsy only. For volumetric analysis, the MRI studies obtained at 6 months after surgery were imported into surgical planning software (Iplan 3.0, BrainLab AG) and residual tumor was segmented. In most cases treated before 2009, a volumetric assessment of the preoperative images was not possible because digital images were not available. Thus, statistical comparisons were only performed on the postoperative findings. The comparisons of mean values of tumor volume in the iMRI and conventional groups were conducted with the Student t-test. A positive finding of residual intrasellar tumor was analyzed using the Fisher exact test.

Kaplan-Meier plots were calculated to assess progression-free survival during the first 30 months after surgery for all primary lesions. Distribution of tumor recurrence was compared using the log-rank test. All statistical analyses were performed using SPSS 15.0 (Lead Technologies, Inc.).

Results

Patient Characteristics

Both groups showed a similar distribution of age. The iMRI group had a lower percentage of females (38% vs 44%) and a higher rate of parasellar tumors (38% vs 25%) than the conventional surgery group. Thus the rate of intended total resection was lower (62% vs 76%). We saw a higher percentage of patients with previous TSS in the iMRI group as well (33% vs 13%) (Table 1).

The majority of patients in both groups suffered from a nonfunctioning pituitary adenoma. The iMRI group included a higher share of functioning tumors, 22 (29%) versus 7 (10%). The distribution of diagnoses is summarized in Table 2.

At the 6-month follow-up assessment, 26 patients (35%) in the iMRI group and 27 in the conventional group (41%) harbored a residual tumor after surgery. The difference was not significant (p < 0.729). Hormone replacement was prescribed in 46 patients (61%) in the iMRI group and in 41 patients (63%) in the conventional surgery group. The difference was not significant (p < 0.590). Worsening of vision was seen in 2 patients (3%) in the conventional group and in 1 patient (1%) in the iMRI group. Vision improved in 23 patients (31%) of this group and in 15 patients in the conventional group (23%). No significant difference was seen based on the Fisher exact test (p < 0.355). Complications were found in 7 patients (9%) in the iMRI group and in 3 (5%) in the conventional surgery group. In the iMRI group 6 patients suffered from a rhinoliquorrhea, of whom 2 were treated with a lumbar drain and 4 had surgical repair. We used a multilayer technique including fascia lata in these cases. One patient in the iMRI group reported an impairment of olfaction. In the conventional surgery group, a single major complication was seen. The patient reported a decrease of vision after surgery. A CT scan revealed an intrasellar hematoma. Despite immediate surgical evacuation, the patient’s vision did not recover to the preoperative level. One patient suffered from postoperative epistaxis, which was treated by nasal packing only. One patient presented at follow-up with a mucocele that has been treated conservatively so far. The Fisher exact test showed no significant difference in complication rates between the groups (p < 0.216). Duration of surgery was shorter in the conventional group, with a mean of 58 minutes, in contrast to the mean of 158 in the iMRI group. This difference was significant (p < 0.025) according to the Student t-test. In a subgroup analysis of intra-, supra-, and parasellar tumors a significant difference in surgery time was seen only for parasellar tumors (p < 0.015).

<p>| TABLE 2: Tumor characteristics in patients treated using TSS with or without iMRI |
|---------------------------------|-------------------------------|-------------------------------|</p>
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Conventional Op (%)</th>
<th>Op w/ iMRI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pituitary adenoma</td>
<td>52 (78)</td>
<td>52 (68)</td>
</tr>
<tr>
<td>nonsecreting</td>
<td>7 (10)</td>
<td>22 (29)</td>
</tr>
<tr>
<td>hormone secreting</td>
<td>6 (9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Rathke cleft cyst</td>
<td>0 (0)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>prolactinoma</td>
<td>1 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>craniopharyngioma</td>
<td>1 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>miscellaneous</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Intraoperative MRI for transsphenoidal pituitary surgery

The overall results at the 6-month follow-up assessment are shown in Table 3. To exclude a learning curve during surgery after introduction of iMRI, the first 20 cases with iMRI were compared with the last 20 cases performed with iMRI. Even though a higher share of parasellar tumors was found in the first cluster of cases (10 vs 3), the mean OR time showed no significant difference (first 20 cases 154 minutes vs 140 minutes for the last 20 cases; p < 0.335). Rates of complications, biochemical remissions, and improvements of vision were not statistically different over time (p < 0.967, p < 0.202, and p < 0.862, respectively).

Resection Rate

**Intrasellar and Suprasellar Tumors.** Furthermore, we evaluated the rate of residual tumor in the first follow-up separately for surgeries with intended gross-total resection and those with planned subtotal resection, as was performed for most of the parasellar tumors.

In 51 patients in the conventional group and in 48 in the iMRI group a complete resection was achieved. In 4 patients in the iMRI group no follow-up at 6 months was present; these cases were therefore excluded from the calculation. The goal was achieved in 37 of 51 patients (73%) in the conventional group and in 40 of 44 (91%) in the iMRI group. This difference was significant (p < 0.034) according to the Fisher exact test (Table 4, Fig. 1).

**Parasellar Tumors.** A volumetric assessment was performed in all other cases. Digital presurgical images were available in only 2 patients in the cases treated in 2007 and 2008. Therefore only postoperative residual volume was compared. Two patients were lost to follow-up in the conventional group and 1 was lost in the iMRI group. The mean volume of residual tumor was 1.2 cm³ in the iMRI group in comparison with 2.1 cm³ in the conventional group. This difference, however, is not statistically significant according to the Student t-test (p < 0.216). An intrasellar tumor remnant was found in 8 of 14 patients (57%) in the conventional group, whereas it was found in only 5 of 27 patients (18%) in the iMRI group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conventional Op (%)</th>
<th>Op w/ iMRI (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>tumor remnant</td>
<td>positive 14 (27) 4 (9)</td>
<td>negative 37 (73) 40 (91)</td>
<td>unknown (lost to follow-up) 0 4</td>
</tr>
<tr>
<td>2-sided Fisher exact test</td>
<td>p &lt; 0.034*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Fisher exact test confirmed this difference to be statistically significant (p < 0.017) (Table 5).

**Progression-Free Survival**

The mean follow-up was 28.9 months in the conventional group and 16.4 months in the iMRI group. Kaplan-Meier assessment showed 9 events in the conventional versus 1 event in the iMRI group. The progression-free survival chart is shown in Fig. 2. No statistically significant difference between groups was shown in the log-rank test (p < 0.103).

**Functioning Adenomas**

Additionally, we performed a subgroup analysis of biochemical remission rates in patients suffering from functioning adenomas. Patient characteristics were different between the iMRI and conventional groups. In the iMRI group (n = 20), patients had a higher share of suprasellar and parasellar tumors (66% vs 27%) and less completely resectable tumors (76% vs 91%) compared with the conventional group (n = 7). Moreover, the proportion of patients with previous TSS was higher in the iMRI group than in the conventional group (23% vs 9%). We retrospectively evaluated dependency on medication after surgery. Patients in both groups had a benefit from surgery in 80% (iMRI) versus 71% (conventional) of cases. In the subgroup analysis we found 5 patients in the conventional group (71%) versus

### TABLE 3: Clinical and radiological findings at 6-month follow-up assessment in patients treated using TSS with or without iMRI*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conventional Op (%)</th>
<th>Op w/ iMRI (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>residual tumor</td>
<td>27 (41)</td>
<td>26 (35)</td>
<td>&lt;0.729†</td>
</tr>
<tr>
<td>hormone replacement</td>
<td>41 (63)</td>
<td>46 (61)</td>
<td>&lt;0.590†</td>
</tr>
<tr>
<td>vision</td>
<td></td>
<td></td>
<td>&lt;0.355†</td>
</tr>
<tr>
<td>worse</td>
<td>2 (3)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>unchanged</td>
<td>48 (74)</td>
<td>47 (62)</td>
<td></td>
</tr>
<tr>
<td>improved</td>
<td>15 (23)</td>
<td>23 (31)</td>
<td></td>
</tr>
<tr>
<td>complications</td>
<td>3 (5)</td>
<td>7 (9)</td>
<td>&lt;0.216†</td>
</tr>
<tr>
<td>mean duration of op in min, range</td>
<td>57.84, 25–200</td>
<td>157.58, 85–361</td>
<td>&lt;0.025‡</td>
</tr>
</tbody>
</table>

* Two patients in the conventional group and 1 in the iMRI group were lost to follow-up; the denominators in this table are 65 and 75, respectively.
† No statistically significant difference (Fisher exact test).
‡ Statistically significant difference (Student t-test).
13 in the iMRI group (65%) to be independent from medication after surgery. Two patients in the conventional (29%) versus 4 patients in the iMRI (20%) group had no endocrinological benefit after surgery (Table 6). The difference between groups was not statistically significant according to the chi-square test (p < 0.875).

**Illustrative Case**

A clinical evaluation for chronic headache revealed the incidental finding of an intrasellar lesion in a 42-year-old woman. Endocrinological workup showed a nonfunctioning adenoma with a slightly elevated prolactin level. Results of the initial ophthalmological examination and visual fields were normal. After thorough counseling the patient decided against surgery; she was followed closely by an endocrinologist. No hypopituitarism was found. After 1.5 years a significant expansion into the suprasellar compartment was seen (Fig. 3). The ophthalmological examination was still without pathological findings; however, because of growth and proximity to the chiasm, we recommended microsurgical TSS performed with iMRI. Even though an intrasellar nonfunctioning adenoma with slight suprasellar extension is not a challenging case, we wanted to obtain the highest chance of a complete removal and the lowest risk of postoperative hypopituitarism for the as yet asymptomatic patient.

After positioning the patient in typical fashion in the

![Fig. 1. Bar graph showing the share of tumor remnants at 6-month follow-up for lesions with intended total resection.](image)

**Table 5: Volumetric evaluation of parasellar tumors at 6-month follow-up in patients treated using TSS with or without iMRI**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conventional Op</th>
<th>Op w/ iMRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>tumor vol in cm³ (% of preop)</td>
<td>NA</td>
<td>10.2 (1.9–36.4)</td>
</tr>
<tr>
<td>preop</td>
<td>2.1 ([NA] 0–8.3)</td>
<td>1.2 ([10%] 0–6.7)</td>
</tr>
<tr>
<td>postop</td>
<td>p &lt; 0.216 †</td>
<td>5 of 27 (18%)</td>
</tr>
<tr>
<td>t-test</td>
<td>8 of 14 (57%)</td>
<td>p &lt; 0.017 ‡</td>
</tr>
<tr>
<td>intrasellar tumor remnant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-sided Fisher exact test</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*NA = not available (no digitalized data of preoperative images before 2009).
†No statistical significance (Student t-test).
‡Statistically significant difference (Fisher exact test).
Intraoperative MRI for transsphenoidal pituitary surgery

head coil, the first intraoperative imaging for neuronavigation was acquired. After that, T2-weighted turbo spin echo sequences in coronal and sagittal planes and T1-weighted spin echo sequences without contrast enhancement in identical planes were obtained. A preoperative contrast-enhanced coronal T1 image was fused to the above-mentioned sequences. The surgical approach was performed as described in the Methods section. Using neuronavigation despite several sphenoidal septae, orientation was unproblematic. The sellar floor was opened in typical fashion; however, no dissolved adenoma tissue was found. Tumor presented as a solid mass suggestive of a meningioma, but a fresh-frozen section nonetheless revealed an adenoma and microsurgical resection proceeded. Typical soft adenoma tissue was found in the dorso-lateral parts of the tumor. After resection, a lowering of the diaphragm and the solid pituitary tissue attached to it could be visualized. After inspection of the cavity no residual tumor was found. Subsequently we performed iMRI. The sequence protocol was used as described above, including a T1-weighted image with contrast enhancement (Fig. 4). Imaging revealed lowering of the diaphragm and an adequate decompression of the suprasellar compartment. However, in the right sellar region with proximity to the carotid artery a contrast-enhancing remnant was found. After the patient was positioned for surgery, the residual lesion was curetted and sent to pathology as a separate specimen. A final iMRI was performed and showed complete removal of the tumor (Fig. 5). Typical closure as described in the Methods section was performed.

Postoperatively the patient recovered without neurological deficits. A transient diabetes insipidus was treated with 2 doses of desmopressin. The final histopathological diagnosis was a gonadotropic adenoma in all specimens. The patient was discharged with routine substitution of

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional Op (%)</th>
<th>Op w/ iMRI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no benefit from op</td>
<td>2 (29)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>reduction of medication</td>
<td>0 (0)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>independent from medication</td>
<td>5 (71)</td>
<td>13 (65)</td>
</tr>
<tr>
<td>total</td>
<td>7 (100)</td>
<td>20 (100)</td>
</tr>
</tbody>
</table>

TABLE 6: Results of 6-month follow-up of functioning tumors in patients treated using TSS with or without iMRI

Fig. 2. Kaplan-Meier plot showing progression-free survival for the 30 months after primary surgery.

Fig. 3. Left: Preoperative MRI (sagittal contrast-enhanced T1 image) depicting an intrasellar pituitary adenoma with suprasellar extension. Right: Preoperative MRI (coronal contrast-enhanced T1 image) including the “objects” (see outlined areas) for adenoma and carotid artery created in the neuronavigation system.
hydrocortisone until the first endocrinological evaluation after 3 to 4 weeks. No signs of hypopituitarism were found during evaluation. At the first follow-up visit after 6 months the patient presented without symptoms. Ophthalmological and endocrinological assessment showed no deficits. On the 6-month follow-up MRI a complete removal was confirmed. The last follow-up was done after 1 year, and showed no recurrent disease (Fig. 6).

Discussion

High-field MRI is a unique tool in the hands of a neurosurgeon. In pituitary surgery it enables the surgeon to reliably visualize tumor remnants in the OR that could previously be detected only after several months.22 It helps us to display vascular structures at risk or demonstrates intraoperatively the level of decompression of the optic system.3,14 Beneficial results have been shown for the challenging resections of craniopharyngiomas and the detection of tumor residua in acromegaly.9,15 Many tertiary referral centers, meanwhile, have established iMRI mainly for routine use in glioma resection. This technique is therefore available to be applied in pituitary surgery too. This, however, raises the following question:

can we justify the routine use of the technique for pituitary surgery, or shall we use it for selected cases only? We therefore conducted a retrospective assessment of all conventional TSSs performed at our center in 2007 and 2008, and compared the results with those from the cases treated between 2009 and 2011 (after introduction of iMRI) to address the above-mentioned questions. Our report is the first comparative study between high-field iMRI-assisted and conventional TSS. We include the highest number of cases (143) in comparison with all previously published reports. A statistically significant benefit for extent of resection when using iMRI in comparison with a control cohort has not been shown before.

Patient Characteristics

Due to the sequential design of the study there is a selection bias between the cohorts. Results for age and sex distribution are balanced between both groups. However, the iMRI group had a higher share of parasellar tumors and hence a lower share of completely resectable lesions. The rate of previous TSS was higher in the iMRI group as well. We can conclude from these data that we have a negative selection bias in the iMRI group, which promotes more favorable results for all assessed items in the conventional group. This negative selection bias might be due to the fact that after introduction of iMRI at our center, primarily complex cases were treated with the help of the new technology. Not until the second half of 2011 were all TSSs performed routinely with iMRI. Introduction of iMRI made intraoperative neuronavigation readily available for all surgically treated cases. Surgical technique and postoperative management of disease were otherwise identical in both groups. In the conventional group, neuronavigation was only performed in selected cases (n = 4) with parasellar extension and recurrent disease. As Thomale et al.29 pointed out, many surgeons see the impact of neuronavigation without intraoperative updating of imaging findings only in a small number of patients. Thus the possible bias in our study due to the few cases in which intraoperative neuronavigation was used might be minute and rather reflects the typical application of the technique. Additionally, the opportunity to have an “updated” neuronavigation route readily available during
surgery is part of the concept of intraoperative imaging and might add to its benefits.

Even though a larger share of complex cases was found in the iMRI group, we see lower rates of residual tumor and higher rates of patients with improved vision after surgery. The proportion of patients requiring hormone replacement for hypopituitarism is slightly lower in the conventional surgery group. This finding as well as the higher rate of complications in the iMRI group might be due to the above-mentioned selection bias. In a detailed assessment of the complications described here, we see CSF leaks as the most common complication with iMRI. It is debatable if this is a side effect of the increased share of previous surgeries, the increased extent of resection, or the higher rates of parasellar tumors in this group. The major complication reported in the conventional group demonstrates a typical case of early bleeding that could have been detected with the use of iMRI before closure. Statistically no significant differences were found for postoperative hypopituitarism and peri- and postoperative complications in our study. For low-field iMRI, Berkmann et al.\(^2\) demonstrated no increase in postoperative hypopituitarism or complications, which was similar to our data. No publication exists so far comparing complication rates between high-field iMRI and conventional surgery.\(^4\)

**Surgical Time**

We have found a significant difference in OR time between the groups; the mean values were more than doubled in the iMRI group. Previously published data do not provide a direct comparison between conventional and iMRI OR times. Nimsky et al.\(^2\) report an interruption of surgical workflow for approximately 15 minutes per scan, but the mean OR times were not provided. Szerlip et al.\(^2\) published a mean duration of procedure of 166 minutes when using iMRI. These authors reported a similar share of parasellar tumors as that found in our series. Gerlach et al.\(^1\) compared conventional surgery versus low-field iMRI–guided surgery and found a significant increase of duration of surgery and anesthesia. The mean surgery time was 116 minutes, versus 78 minutes for conventional surgery. The rate of parasellar tumors was considerably lower in this series, which might explain the shorter OR times. The mean duration of conventional surgery without iMRI in our series is lower than the average time of 78–170 minutes published in the literature. This fact might influence the results as well as the high incidence of “complex” cases in the iMRI group. If the cases with parasellar tumor extension are excluded, no statistical significance for OR time can be found between the iMRI and conventional groups.

A comparison of the first 20 with the last 20 cases in the iMRI cohort excluded a significant difference of surgical time as well as complications, biochemical remission rates, and improvement of vision. This finding might be due to the fact that iMRI was mainly used for glioma surgery in the beginning. Thus, our surgical team might have completed the usual learning curve at the time of inception of iMRI-supported pituitary surgery.

**Rate of Resection**

**Intrasellar and Suprasellar Tumors.** The main goal of any type of intraoperative imaging in neurosurgery is to increase the rate of tumor resection. In our study we saw a higher proportion of total resections in the iMRI group. The results were not statistically significant because a total resection was intended in only 62% of cases. When we assessed only cases with intended total resection, we saw significantly higher resection rates in the iMRI group. To our knowledge, we provide the first report demonstrating a statistical benefit for resection rates in operations in which high-field iMRI is used. In our study resection rates were as high as 91% with the use of iMRI, in comparison with 73% in the conventional group. The report by Berkmann et al.\(^2\) demonstrated a benefit in resection rates when low-field iMRI was used; however, that study was limited by a small retrospective control cohort of only 30 patients. The published resection rates were 85% for low-field iMRI and 68% for the conventional group. Similar results were provided by Wu et al.,\(^2\) with a gross-total removal rate of 83% with the low-field technique. The resection rate in our study, which was determined using a 1.5-T MRI unit, is comparable to the results in 91.8% of cases in the Prague group, in which a 3-T device was used.\(^2\) Nimsky et al.\(^2\) published a resection rate of 82% in operations performed with the aid of intraoperative high-field (1.5-T) MRI.

Our report is the only high-field MRI study providing a control cohort; thus, comparability might be limited. Our actual data demonstrate a significant advantage of high-field iMRI in comparison with a conventional procedure, especially for “straightforward,” completely resectable tumors. Furthermore, compared with the literature, the results suggest higher resection rates with application of the high-field technique. No additional benefit to resection rates has been shown so far with the 3-T technique. However, more data are needed to evaluate this technique in greater detail. Similar resection rates of 91% for endocrine-inactive tumors were recently published by McLaughlin et al.\(^9\) after performing an endoscope-assisted transsphenoidal approach. An improved intrasellar visualization attained using an endoscopic technique might improve resection rates to a comparable extent as with high-field iMRI. To our knowledge, so far no study exists comparing microsurgical versus endoscopic or endoscope-assisted surgery directly. Schwartz et al.\(^27\) describe the combined use of a low-field iMRI and endoscope-assisted surgery, reporting complementary information from each imaging modality.

**Parasellar Tumors.** When we were establishing iMRI at our center, the patient group we thought would benefit most from intraoperative imaging did not comprise the above-mentioned “straightforward” cases, but the more complex giant adenomas with parasellar extension. The iMRI technique provides updates of navigation routes and crucial information about vascular structures at risk.\(^14\) To evaluate the impact of iMRI on the extent of resection in lesions with intended subtotal resection, we used a volumetric measurement and assessed the presence of intrasel-
lar tumor remnants. Our study is the only report at time of publication providing this type of detailed assessment of parasellar tumors. However, the data are limited by the relatively small number of cases in the subgroup, which might lead to a Type I error. Even a 50% smaller mean volume after surgery in the iMRI group showed no statistically significant difference on the Student t-test. Yet, intrasellar tumor remnants were found significantly less often in the iMRI group. In our opinion this finding best demonstrates the goal of a successful subtotal TSS.

Although intrasellar tumor remnants are not an issue for compression of the optic system, these residua represent resectable parts of the adenoma that might require repeated surgery. A limitation of the comparison is that preoperative imaging was available for volumetric measurements in only 2 patients in the conventional group. Thus, no information about individual extent of resection is provided in this group. The results might be biased by the presence of differing preoperative tumor sizes. As of this writing, there are no data provided in the literature concerning volumetric assessment of extent of resection in parasellar tumors. Our data suggest a benefit regarding extent of resection with iMRI in parasellar tumors and demonstrate significantly lower rates of intrasellar tumor remnants. To our knowledge no study exists providing comparable information about resection of parasellar tumors in operations in which iMRI was used. A limitation of assessing resection rates is that the observer was not blinded to type of surgery when determining residual or recurrent tumor.

**Progression-Free Survival**

Evaluation of progression-free survival is the most important factor in ultimately assessing the value of a new technique that provides higher resection rates. Unfortunately, due to the novelty of the technique no published data exist so far in this regard.

We assessed our patients' data concerning recurrence rates. Follow-up for the patients treated with the aid of iMRI is shorter, given the fact that we compared a cohort from 2007 and 2008 with a cohort from 2009 to 2011. We therefore calculated Kaplan-Meier plots for the first 30 months after surgery to make the cohorts comparable. The difference we found looks very beneficial for the use of iMRI, especially because a higher share of parasellar tumors is included in the iMRI cohort. The evaluation is limited by the relatively short follow-up. Even though a meta-analysis by Roelfsema et al. describes the peak for tumor recurrence as occurring between the 1st and 5th years after surgery, further follow-up for iMRI is needed to draw a final conclusion.

**Functioning Adenomas**

Functioning adenomas are a unique challenge in the field of pituitary surgery. Small tumor remnants can lead to persisting hormone excesses, making patients still dependent on medication after surgery. So far no distinctive visualization of microadenomas has been achieved with low-field iMRI; in particular, adenomas invading the cavernous sinus could not be detected. In our study population a higher share of functioning adenomas in the iMRI than in the conventional surgery group was present. The data suggest a slightly higher rate of biochemical remission in the conventional group in comparison with the iMRI group. The limitation of the comparison is the low number of cases in the conventional group and the heterogeneity of both groups. Size of adenoma and tumor extension as well as the pattern of hormone secretion considerably influence the prognosis of a complete biochemical remission. Remission rates of 74% have been published for microadenomas, whereas macroadenomas invading the cavernous sinus have cure rates as low as 39%–43%. Although the report of Fahrbusch et al. concerning the impact of high-field iMRI in acromegaly is very promising, no final conclusion concerning the benefit of biochemical cure rates with the use of iMRI can be drawn. Because our data are limited by the small subgroup of functioning adenomas in our cohorts, further studies are needed.

Our data support the routine use of high-field iMRI for pituitary surgery. Especially for the “straightforward” intra- and suprasellar nonfunctioning adenomas, we were able to demonstrate a significant benefit regarding total resection rates. The study is limited by its retrospective design and the absence of randomization. However, even with the negative selection bias of more complicated cases in the iMRI group, which favors positive results for the conventional group, preservation and improvement of vision was higher and no significant increase in complications or hypopituitarism was found. A possible bias in a retrospective control cohort might be the progress in surgical technique or medical treatment over time, which might lead to an improvement in patient outcome independently from iMRI usage. In our study we hope to have minimized this effect because all evaluated surgeons in our study were far beyond their learning curve and did not change their surgical technique after or during the introduction of iMRI at our center.

A disadvantage of the intraoperative resection control might be the increased OR time. Part of the data for iMRI cases was acquired right after introduction of the technique at our center; therefore, a learning curve might bias the results. Nevertheless, an experienced transsphenoidal surgeon might have his or her OR time almost doubled with iMRI. This is indeed an important issue to discuss, especially with regard to OR cost and hospital efficiency. In our opinion the benefit of a complete resection in more than 90% of cases without the need for a repeat surgery outweighs this argument significantly. In our series we have seen 11 cases of patients who had to have surgery for a recurrent tumor. All patients underwent conventional operations without the help of intraoperative imaging. Additionally, during the first 30 months, 9 patients in the conventional group and only 1 patient in the iMRI group had recurrent disease. In particular, we demonstrated that huge parasellar tumors have a significantly lower rate of intrasellar tumor remnant, which is the major goal in tumors that are only subtotaly resectable. This was achieved with similar rates of hypopituitarism. No data exist to date in this regard. Based on our experi-
Intraoperative MRI for transsphenoidal pituitary surgery

ence since 2009, we advocate the routine use of iMRI for pituitary surgery if available at the institution. Detailed studies are needed to evaluate the impact of iMRI for surgery in functioning adenomas. Our data as well as the few published papers addressing this topic suggest a benefit in regard to biochemical remission rates with use of iMRI. The data in our study support the benefit of high-field iMRI in comparison with the conventional microsurgical approach.

No endoscopic device was used in our series. Further studies are needed to evaluate resection rates and outcome in patients undergoing iMRI-assisted versus endoscopic TSS. Because many centers have established iMRI for resection control in glialoma surgery, often as two-or-more–room solutions, increased costs of iMRI in comparison with the endoscopy equipment, at least at these institutions, would not be such a big issue anymore. Both techniques seem to be beneficial for adenomas with supra- and parasellar extension. It would be interesting to compare the techniques with regard to small intrasellar lesions. No benefit was shown for using endoscopically guided in comparison with microsurgical resection for this entity. Systematic reviews and meta-analyses so far have shown no significant benefit for resection rates by using endoscopic surgery. Results for complication rates are heterogeneous. However, Ammirati et al. described a significantly higher rate of vascular complications when using the endoscopic technique in comparison with the conventional microsurgical approach. Intraoperative updates of neuronavigation routes and depiction of vascular structures are important advantages of high-field iMRI. However, to our knowledge at the time of this writing, no meta-analysis exists for the use of iMRI in TSS.

Most likely the combined use of endoscopy-assisted surgery and intraoperative resection control attained using iMRI could be the most favorable solution. Intraoperative MRI provides the possibility to “look behind” structures and not only “around the corner,” whereas an endoscope provides improved visualization during surgery and thus might prevent multiple iMRI scans in case of a residual tumor. We are in need of a large prospective randomized study to elucidate this issue.

Conclusions

The use of high-field iMRI leads to a significantly higher rate of complete resection in comparison with the conventional microsurgical transsphenoidal approach. In parasellar tumors a lower residual volume and a significantly lower rate of intrasellar lesion remnants were shown with the technique. Follow-up concerning recurrence rates so far is limited for iMRI; however, after 2 years Kaplan–Meier analyses show a distinctly lower rate in the iMRI group. No significant benefit of iMRI was found for biochemical remission rates and improvement of vision. Even though surgical time was longer with the addition of iMRI, it did not increase the complication rate significantly. We therefore recommend the routine use of high-field iMRI for pituitary surgery if this technology is available at a particular center.

Disclosure

Dr. König is a consultant for BrainLab. The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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References