Neurochirurgie 64 (2018) 155–160

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Original article

High-field intraoperative MRI in glioma surgery: A prospective study with volumetric analysis of extent of resection and functional outcome

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ARTICLE INFO

Article history:
Received 21 August 2017
Received in revised form 14 January 2018
Accepted 17 February 2018
Available online 10 May 2018

Keywords:
High-field intraoperative MRI
Low-grade glioma
Extent of resection
Functional outcome

ABSTRACT

Background. – High-field intraoperative MRI (IoMRI) is a useful tool to improve the extent of glioma resection (EOR).
Objective. – To compare the interest of 1.5 T IoMRI in glioma surgery between enhancing and non-enhancing tumors, based on volumetric analysis.
Methods. – A prospective single-center study included consecutive adult patients undergoing glioma surgery with IoMRI. Volumetric evaluation was based on FLAIR hypersignal after gadolinium injection in non-enhancing tumors and T1 hypersignal after gadolinium injection in enhancing tumors. Endpoints comprised: residual tumor volume (RTV), EOR, workflow and clinical outcome on Karnofsky performance score (KPS).
Results. – Fifty-three surgeries were performed from July 2014 to January 2016. Thirty-four patients underwent one IoMRI, and 19 two IoMRIs. In non-enhancing tumors, intraoperative RTV on 1st IoMRI T2/FLAIR was higher than in enhancing tumors on T1 sequences (7.25 cm^3 vs. 0.74 cm^3, respectively; $P = 0.008$), whereas the RTV on 2nd IoMRIs and final RTV were no longer significantly different. After IoMRI, 72% of patients underwent additional resection. In non-enhancing tumors, EOR increased from 77.3% on 1st IoMRI to 97.4% on last MRI ($P < 0.001$). Taking all tumors together, final RTV values were: median = 0 cm^3, mean = 3.9 cm^3. Mean final EOR was 94%. In 25% of patients, KPS was reduced during early postoperative course; at 3 and 6 months postoperatively, median KPS was 90.
Conclusion. – Intraoperative MRI guidance significantly enhanced the extent of glioma resection, especially for non- or minimally enhancing tumors, while preserving patient autonomy.

1. Introduction

The extent of resection (EOR) in glioma surgery plays a crucial role in prolonging patients' survival, for both de novo and recurrent tumors [1–3]. Optimal resection improves response to adjuvant treatment and enhances and prolongs quality of life [4,5].

The neurosurgeon faces three main obstacles to this goal of optimal resection. Firstly, it is difficult, even under microscopy, to distinguish the gross tumor boundaries between solid tumor tissue and infiltrated peritumoral brain tissue, especially in low-grade glioma (LGG). Secondly, there is a "brainshift" phenomenon, consisting in offset between neuronavigation images and reality, due to depletion of cerebrospinal fluid through the opening of the dura mater. Thirdly, the surgical approach has to take account of and respect surrounding functional areas.

Intraoperative MRI (IoMRI) helps to address these issues. It takes "brainshift" into account by updating neuronavigation data with intraoperative imaging. It also allows the surgeon to control the EOR at any time and to specify the location and volume of tumor remnants. From a functional point of view, diffusion tensor imaging (DTI: tractography) help to preserve motor or visual neurologic functions [6]. IoMRI was reported to significantly increase the extent of LGG and high-grade gliomas (HGG) resection, while preserving function [7–10].

Based on the Response Assessment in Neuro-Oncology (RANO) criteria, surgical goals differ between HGG and LGG [11]. In HGG, removal of all enhancing tumor is the primary goal of complete

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https://doi.org/10.1016/j.neuchi.2018.02.003
0028-3770/

resection, and not all FLAIR hyperintense tissue surrounding the enhancing tumor is typically resected. In LGG, the goal is to remove all detectable tumor tissue on T2/FLAIR sequences.

We report our experience using 1.5 T high-field IoMRI in glioma surgery for both contrast-enhancing and non-enhancing tumors. The objective was to assess the impact of IoMRI on glioma surgery in terms of EOR and functional outcome. We evaluated the surgical workflow and EOR on volumetric measurement and compared these results between enhancing and non-enhancing tumors.

2. Materials and methods

2.1. Patients

All patients undergoing glioma surgery using a high-field IoMRI platform from July 2014 to January 2016 were prospectively included. Inclusion criteria were: age > 18 years, histologic diagnosis of glioma, and comprehensive imaging data (pre-, intra- and postoperative MRI).

Preoperatively, a senior neurosurgeon assessed Karnofsky Performance Scores (KPS).

Patients were divided into 2 groups, with T2/FLAIR sequences for non-enhancing or minimally enhancing tumors and T1G+ sequences for strongly enhancing tumors.

Tumor location was categorized as left or right frontal, fronto-callosal, fronto-temporo-insular, temporal, parietal or occipital. The following brain areas were considered "eloquent": primary sensorimotor areas, supplementary motor areas, visual areas, language areas (dominant hemisphere fronto-opercular cortex and posterior temporal cortex, arcuate fasciculus, and inferior fronto-occipital fasciculus), limbic and paralimbic structures (including both insulae), and basal nuclei.

All patients harboring a lesion potentially close to language areas underwent preoperative functional MRI with language activation to identify the dominant hemisphere. Lesions in the language areas on the dominant side were preferentially treated under awake surgery rather than with IoMRI. Complementary DTI with fiber tracking (DTI-FB) was performed if necessary to specify the position of major neurological bundles (corticospinal tract, arcuate fasciculus, inferior fronto-occipital fasciculus, optical radiations). All patients had a recent preoperative MRI neuronavigation sequence, in most cases the day before surgery.

Postoperatively, control MRI was performed within 48 hours of surgery, and at 3 and 6 months. Functional outcome was assessed on KPS by a senior neurosurgeon at discharge and at 3 and 6 months. Definitive histologic subtypes were reviewed on the 2007 WHO classification by a senior neuropathologist.

2.2. Surgical procedures

All patients were operated on in our integrated imaging platform, with dedicated software (Brainlab®, Munich, Germany) and 1.5 Tesla MRI (General Electric®, Boston, MA) located in a room adjacent to the operative room. Thus, patients underwent surgery outside the 5-Gauss line, and normal instruments and a surgical microscope could be used. Patients were positioned using an MRI-compatible head-holder. Procedures were performed under general anesthesia. The imaging sequences used for neuronavigation were 3D T1 after gadolinium injection, or 3D FLAIR. The surgical microscope (OPMI Pentero® Zeiss, Germany) was connected to the imaging network and could be used for neuronavigation.

For enhanced tumors on gadolinium-injected T1 sequence, the resection goal was to remove all enhancing tumor. For non-enhanced tumors, in both suspected grades II and III, the goal was to remove all detectable tumor tissue on T2/FLAIR sequence. A second IoMRI scan was performed when the neuronavigation became insufficiently accurate and/or to assess the presence of residual tumor. The IoMRI images were used to update the navigation data after each control.

Ahead of MRI, a checklist was methodically filled out to ensure absence of metallic material in the surgical site that could interfere with the magnetic field. For IoMRI, after sterile draping, the patient transferred to the MRI scanner. IoMRI systematically included a volumetric 3D T1 sequence to readjust neuronavigation. Additional sequences, such as 3D FLAIR (especially for LGG), DTI (B1000 and ADC) or T2 with gradient echo could also be performed. Intraoperative tractography was performed for gliomas close to functional areas (e.g., corticospinal tract). Neuronavigation updating used the automatic coregistration provided by the Brainlab® software, with quality and accuracy double-checked by an imaging engineer and the senior neurosurgeon.

2.3. Volumetric analysis

Two independent observers (radiologist and senior neurosurgeon) measured pre-, intra- and post-operative glioma volumes, using the "Tumor tracking" module of the IntelliSpace Portal package (Philips®, Amsterdam, Netherlands). Lesions showing no or slight contrast enhancement after gadolinium injection were contoured using the T2/FLAIR hypersignal. High-uptake tumors were segmented using the T1 hypersignal after gadolinium injection (T1G+). After segmentation, volumes were calculated in cubic centimeters. In case of > 10% discrepancy between the 2 observers, both segmentations were compared so as to obtain a consensus volume. EOR was reported as percentage: (preoperative tumor volume – postoperative tumor volume)/preoperative tumor volume.

2.4. Statistical analysis

Statistical analyses were performed by our institutional biostatistics department. Qualitative variables were expressed as numbers (percentage), and quantitative variables as median (interquartile range [IQR]). Distribution normality was assessed using histograms and Shapiro-Wilk test. Inter-group comparisons (T2/FLAIR vs. T1G+) used Mann-Whitney U-test for quantitative variables and chi-square test for qualitative variables. To study the impact of the number of IoMRI controls on postoperative tumor volume, non-parametric analysis of covariance was performed, adjusting on the baseline parameters: preoperative volume, de novo tumor or recurrence, and eloquent area. KPS was compared between the various postoperative time-points and the preoperative value, on Wilcoxon signed-rank test. Tests were 2-tailed, with $\alpha = 0.05$, using the SAS software package, release 9.3 (SAS Institute, Cary, NC).

3. Results

3.1. Key-points

In this series of 53 gliomas, 34 non-enhancing or minimally enhancing tumors (T2/FLAIR group) and 19 enhancing tumors (T1G+ group) underwent at least one IoMRI. On first IoMRI, median RTV was 3.01 cm^3. Additional resections were then performed in 38 patients (72%), improving the EOR by 13.9%. Nineteen patients (36%) underwent a 2nd IoMRI, which further improved the EOR by 4.8%. On the last MRI, final median RTV dropped to 0 cm^3 ($P < 0.001$). Taking all tumors together, median EOR increased from 82% on 1st IoMRI to 100% on final control ($P < 0.001$). There was no significant difference in EOR between de novo and recurrent glioma. T2/FLAIR group glioma showed greater benefit from IoMRI: median

Table 1
Anatomical distribution of operated tumors, according to hemisphere. EA: tumors close to eloquent area.

Lesion location	Hemisphere				Total
	Right	EA	Left	EA	
Frontal	9	2	9	5	18
Fronto-callosal	2	2	1	1	3
Fronto-temporo-Insular	11	11	1	1	12
Temporal	6	1	7	2	13
Parietal	4	1	2	1	6
Occipital	1	0	0	0	1
Total	33	(17)	20	(10)	53

RTV = 7.25 cm^3 on 1st IoMRI and 1.03 cm^3 on last MRI, while EOR increased from 77.3 to 97.4% between 1st and last MRI ($P < 0.001$).

Functionally, KPS was lower at discharge for 13 patients (25%), while median postoperative KPS at 3 and 6 months was 90.

3.2. Population data

Fifty-three patients were included: 34 men, 19 women; M/F sex ratio = 1.8. Median age at diagnosis was 45 years (range, 24–72 years). Forty-four patients (83%) were right-handed, 6 left-handed and 3 ambidextrous. Forty-nine patients (92%) had KPS $\geq$ 80 at diagnosis. The most common diagnostic presentations were: seizures in 33 patients (62%), headache in 10 (19%), radiological progression of previous tumor in 10 (19%), motor or sensory deficits in 8 (15%), and phasic disorder in 5 (9%). Median hospital stay was 8 days (IQR, 7–9 days).

Thirty-three patients (62%) presented with de novo tumor, and 20 (38%) with recurrent tumor: 7 (35%) WHO grade II oligodendrogliomas, 6 (30%) grade II oligoastrocytomas, 6 (30%) grade IV glioblastomas and 1 (5%) grade III malignant glioneuronal tumor.

Anatomical distribution is reported in Table 1: frontal in 18 patients (34%), temporal in 13 (24%) and fronto-temporo-insular in 12 (23%). Thirty-four patients (64%) underwent preoperative functional MRI and/or DTI. Twenty-seven patients (51%) had a lesion close to an eloquent area (e.g., language or primary motor areas) on functional MRI and/or DTI.

On preoperative MRI, 34 tumors (64%) were contoured on T2/FLAIR and 19 (36%) on T1G+ sequences.

Two patients with very large lesions, for which the surgical objective was debulking, were not included for statistical analysis.

3.3. Operative data

All patients had at least one IoMRI. No technical incidents were reported. However, accuracy was not immediately satisfactory after automatic neuronavigation updating in the light of IoMRI, and was optimized in most cases by changing the location of the operating fields, as accuracy was impaired if there were too many fields between star tracking and mounting base, or by renewing the computer registration procedure. Median duration of 1st IoMRI control (including patient transfer) was 38 minutes (IQR, 30–46 min). Nineteen patients (36%) underwent a 2nd IoMRI, with a median duration of 26 minutes (IQR, 18–30 min). None had more than 2 IoMRIs. Median total operative time was 4 hours 25 min (IQR, 4 h 02 min to 5 h 37 min).

There was no significant difference between the T2/FLAIR and T1G+ groups in median duration of each IoMRI (1st control: $P = 0.06$; 2nd: $P = 0.76$), number of IoMRIs ($P = 0.74$), or median duration of surgery ($P = 0.42$).

Table 2
Final EOR per group: T2/FLAIR and T1G+.

	T1G+ (%)	T2/FLAIR (%)	*P* value	Total (%)
EOR > 90%	18 (95)	25 (74)	0.07	43 (81)
EOR > 98%	14 (74)	17 (50)	0.09	31 (58)
EOR = 100%	12 (58)	16 (47)	0.26	28 (53)

3.4. Outcome data: volumetrics

IoMRI helped to reduce median RTV from 3.1 cm^3 at 1st IoMRI to 0 cm^3 on the final control ($P < 0.001$). Number of IoMRIs was not significantly associated with RTV, for all tumors taken together ($P = 0.5$), or for the T2/FLAIR ($P = 0.68$) or T1G+ groups ($P = 0.24$).

Median EOR improved from 82% at 1st IoMRI to 100% at last control ($P < 0.001$). Mean final EOR was 94% (SD = 10).

Taking all patients together, resection was complete in 28 cases (53%), > 98% in 31 (58%) and > 90% in 43 (81%) (Table 2). Twenty-six of the 33 patients with contrast-enhancing tumors (78.8%) had complete resection of the contrast enhancement. A tumor remnant in the corpus callosum was found in 100% of fronto-callosal tumors. In fronto-temporo-insular tumors, a remnant was found in nearly 90% of cases, often in the posterior insula or medial temporal lobe.

There was no significant difference in EOR between de novo and recurrent gliomas ($P = 0.45$).

3.5. Additional resection after IoMRI controls

The procedural flow-chart is shown in Fig. 1. After the first IoMRI, no additional resection was performed in 15 patients (28%) (7 T2/FLAIR and 8 T1G +), due to initial complete tumor removal.

On the other hand, 38 patients (72%) (27 T2/FLAIR and 11 T1G +) underwent at least one additional resection. At the time of the first IoMRI, these patients had significantly higher median RTV (7.3 cm^3 (IQR, 2.9–19.4 cm^3); $P < 0.001$) and lower EOR (74.6% (IQR, 66.6–86.2%); $P < 0.001$) than the 15 patients without additional resection.

For the 30 patients who had only 1 IoMRI with 1 additional resection, median improvement in EOR was 13.9% (IQR, 7.7–26.9%).

Nineteen patients (36%) had a second IoMRI control. Eight (42%) underwent additional resection (7 T2/FLAIR and 1 T1G+). For the 11 other patients, the surgeon decided not to perform a 2nd resection, considering primary resection to be maximal (e.g., contact with eloquent areas).

For T2/FLAIR tumors, 2nd IoMRI led to 7 additional resections out of 13 patients (54%). For T1G+ tumors, 2nd IoMRI led to 1 additional resection out of 6 patients (16%). Second IoMRI improved median EOR by 4.8% (IQR, 2.7–8%) for all these tumors.

EOR in the T2/FLAIR group increased from 77.3% at 1st control to 97.4% at last MRI ($P < 0.001$). For T1G+ tumors, gain was less than 3%.

3.6. Postoperative outcome

3.6.1. Functional evaluation

Median KPS was 90 (range, 50–100) preoperatively, 80 (range, 30–100) at the early postoperative stage, 90 (range, 20–100) at 3 months and 90 (range, 0–100) at 6 months. Early postoperative, 3 month and 6 month KPS were significantly lower than preoperatively (respectively, $P < 0.0001$, $P = 0.0184$ and $P = 0.0475$). The percentage of patients with KPS < 80 was 7.6% (4/53) preoperatively, 32.1% (17/53) at the early postoperative stage, 15.1% (8/53) at 3 months and 13.2% (7/53) at 6 months.

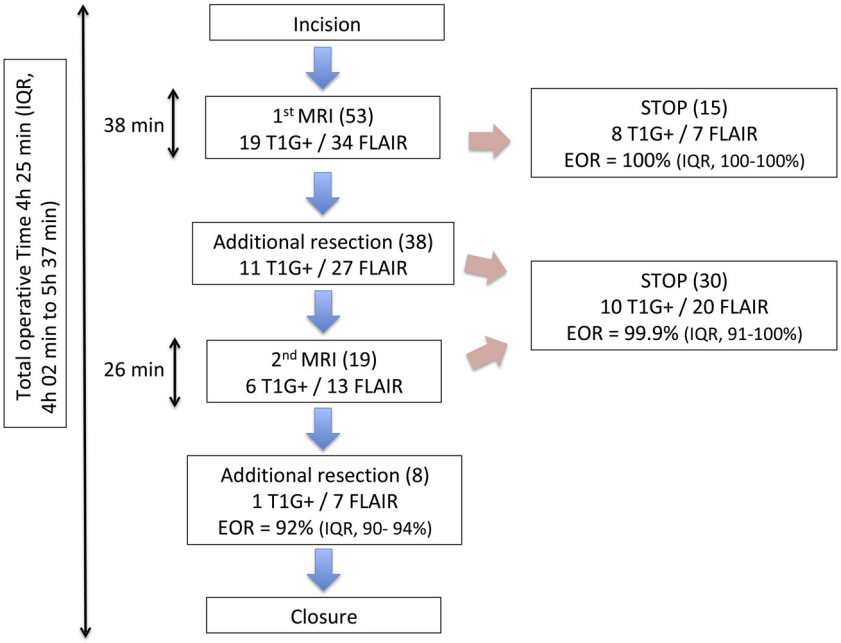

Fig. 1. Procedural flowchart. Numbers between brackets correspond to the number of patients at each step of the intervention. EOR: extent of resection, IQR: interquartile range.

3.6.2. Morbidity/mortality

Thirteen patients (25%) showed decreased KPS (< 80) during the early postoperative course, indicating a need for assistance, however minimal, in daily life. The main complication was onset or increase of motor deficit in 12 patients (23%), followed by phasic disorder in 8 (15%) and visual field impairment in 8 (15%). Six patients (11%) had supplementary motor area syndrome, with full motor and phasic recovery at discharge.

At 3 months, phasic disorder and motor deficit had completely resolved, except for 1 case of moderate persistent central facial paralysis. Three patients (6%) showed behavioral change, with apragmatism or disinhibition related to surgery of the frontal or temporal lobe. Campimetric impairments persisted for 6 patients (11%). Overall, permanent morbidity at 3 months was 17%. One patient had late infection requiring removal of the craniotomy flap. There were no cases of compressive hematoma in the operative cavity. One patient with recurrent glioblastoma died during the 6 months after IoMRI-guided surgery, due to disease progression.

4. Discussion

4.1. Surgical procedure workflow

Median surgery time from skin incision to closure was 4 hours 25 min, consistent with the time reported by Senft (4 hours 10 min) [7] and shorter than for Mohammadi (6 hours 40 min, including anesthesia induction time and initial recovery) [9]. There was no difference in surgery time between the T2/FLAIR and T1G+ groups. IoMRI lengthened surgery by at least 1 hour in comparison with classic neuronavigation [12]. In the present study, 1st IoMRI was longer than 2nd, due to acquisition of contrast-enhanced sequences during 1st IoMRI. First and second imaging time varied over 15 min between interventions. Standardization of the MRI protocol according to type of tumor (low or high grade) could improve the relevance of the data obtained [13]. There was no difference in number of IoMRIs between the T2/FLAIR and T1G+ groups.

Additional resections were performed in 72% of cases, in most cases for non-enhancing (FLAIR) lesions. Our practice is in line with other experienced centers using IoMRI [14]. In most cases, additional resection was planned from the outset, in a strategy we called “strategic residual tumor”, to avoid functional impairment, as mentioned in the Morbidity section below.

In the present series, 9 senior neurosurgeons with various levels of neuro-oncological experience performed the 53 procedures. Some aimed for maximal tumor resection and then performed the first IoMRI, whereas others performed IoMRI much earlier in resection. Khan et al. reported a difference in survival and hospital stay according to the neuro-oncological experience of the main operator [15]. EOR is also influenced by the surgeon’s experience. Even in experienced neuro-oncological surgeons, surgical aggressiveness varies, as recently reported by Sonabend et al. [16]. In the present study, despite the varying operator experience, IoMRI enabled very high and reproducible EOR values.

4.2. Volumetrics

In the present series, the median preoperative tumor volume of 26.3 cm^3 was similar to previous reports (Mohammadi et al.: 20.1 cm^3, Kuhnt et al.: 27.82 cm^3) [9,17]. IoMRI controls reduced the median RTV from 3.1 cm^3 to 0 cm^3 ($P < 0.001$). Median EOR increased from 82 to 100% ($P < 0.001$) between 1st and last MRI. These results highlight the role of IoMRI in glioma surgery to optimize EOR, as previously reported (Ius: 87.5% [18], Mohammadi: 99.4% [9], Senft: 100% [7]).

Taking all tumors together, 58% of patients had > 98% and 81% > 90% resection, in line with previous reports with IoMRI [17,19]. For strongly enhancing tumors contoured in T1G+ (glioblastomas in a vast majority), 74% of patients had > 98% resection, and 100% had > 78% resection, the threshold reported by Sanai et al. as increasing overall survival in patients with glioblastoma [3].

Non- or minimally enhancing tumors (mainly LGG) benefited more from IoMRI [20]. On 1st IoMRI, their median RTV was 7.25 cm^3, dropping to 1.03 cm^3 on final control: i.e., 86% tumor volume reduction. Using IoMRI, intraoperative EOR was greater for non- or minimally enhancing gliomas than for enhancing tumors (mostly HGGs), although the difference was non-significant at end of surgery ($P = 0.095$) (Table 3). Only one previous study with

Table 3
Median RTV in cm^3, and median EOR in percentage per IoMRI and T1G+ and T2FLAIR group. Total: median value for each parameter for the whole cohort (53 patients).

	T1G+	T2/FLAIR	*P* value	Total
Preop. Volume	14.9 Range, 3.2–251	37.46 Range, 1.4–199	0.07	26.3
1st IoMRI				
RTV	0.74	7.25	0.008	3.1
EOR	97.6	77.3	0.017	82
2nd IoMRI				
RTV	0.33	6.97	0.047	4.44
EOR	99.35	84.9	0.07	89.6
Postop. MRI				
RTV	0 Range, 0–15.9	1.03 Range, 0–124	0.086	0
EOR	100	97.35	0.095	100

volumetric data reported such results [9]. High-definition intraoperative imaging has changed preoperative planning completely. In the present study, we did not aim at maximal resection in one step before the first IoMRI, but rather performed staged surgery, with iterative IoMRI when neuronavigation became less accurate or when the surgeon was approaching an eloquent area or still had a doubt concerning a possible tumor remnant. We described above the concept of strategic residual tumor to ensure safe and accurate resection by means of navigation updates.

Two tumor locations were associated with high risk of residual tumor: fronto-callosal and fronto-temporo-insular gliomas. In fronto-callosal glioma, the probability of residual tumor was 100%. Dissection of the corpus callosum remains controversial. A patient with partial infiltration of the rostrum of the corpus callosum may benefit from complete resection when the ipsilateral frontal pole is also resected; however, when infiltration clearly crosses the midline, complete resection is not indicated.

Regarding the number of surgical revisions after IoMRI checks, it was paradoxically found that tumors with 2 IoMRIs and 2 additional resections showed the lowest final EORs, at 92.4%. These tumors were exclusively in the T2/FLAIR group and all located in fronto-temporo-insular area, which explained the lower EOR rate, although this was still better than for fronto-temporo-insular gliomas without IoMRI as previously reported [21,22].

Surgery of recurrent tumor, which previously consisted in surgical resection with radiotherapy or chemotherapy, remains challenging due to the difficulty of determining lesion boundaries. Using IoMRI, EOR did not significantly differ between de novo and recurrent glioma.

4.3. Morbidity

During the early postoperative course, 13 patients (25%) experienced clinical deterioration, with KPS < 80, mainly implicating motor deficits (hemiparesis), phasic disorders (loss of verbal expression: aphemia) and visual field impairment (homonymous hemianopia). Half of the motor deficits and phasic disorders were involved in a supplementary motor area (SMA) syndrome, which promptly resolved during hospital stay. At 3 months, overall morbidity was 17%. In previous reports, the rate of new or worsened deficits (mainly motor and phasic) in IoMRI-guided surgery ranged from 10% [7,9] to 28% [23] during the early postoperative period. Concerning these early deficits, many techniques (e.g., fluorescence-guided surgery, awake surgery) aiming at enhancing EOR have been reported to increase the rate of deficits, most of which were transient [24–27]. In the present study, the high rate of deficits can be explained by the large number of frontal lesions, including recurrences, close to the SMA [28]. The infection rate was lower than previously reported and similar that for procedures without IoMRI [12]. There were no hemorrhagic complications.

At 3 months postoperatively, there was clear improvement in KPS was reported compared to the early postoperative course. There were no persistent motor deficits except for 1 case of moderate central facial paralysis. At 6 months, median KPS remained stable, taking account of disease progression and adjuvant therapies, especially in HGG patients: the lower quartile reached 0; 1 patient died at 6 months from a 2nd recurrence of glioblastoma multiforme.

In the present study, IoMRI-guided surgery did not increase the number of permanent neurological deficits, even including patients harboring tumors close to eloquent areas. In our experience, using the concept of staged volume surgery with strategic residual tumor helped improve patients' outcomes. Median KPS was still 90 at 3 and 6 months after surgery.

4.4. Limits

The present series included different tumor grades (WHO grades I to IV) and various anatomical locations. Among our 53 patients, there were 2 cases of very large preoperative tumor volume (250 and 199 cm^3, compared to a study median of 26.3 cm^3), in which the surgical objective was tumor debulking, given the mass effect on the brainstem. These 2 patients (1 grade II oligoastrocytoma, and 1 glioblastoma) showed significantly higher RTV than the other patients (30 and 124 cm^3), and were excluded from the statistical analyses. These findings raise the question of the interest of IoMRI in large tumors for which complete resection is not the objective. In our experience, IoMRI may still have an interest in these surgeries, to maximize EOR and especially to enhance safety operative for the surgeon. Brainshift was maximal in these cases of large tumor volume dissection. Neuronavigation updating in this context ensures better surgical safety, especially when eloquent areas are near [10].

We did not analyze the impact of IoMRI on overall (OS) or progression-free survival (PFS). Follow-up was too short and samples too small for appropriate statistical analysis. However, benefit for OS and PFS of gross total resection for gliomas was reported elsewhere [2,18,20,29–31].

In the present series, fluorescence-guided resection (FGR) for HGGs was not associated to IoMRI. We did not want to add an additional bias between LGGs and HGGs. Thanks to IoMRI, EOR was equivalent to or better than FGR alone for HGGs [32,33].

A further study will implement intraoperative direct electrical stimulation mapping in awake patients associated to IoMRI to combine image-guided and functional-guided surgery to optimize patient outcome [34].

5. Conclusion

IoMRI-guided surgery significantly enhanced the EOR of gliomas, especially for non- or minimally enhancing tumors (mainly LGG). IoMRI led to additional resection in 72% of cases, increasing EOR by almost 20%. Median EOR was 100% (mean 94%). Such high EOR values were achieved regardless of tumor type (de novo or recurrent), location (including tumors close to eloquent areas, and fronto-temporo-insular gliomas) or even the surgeon (9 different senior surgeons). Thus, IoMRI ensures a high standard of care for patients harboring gliomas. This use of IoMRI introduced the concept of "staged volume" surgery with "strategic residual tumor". This strategy was safe and effective, with acceptable morbidity.

Ethical statement

Ethical approval: all procedures performed in studies involving human participants were in accordance with the ethical standards

of the institutional and/or national review boards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent: informed consent was obtained from all individual participants included in the study.

Disclosure of interest

The authors declare that they have no competing interest.

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