Real Impact of Intraoperative Magnetic Resonance Imaging in Newly Diagnosed Glioblastoma Multiforme Resection: An Observational Analytic Cohort Study From a Single Surgeon Experience

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■ BACKGROUND: **The goal of surgery for brain glioma is to maximize the extent of tumor resection, avoiding postoperative functional impairment. Intraoperative (Io) magnetic resonance imaging (MRI) has emerged as an effective tool to guide a safer glioma resection. The objective of this study is to assess the real impact of Io MRI in O-6-methylguanine-DNA methyltransferase and non-O-6-methylguanine-DNA methyltransferase methylated glioma surgery.**

■ METHODS: **A total of 129 patients suffering glioblastoma who underwent craniotomy for tumor resection were retrospectively evaluated between March 2009 and January 2017 at 2 different affiliated hospitals of the same university. We compared a subgroup of 65 patients operated on without Io MRI (group A) with a second subgroup of 64 patients who underwent surgery with the aid of Io MRI (group B). Volumetric analyses of the extent of resection (EOR) were performed using gadolinium-enhanced T1-weighted imaging. All surgical procedures were performed by a single surgeon (the senior author).**

■ RESULTS: **The average EOR increased from 86.23% ± 10.51% for group A to 94.01% ± 7.42% in patients included in group B. The secondary end points of this study were progression-free survival (PFS) and overall survival (OS). PFS was found to be 5.38 ± 2.32 months for group A versus 7.89 ± 2.75 months for group B. Regarding OS, the average value was 13.38 ± 4.06 months for group A versus 16.43 ± 3.41 months for group B.**

■ CONCLUSIONS: **We can affirm that 1.5-T Io MRI is a safe and effective technique, and its use optimizes significantly both the extent of glioma resection and the survival of patients.**

INTRODUCTION

Background and Rationale

The target of glioma surgery is to improve overall survival (OS) while maximizing the extent of resection (EOR) of the tumor and avoiding postoperative neurologic morbidity.[1-5] Preservation of function predicts quality of life, eligibility for adjuvant therapies, and OS.[2,5] Intraoperative (Io) magnetic resonance imaging (MRI) has been shown to be useful in maximizing the EOR.[6-8]

The main reasons for performing a glioma resection with the aid of Io MRI are the Io resection assessment and brain shift control.[7-10] Io MRI notably enhances neuronavigation accuracy and provides precise and dynamic imaging.[7-9,11] Additionally, we currently know that glioblastoma multiforme (GBM) is in any case a highly malignant brain tumor,[12] but it is not a single entity. The role of O-6-methylguanine-DNA methyltransferase (MGMT) methylation status on response to temozolomide and subsequently on survival, has been investigated and demonstrated[13]; however, the impact of Io MRI on the differential molecular pattern remains somewhat unexplored and deserves specific mention.

Key words
- EOR
- Glioblastoma
- Intraoperative MRI
- Overall survival
- PFS

Abbreviations and Acronyms
EOR: Extent of resection
GBM: Glioblastoma multiforme
GTR: Gross total resection
Io: Intraoperative
MGMT: O-6-methylguanine-DNA methyltransferase
MRI: Magnetic resonance imaging
OS: Overall survival
PFS: Progression-free survival

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Objectives

To our knowledge, this is the first single surgeon study describing and quantifying the exquisite effect of Io MRI on EOR, OS, and progression-free survival (PFS) according to the weight of MGMT methylation on such parameters. Therefore, the aim of this work is to retrospectively review and compare 2 subsets of patients suffering from GBM operated on by the same surgeon, with or without the aid of an Io MRI system.

MATERIALS AND METHODS

Study Design and Setting

We report a retrospective analysis of surgical (EOR) and oncologic results (PFS and OS) of patients affected by GBM who underwent surgical resection by the senior author in the period ranging between March 2009 and January 2017. All patients were operated on in 2 different neurosurgical departments affiliated with the same university: one is equipped with an Io MRI operative theater and the other has a standard operative theater. The use of Io MRI was not randomized. The resulting design of the study is a retrospective observational cohort study in which the data analyzed were collected by 2 independent researchers, who were blinded to the objective and design of the study. This team, when reviewing the radiologic data, was not blind to the use/not use of Io MRI, but was completely blind to the purpose of this investigation.

Patient data (age, sex, tumor location, Karnofsky Performance Status, neurologic status pre- and postsurgery, and pre- and postoperative tumor volume) and MGMT methylation status were recorded.

Participants and Eligibility

For the initial GBM patient cohort, we applied the following inclusion criteria:

1) A preoperative Karnofsky Performance Status score >70% was necessary.
2) We included only patients presenting with an American Society of Anesthesiologists score between II and III.
3) All patients suffered from GBM (according to the World Health Organization[12]).
4) The patients were included only if a successful complete Stupp protocol[13] was applied.
5) All patients received standard conformational planning with a linear accelerator, and no stereotactic radiosurgical treatment was performed.
6) Once the progression of the disease was noticed, the patient and the relevant imaging were referred again to our attention to evaluate the feasibility of a second surgery or to address the patient to a second line of adjuvant treatment.
7) The estimated target of the surgical procedure was the total or subtotal resection of the lesions, and no biopsies were included.
8) All patients included in the study were newly diagnosed with GBM at their first surgery; operating on recurrences makes a complete difference.[14]
9) Patients were excluded for incomplete or wrong data on clinical, radiologic, and surgical records and/or lost to follow-up.

A total of 129 patients matched the inclusion and exclusion criteria and their clinical records were retrospectively reevaluated for this study: 65 patients were in group A (conventional microsurgical resection), whereas 64 were in group B (Io MRI–aided microsurgical resection).

All patients included underwent a preoperative brain MRI scan including a high-field 1.5-T volumetric study with the following sequences: T2-weighted imaging, fluid attenuated inverse recovery, and isotropic volumetric T1-weighted magnetization-prepared rapid acquisition gradient echo before and after intravenous administration of paramagnetic contrast agent. Diffusion tensor imaging sequences with 3-dimensional tractography and functional MRI completed our protocol for gliomas affecting eloquent locations.[7,8]

All procedures for group B (Io MRI–aided) were performed in BrainSuite (Feldkirchen, Germany). Patient heads were placed in a magnetic resonance head coil frame, with integrated fiducials that were preoperatively recognized by a frame-based neuronavigation system (VectorVision [BrainLAB AG, Feldkichen, Germany]) (Figure 1). A dedicated pointer equipped with fiducials was recognized by the neuronavigator and used to identify the lesion and localize the proper skin incision.

After dural opening, we acquired an Io volumetric MRI for neuronavigation to correct the potential brain shift in about 15 minutes of total acquisition and average processing time.[1,8] BrainSuite has an integrated operative microscope (NC4 Multivision [Zeiss, Oberkochen, Germany]). At the end of the procedure, the last MRI was performed in all cases to verify the complete resection or the presence of residual tumor that needed further resection.

All procedures for group A (conventional resection) were performed with an infrared-based neuronavigator (Stealth III [Medtronic, Minneapolis, Minnesota, USA]), in a standard neurosurgical theater, with a standard operative microscope (OPMI/NC4 [Zeiss]). On the first postoperative day, patients underwent volumetric brain MRI scan to evaluate the EOR.

Because surgery in BrainSuite is performed outside the 5-G line, for both subgroups all the ordinary surgical and microsurgical instruments were used.

For both subgroups, a standard total intravenous anesthesia protocol with propofol (1 mg/kg) and remifentanil (0.5 μg/kg/min) was used. If Io neuromonitoring of the motor pathway was performed, no muscle relaxants were administered. For patients operated on in BrainSuite, an MRI-compatible respirator and an anesthesia care monitor were provided. Io monitoring methodology and Io MRI compatible devices have been previously reported elsewhere.[9]

We used a functional neuronavigation approach combined with Io neuromonitoring.

The necessity of further resections after a first Io MRI was recorded.

In general, both with or without Io MRI, it was intraoperatively judged necessary to stop tumor excision when 1) white matter appeared free of disease in any aspect of the surgical cavity; 2) despite a directly visualized or Io MRI–proven remnant,

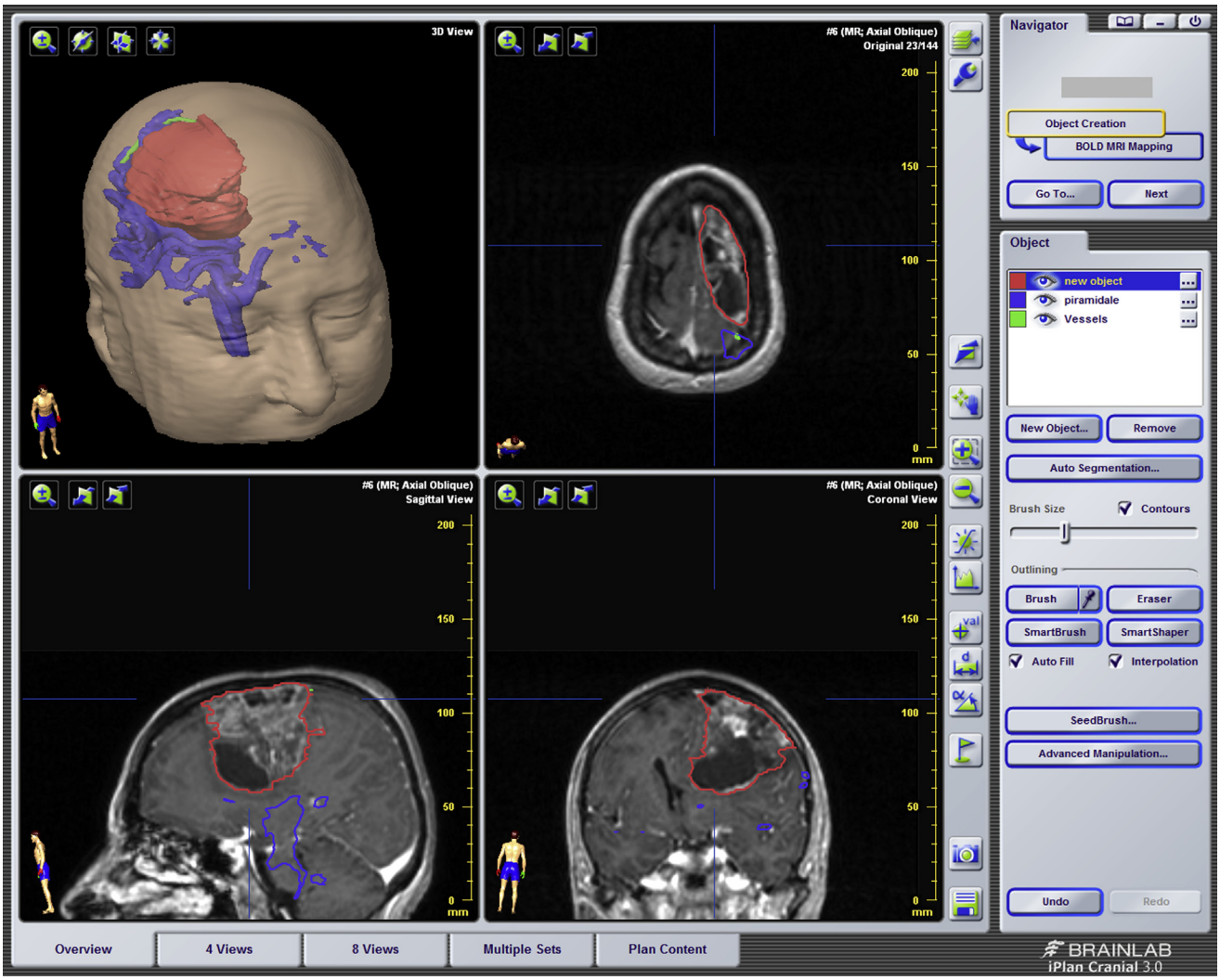

Figure 1. Intraoperative neuronavigation image.

neuromonitoring outlined a risk for postoperative motor morbidity; and 3) Io MRI (for patients treated with the aid of Io-MRI) showed gross total resection (GTR) of the contrast-enhancing lesion.

Data Sources and Quantitative Variables

The EOR was determined by a team of independent researchers, blinded to the objective of the study, through a comparison between the magnetic resonance images obtained before surgery and the last postsurgical Io MRI (group B) or the first MRI after surgery (group A). The EOR was calculated on the ground of a manual segmentation of the tumor outline in the planning software. The GTR was defined as a confirmed reduction of the preoperative volume of the tumor of at least 95%.

In case of GTR, tumor progression was defined as the first MRI scan demonstrating the presence of pathologically enhancing tissue characterized by an MRI pattern (relying mostly on perfusion weighted imaging) inconsistent with a cerebral radiation injury (which is in fact a pseudoprogression[15]). In case of incomplete resections (<95% volume reduction) a volumetric increase of the residual disease detected at the first postoperative MRI scan was considered as disease progression.

A close range—dedicated neuroimaging follow-up program was routinely performed in both institutions. This program included the following: 1) a standard early (maximum 24 hours after surgery) postoperative volumetric brain MRI (for group A) or the last Io volumetric MRI (for group B); 2) at approximately 1 month from surgery (25–35 days), a volumetric brain MRI scan was repeated for a first step follow-up control and to provide information for the radiation treatment planning; and 3) after the end of irradiation, a volumetric brain MRI scan was performed every 3 months.

Table 1. Patient Demographics (N = 129)

Demographic	Group B (Io MRI) (n = 64)	Group A (Non–Io MRI) (n = 65)	*P* Value
Sex	Male: 35 (54.7)	Male: 33 (50.8)	
	Female: 29 (45.3)	Female: 32 (49.2)	
Age, years	56.61 ± 10.49	57.56 ± 13.52	
KPS score at admission	Mean 86.4% (range: 70–100)	Mean 87.1% (range: 70–100)	NS
Volume, cm^3	26.8 ± 11.3	27.4 ± 10.9	NS
MGMT methylated	16 (25.0)	15 (23.1)	NS
EOR, %	94.01 ± 7.42	86.23 ± 10.51	0.005
GTR (>95% reduction)	43 (67.2); further resection after a first procedure for 38 (59.37)	28 (43.1)	0.001
PFS at 6 months	50 (78.12)	32 (49.23)	0.001
PFS, months	7.89 ± 2.75	5.38 ± 2.32	0.001
OS, months	16.43 ± 3.41	13.38 ± 4.06	0.001
Location	Frontal: 27 (42.2)	Frontal: 29 (44.6)	
	Temporal: 15 (23.4)	Temporal: 17 (26.1)	
	Occipital: 9 (14.1)	Occipital: 7 (10.8)	
	Parietal: 8 (12.5)	Parietal: 9 (13.8)	
	Insular: 5 (7.8)	Insular: 3 (4.6)	
Eloquence of location, according to function	Noneloquent location: 32 (50.0)	Noneloquent location: 33 (50.7)	
	Motor (CST): 17 (26.6)	Motor (CST): 15 (23.1)	
	Visual (OR): 4 (6.3)	Visual (OR): 5 (7.7)	
	Speech (AF/UNC/IFOF): 11 (17.2)	Speech (AF/UNC/IFOF): 12 (18.5)	

Values are number of participants (%), mean ± SD, or as otherwise indicated.
Io, Intraoperative; MRI, magnetic resonance imaging; KPS, Karnofsky Performance Status; NS, not significant; EOR, extent of resection; GTR, gross total resection; PFS, progression-free survival; OS, overall survival; CST, corticospinal tract, OR, optic radiation; AF, arcuate fasciculus; UNC, uncinate fasciculus; IFOF, inferior fronto-occipital fasciculus; MGMT, O-6-methylguanine-DNA methyltransferase.

Generally, the treatment was considered to be stopped when disease showed volumetric progression despite the second line of adjuvant treatment. Both subgroups received a surgical and adjuvant treatment with 1) the same operative microscope, 2) a similar infrared-based neuronavigation system, 3) similar microsurgical instruments, 4) the same microsurgical technique performed by the same surgeon (the senior author), and 5) the same adjuvant treatment and follow-up program.

PFS was defined as the interval between the last Io or the first postoperative day MRI scan and the first MRI scan demonstrating tumor regrowth and was coded as a continuous variable. For statistical purposes, to compare the 2 subgroups, PFS was also considered at 12 months and coded as a dichotomous variable (1 [yes] or 0 [no]). Because the present cohort is extremely biologically homogeneous, we found it useful to add OS data. OS data were retrospectively retrieved by phone calls.

Statistical Methods

The sample was analyzed with SPSS version 18. Comparison between nominal variables was made with the χ^2 test. EOR and PFS means were compared with 1-way and multivariate analysis of variance along with contrast analysis and post hoc tests. Kaplan-Meier survival analysis assessed survival. Continuous variable correlations were investigated with Pearson bivariate correlation. Threshold of statistical significance was considered $P < 0.05$.

Potential Source of Bias and Study Size

We addressed no missing data because incomplete records was an exclusion criteria. A potential source of bias was expected from exiguity of the sample, which nevertheless, regarding the end points selected, presents an excellent post hoc statistical estimated power ($1 - \beta = 0.96$ for $\alpha = 0.05$ and effect size = 0.6).

This study was approved by the institutional review board of our institution. Before the surgical procedure, all patients gave informed written explicit consent after receiving the appropriate information. Data reported in the study have been completely anonymized. No treatment randomization has been performed. This study is consistent with the Declaration of Helsinki.

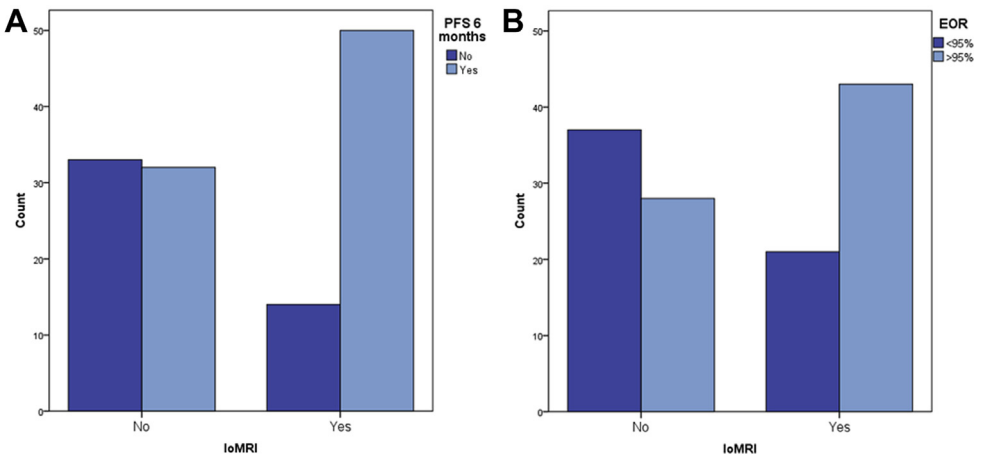

Figure 2. (**A**) PFS at 6 months and (**B**) Extent of Resection of the 2 groups for the use of intraoperative magnetic resonance imaging. EOR, extent of resection; IoMRI, intraoperative magnetic resonance imaging; PFS, progression-free survival.

RESULTS

Participants

In the period between March 2009 and June 2016, 129 patients, matching the exclusion and inclusion criteria and suffering from GBM, underwent surgery in our departments and were retrospectively evaluated for this study. The senior author performed all the resections.

Descriptive Data

The final cohort consisted of 68 men and 61 women, and the average age was 57.04 ± 11.87 years (range, 36–78 years). Fifty-six tumors (43.4%) were located in the frontal lobe, 32 (24.8%) were in the temporal lobe, 17 (13.1%) were in the parietal lobe, 16 (12.4%) were in the occipital lobe, and the remaining 8 (6.2%) were insular or deep-seated. All relevant details are included in Table 1. The 2 groups appeared to be adequately matched (Table 1).

The average EOR was 86.23% ± 10.51% for group A and 94.01% ± 7.42% for group B. This difference was statistically significant (P = 0.005). GTR (>95% tumor volume reduction) was completed in 28 of 65 patients (43.1%; group A) versus 43 of 64 patients (67.2%; group B), realizing a GTR rate increase of 24.1% (Figure 2A).

Group B patients underwent an Io MRI after the first resection to assess the EOR. During the surgical procedure, in a total of 38

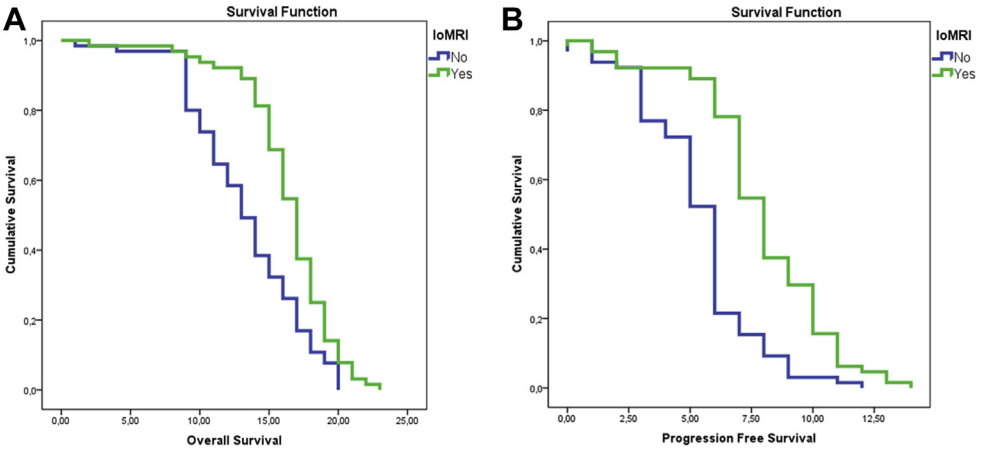

Figure 3. Kaplan-Meier survival curve that describes the impact of intraoperative magnetic resonance imaging on (**A**) progression-free survival and (**B**) overall survival. IoMRI, intraoperative magnetic resonance imaging.

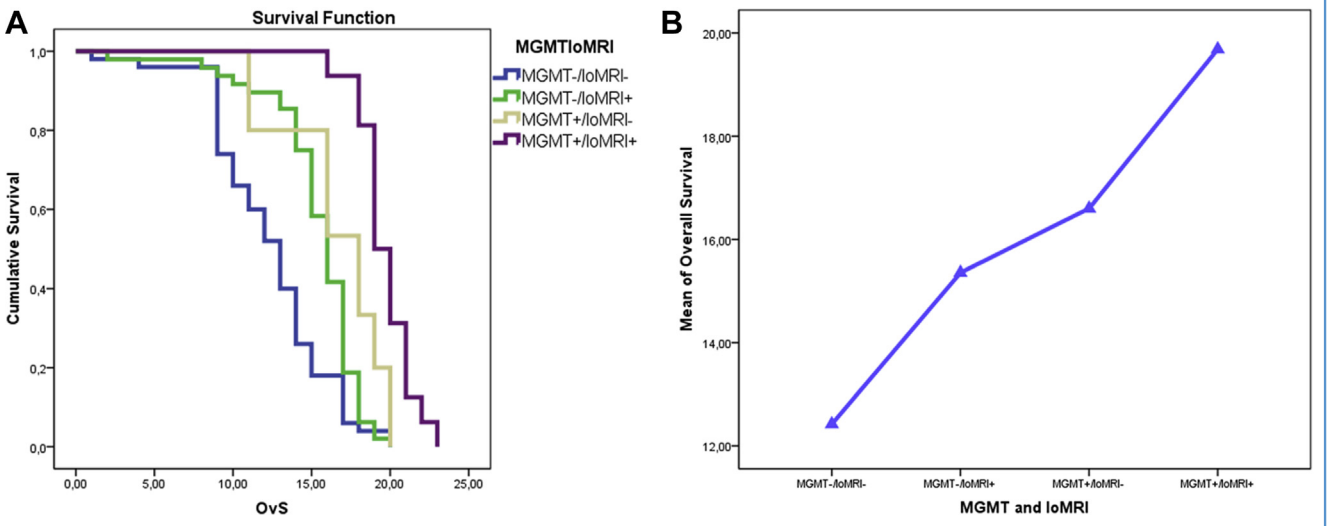

Figure 4. (**A**) Kaplan-Meier survival curve that describes the impact of intraoperative magnetic resonance imaging plus MGMT methylation status on overall survival. (**B**) Analysis of variance chart disclosing the relevant trend of survival for the aforementioned 4 subgroups of patients. IoMRI, intraoperative magnetic resonance imaging; MGMT-, not methylated; MGMT+, methylated; Io-MRI-, operated on without Io-MRI; Io-MRI+, operated on with Io-MRI.

of 64 patients (59.37%), the Io MRI disclosed a remnant that deserved a further resection, which was safe and feasible according to Io neuromonitoring findings and anatomic and functional imaging eloquent area landmarks. Direct experience with Io MRI brought the first operator (the senior author) to adopt a strategy of a first cautious resection before completing a more aggressive debulking after Io control. Therefore, whenever available, the use of Io MRI definitely modifies the resection strategy.

Outcome Data and Main Results

The median PFS was 5.38 ± 2.32 months for group A versus 7.89 ± 2.75 months for group B; the mean OS was 13.38 ± 4.06 months for group A versus 16.43 ± 3.41 month for group B. These differences were statistically significant ($P = 0.001$ and $P = 0.001$, respectively). PFS at 6 months accounted for 49.23% (32/65) of group A and 78.12% (50/64) of group B; the PFS increase was as high as 28.89% ($P = 0.001$) (Figure 2B).

PFS, OS, and EOR showed a strong statistical correlation, coherently with what was expected for a homogeneous cohort of patients with GBM (OS-PFS: $r = 0.454$; EOR-OS: $r = 0.718$; EOR-PFS: $r = 0.416$; P value between 0.001 and 0.002).

Other Analyses

Regarding Kaplan-Meier survival curves, Io MRI demonstrated a strong positive effect on all the investigated outcome variables: PFS, OS, and EOR ($P > 0.001$, $P > 0.001$, and $P = 0.002$, respectively) (Figures 3A and 3B).

To assess the impact of Io MRI on the differential MGMT methylation status, we furthermore classified our patients in 4 nominal variables: 1) 50 patients operated on without Io MRI presenting a not methylated MGMT; 2) 48 patients operated on with Io MRI presenting a not methylated MGMT; 3) 15 patients operated on without Io MRI presenting a methylated MGMT; and 4) 16 patients operated on with Io MRI presenting a methylated MGMT.

Interestingly, Kaplan-Meier analysis (Figure 4A), along with univariate analysis of variance (Figure 4A), disclosed that MGMT methylated plus Io MRI convey a progressive survival advantage among the 4 different subgroups, with the most effective advantage being the one obtained by treating MGMT methylated patients with Io MRI. Precisely, the survival difference between the MGMT methylated and unmethylated patients regarding the use of Io MRI is a statistically significant amount of approximately 2.7 months for both the eloquently and noneloquently located lesions.

Complications

In the entire cohort we recorded the following surgical complications: 3 patients (2 belonging to group A and 1 in group B) presented a hemorrhagic complication (surgical cavity hematoma/venous infarction: 2.32% of patients), and 2 of those patients required surgical revision and 1 of them suffered from a postoperative neurologic vegetative state and died on postoperative day 20. A total of 4 patients (2 belonging to group A and 2 in to group B) presented a cerebrospinal fluid flow disturbance, and 1 patient developed a surgical cavity infection (belonging to group A) for an overall surgical complication rate of 6.2% in the entire cohort. Three of the cerebrospinal fluid disturbances were managed surgically; the remaining, a mild temporal horn entrapment, was stable in serial follow-up MRI scans and was deemed to be managed conservatively. The surgical cavity infection required a

surgical revision. Surgical complication did not show significant differences between the 2 subgroups.

We also recorded a total of 4 medical complications: 3 cases of pneumonia, 1 case of myocardial infarction, and 1 case of kidney failure. One of the patients suffering from pneumonia and the patient affected by myocardial infarction died. Therefore, the resulting overall mortality rate was 3 of 129 (2.32%).

We furthermore recorded a total of 20 neurologic postoperative deficits: 11 patients presented a new or worsening of a preexisting motor deficit (6 belonging to group A and 5 in group B), with 9 of such patients presenting a minor transient impairment which resolved within 30 postoperative days, and in 2 cases the deficit was permanent (1.55%). We recorded a total of 6 new or worsening preexisting speech disturbances (1 improved at 30 days, 3 were stable at follow-up, and 2 completely resolved within 30 days) and 2 new visual field deficits (permanent at follow-up), plus the vegetative state patient. We did not find statistically significant difference among the 2 subgroups regarding the incidence of surgical or neurologic complications, a fine analysis of the complications incidence, however, did not in the main end points of the present work.

DISCUSSION

In this study we investigate the impact of a 1.5-T Io MRI on EOR and therefore on the PFS in a uniform cohort of patients affected either by MGMT methylated and unmethylated GBMs. The target of glioma surgery is not only to improve survival but also to increase the time of acceptable quality of life.[1-5]

GTR as measured by absence of contrast-enhancing tumor or T2-weighted imaging/fluid attenuated inverse recovery hyperintensity after surgery has being widely accepted to be associated with extended OS and PFS in high-grade gliomas, low-grade gliomas, and even recurrent gliomas.[4,16-18]

There is a growing evidence in the current literature supporting the role of extensive resections to improve survival in GBM patients. Lacroix et al.[17] reported a large series of GBM, with a longer survival (13 months) in patients with 98% resection of the tumor versus resection of <98% (8.8 months). Sanai and Berger[18] analyzed in a review all the relevant literature reporting that the higher the EOR the longer the OS and PFS, both for low- and high-grade gliomas.

Io MRI systems were developed as surgical tools to improve visualization of tumor remnants that would otherwise remain unresected[7-9,19-21]; nevertheless, the true impact of Io MRI in GBM surgery has not been completely investigated, and surprisingly, when analyzing the literature, some of the experiences reported do not support its use in high-grade glioma surgery.[22]

Kubben et al.[19] in a systematic review regarding the use of Io MRI, analyzing a limited number of highly comparable short series of patients, reported class II evidence supporting the use of Io MRI in increasing EOR, enhancing quality of life, and prolonging survival after resection of gliomas with respect to conventional microsurgical resection.

Key Results and Interpretation

In our experience, the key advantages of Io MRI are 1) to restore neuronavigation accuracy during surgery, 2) to solve the problem of brain shift, and 3) to intraoperatively identify residual tumor.[7-9]

A prospective, randomized controlled trial by Senft et al.[23] reported a significant improvement in PFS at 6 months in the Io MRI group versus the conventional surgery group, without any difference in postoperative neurologic deficits. However, the impact of this prospective trial is slightly limited by the small number of patients recruited. This trial provides preliminary strong evidence that supports the use of Io MRI in resection of newly diagnosed GBM. However, apart from the study size, there are several limitations, including 1) the patients included suffered from different World Health Organization grading of gliomas, 2) different neuronavigators were used, and 3) 1.5- and 3-T Io MRI are, in our experience, completely different instruments, and results are not completely superimposable for such a fine analysis because 1.5-T MRI presents a lower spatial resolution and may underestimate residuals with respect to 3 T, which presents more artifacts than conventional 1.5-T imaging.[24,25] In other words, to draw definitive conclusion on EOR, all patients should be investigated with a similar MRI and with the same radiologic protocol.

Our results and our experience are consistent with the results of Senft et al.,[23] and we definitely agree with their findings. The aim of our study was to empower this evidence and drive it one step beyond through a retrospectively analyzed, strongly comparable, and strictly matched cohort of patients in which the weight of multiple potential sources of bias is excluded.

Further notable prospective trials,[26] outlined the role of Io MRI in increasing the EOR. Similar to the work of Senft et al.,[23] the trial of Hatiboglu et al.[26] focused on the exquisite impact of Io MRI on the EOR, providing the evidence (44 patients) that such a tool increased significantly the EOR from 84% to 99% with additional tumor removal after the Io scan for enhancing gliomas and from 63% to 80% for nonenhancing gliomas. In this paper, importantly, n 15 (52%), this was achieved with the contribution of Intraoperative MRI.

Regarding our experience with Io MRI—aided GBM surgery, at the beginning of the resection, it is usually simple to differentiate, under operative microscope, between normal and pathologic tissue. However, when dealing with smaller remnants, after most of the resection has been carried out, the transition between normal and pathologic tissue becomes generally more difficult. In such conditions, we noticed the real utility of the Io MRI.

Furthermore, notable is the cumulative progressive impact of the Io MRI in the surgical treatment of GBM patients according to their MGMT methylation status. It conveys an additional progressive survival advantage with respect to the simple effect on survival of the sole MGMT, with which positive impact on OS has been extensively investigated and recognized.[13]

Naturally, Io MRI is more time consuming than conventional surgery, and the costs are usually higher. However, immediate intervention for incomplete procedures (e.g., residual tumor) or possible complications can prevent reoperation and decrease hospitalization length and treatments cost.[27]

Indeed, EOR, according to the literature,[17] is the main prognostic factor determining the final OS. Therefore, whenever possible, a second surgery after a first partial resection should always be planned, determining an increase in the overall hospitalization and treatment-related cost.

It is important to mention the possibility to perform a brain shift correction, critical to approach eloquent areas gliomas.[7,8] Eloquent structures such as the corticospinal tract or arcuate fasciculus may move on average up to 4 mm. In other cases, the displacement of the eloquent structures is caused by the resection itself.[7-10] An Io correction is therefore critical for satisfactory safety of the resection.

Since its introduction, Io MRI underwent important comparison trials with Io ultrasonography, a more accessible and less time-consuming Io imaging. These reports outlined the superiority of Io MRI in improving EOR and detecting residual disease,[28,29] outlining a role limited to an accurate predebulking tumor delineation performed with Io ultrasonography.

Strong, prospective controlled trials are necessary to validate and describe the role and real impact of Io computed tomography and ultrasound imaging on the results of Io MRI–aided glioma surgery.

Therefore, to date, Io-MRI remains, according to the literature and our experience, the most accurate instrument to visualize tumor remnants after resection.

Limitations and Generalizability

The main limitation of the study lies in its retrospective nature. Furthermore, the patients were not randomly allocated to the subgroups. With respect to other retrospective trials,[20] we had the same adjuvant treatment protocols, similar MRI scanners, similar instruments, the same neuronavigator, the same operative microscope, and the same surgeon, in the context of 2 ultraselected and completely superimposable cohorts of patients.

CONCLUSIONS

We present the experience of a single surgeon in performing surgery for GBM with the aid of a 1.5-T Io MRI. Once the follow-up and adjuvant therapies are completely homogenized for all the patients included in the cohort, it appears surprisingly clear that Io MRI, similar to what was previously demonstrated in another similar retrospective investigation,[30] is a safe and effective tool that optimizes significantly both the EOR and OS of the patients.

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