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RESEARCH ARTICLE

Intraoperative Magnetic Resonance Imaging in Brain Glioma Surgery Using Low-field system. Presentation of the First Twenty-eight Procedures

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ABSTRACT

Background: Imaging systems placed into the operating theatre is becoming a standard practice in glioma resection surgery.

Aim: To evaluate feasibility, safety, and utility of an intraoperative open low-field magnetic resonance imaging (iMRI) to assess the extent of glioma resection.

Methods: Study population sample included 28 patients undergoing first time surgical resection for brain gliomas. All patients underwent preoperative and postoperative high-field MRI scans, and one to four intraoperative MRI acquisitions, using a side-opening 0.25 T MRI system. Pre- and postoperative MRI scans were assessed to measure volumetric changes and the extent of resection. Surgical timing was also registered.

Results: n=28 patients (19 men and 9 women, range: 6 - 71 years), underwent microsurgical resection of brain glioma for the first time (18 high-grade and 10 low-grade gliomas). Postoperative MRI indicated that gross total resection (>99%) was achieved in 23/28 (82%), subtotal resection (90-99%) in 4/28 (14%) patients; in the latter, residual tumor volume ranges between 0.5 and 8.2 cm^3; and partial resection (<90%) in 1/28 (4%). Three patients (10.7%) experienced worsening of neurological symptoms (only one permanent). The average time required for each imaging session was 12 minutes.

Conclusion and Relevance: Intraoperative low-field MRI-guided resections maximizes the extent of glioma resections, without significant interferences with surgical and anesthesiologic procedures and without excessive prolongation of the surgery, playing a relevant role in patient survival and quality of life.

Keywords: intra-operative magnetic resonance, glioma, extent of resection

Introduction

Maximizing the extent of resection (EOR) while preserving the surrounding functional brain tissue[1,2] is essential in glioma surgery. Numerous studies have shown that the progression-free survival and quality of life depends on EOR. In 216 adults with low-grade gliomas, when EOR >90% was achieved, 5- and 8-year overall survival increased by 21% and 31%, respectively[3]; in other study that included 416 patients with multiple glioblastomas, the median survival was 13 months when EOR was ≥98%, against 8.8 months when EOR was lower[4]. However, differentiating glioma tissue from normal tissue is often difficult, and achieving maximum resection becomes challenging. Neuro-navigation, the precision of which is hampered by intraoperative displacement of intracranial structures, becomes limited for such purposes. Brain shift, caused by lesion removal, cerebrospinal fluid volume reduction and edema[5], can reach up to 30 mm at the level of the brain surface and more than 10 mm in the midline, requiring repeated imaging-based intraoperative neuro-navigation adjustment[6].

Intraoperative imaging is becoming standard practice in glioma surgery[1,2,7]. Ultrasound (US) and magnetic resonance imaging (MRI) can be used for this purpose. Intraoperative US is a low-cost tool that minimally prolongs operative time, but it is has several drawbacks, including limited image quality in patients with previous radiotherapy, the necessity to use different probes for lesions localized in different depths and the presence of ultrasound artifacts; most importantly, the 2-D ultrasound image depends on the orientation of the ultrasound probe and obtaining an US scan of a certain part of the brain in at least two exact orthogonal planes may be challenging, especially in small craniotomies[8,9].

The use of intraoperative MRI (iMRI) in brain surgery began in the late 1990s[10,11] and led to an increase in the EOR of gliomas[11-14]. Both high- and low-field MRI systems have been used for intraoperative monitoring, and both have its own set of advantages and disadvantages, as with iMRI there is a constant trade-off between signal-to-noise ratio and access to the patient.

High-field systems (1.5, 3 or 7 T) have an optimal image quality but are expensive and require extensive structural modifications for their installation. The intraoperative use of the high-field system is further complicated by the fact that their 5-G magnetic field zone. The surgical procedure can be performed outside of it, and this localization is very distant from the center of the magnet, modifying significantly the surgical procedure and representing a challenge for anesthesiologist to avoid the risk of dislodged IV lines, catheters and/or endotracheal tubes during the transfer to patient from the operating room to the MRI scan[15]. Time for transportation, together with the time required for scanning, can add up to 2 hours to the intervention, which significantly extends the duration of anesthesia and increases the risk of postoperative complications[16,17]. Meta-analysis of 66 studies has demonstrated a 14% increase in the likelihood of complications for every 30 minutes of additional operative time[18].

To overcome the shortcomings of high-field MRI, low-field MRI systems have been proposed for intraoperative neurosurgical use. Its main advantage lies on the fact that these systems can be placed directly inside the operating room and allow for intraoperative evaluation of tumor resection without moving the patient and prolonging the time of anesthesia[18]. However, the magnets and coil settings of intraoperative systems, as well as surgical instruments, and neurophysiological monitoring equipment must be adapted to ensure the image quality necessary to guarantee the detection of tumor remains.

In the present paper, we described our experience with the use of the open low-field (0.25 T) iMRI system applied in the first 28 patients who underwent glioma resections.

Material and Methods

This was a descriptive pilot study with 30 patients who underwent a glioma surgical resection under intraoperative low-field resonance at the Neurosurgery Department of Clínica Adventista Belgrano (Buenos Aires, Argentina) between June 2022 and January 2024. Surgeries were performed as standard micro-neurosurgical procedures using regular instrumentarium. In all patients, the diagnosis of glioma was confirmed by histology and they were classified according to 2021 WHO classification as low-grade gliomas (grade I-II neuroepithelial tumor) or high-grade (grade III-IV glial tumors)[19]. Two patients with previous glioma surgery were excluded. All participants (n=28) were informed about the use of iMRI system and gave their written consent to participate. The study protocol followed the principles of the Declaration of Helsinki and was approved by the institutional Ethics Committee.

Pre-and post- operative MRI requirements. Pre- and post- operative MRI imaging was performed with a standard high-field MRI system (General Electric® and Philips® Systems, 1.5 and 3 Tesla), to ensure greater accuracy and reduce the margin of error in detecting residual tumor. We used gadolinium-enhanced T1 sequences for tumors that uptake contrast (pilocytic astrocytoma, ganglioglioma, anaplastic gliomas). For non-T1-enhancing tumors, enhanced T2 and fluid-attenuated inversion recovery (FLAIR) images were used (Figure 1).

Inside the iMRI surgical room. An MRI equipment was installed inside a 50.3 m² Faraday cage, which includes an operating area equipped with a 100% particle-free unidirectional laminar air flow air-conditioning system, with a positive pressure gradient inside relative to the outside.

A standard side-opening low-field MRI system (S-scan, Esaote™ S.p.A., Genoa) was located in the surgical room together with an MRI table specifically modified by the authors. The MRI system operates with a 0.25T permanent magnet, having a 5-G limit of 180 cm and controlled access area (0.5 mT) of 157 cm. The opening between the poles of magnet is 37.2 cm in the narrowest part, which completely covers the maximum diameter of the patient head. The low-field MRI system allows obtaining high-quality images using T1, T2 and FLAIR sequences and achieving visualization in axial, sagittal and coronal planes in a total time of 6 minutes. The view display field is 27 cm. (Figure 2).

Figure 1: High-grade glioma in right temporal lobe region on **(a)** preoperative and **(b)** postoperative images obtained with high-field MRI system.

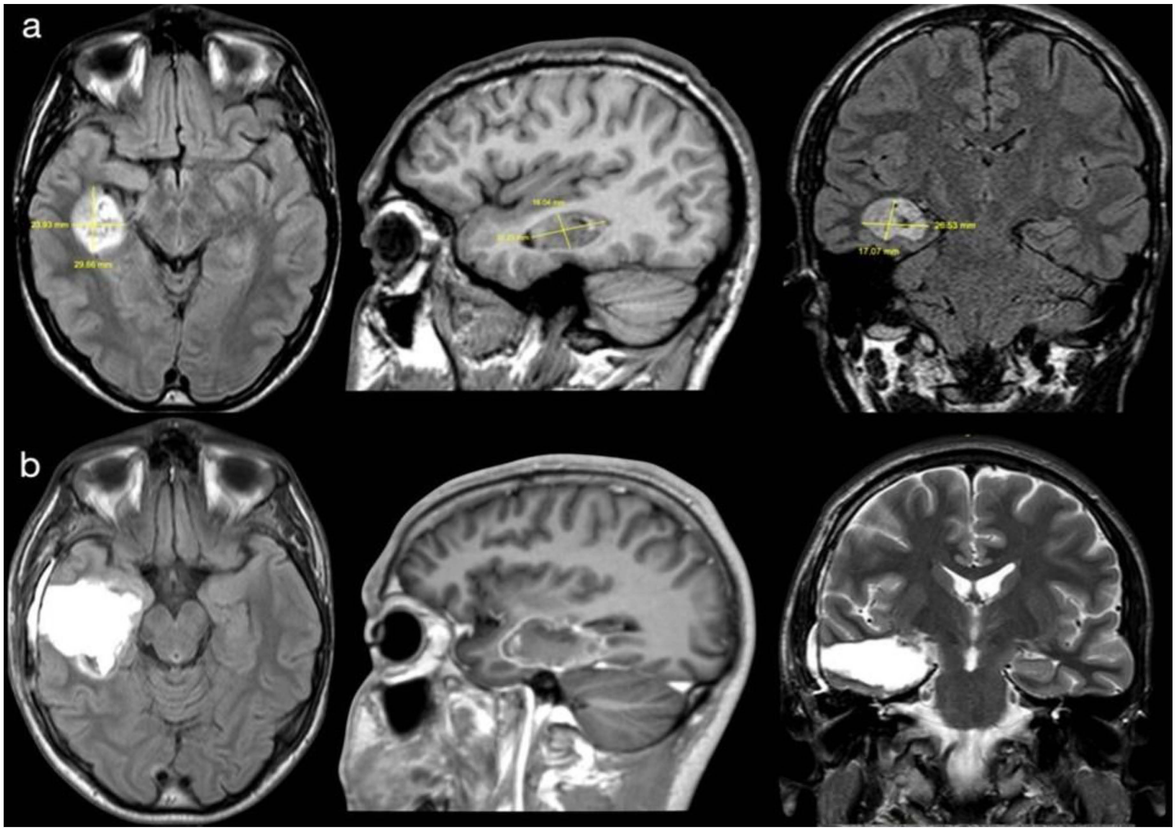
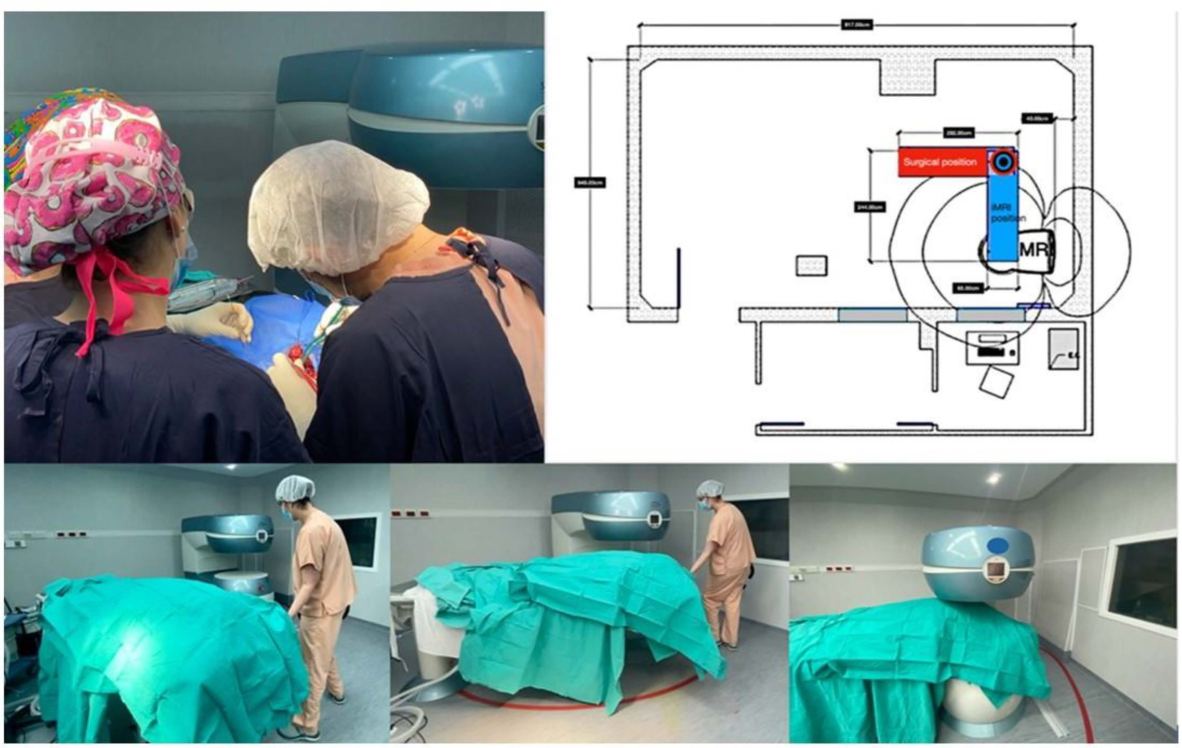


Figure 2: Operating theatre scheme. An open low-field (0.25 T) MRI system S-scan is installed inside a Faraday cage. The operating table has been set in the surgery position (red) to keep easy and quickly rotate it towards the inside of the magnet (blue) for the acquisition of intraoperative images (below).



Surgical Procedure. During surgery, the patient is placed directly on the MRI table and the surgical procedure is performed approximately 2.5 meters from the center of the magnet. The specific design of the table allows for a semicircular rotation that within seconds places the patient in the center of the magnet at any time during the surgery (Figure 2).

Before image acquisition, a vitamin E capsule placed in a finger of sterile surgical glove is positioned into the surgical cavity to localize accurately the residual tumor in the operating field. T1, T2 and FLAIR sequences are used for iMRI scans. After the image acquisition, the table with the patient is returned to the surgical position.

Intraoperative frozen biopsy was performed in all surgical procedures. In tumors close to eloquent areas, we added intra-operative neurophysiology, evoked potentials and cerebral stimulation.

After surgery, all patients were strictly monitored with high-field MRI.

Volumetric Resection. Volumetric measurement of original and residual tumors was performed with OsiriX™ v.58 32-bit software (Pixmeo SARL, Geneva, Switzerland). The extent of resection (EOR) was classified as gross total resection (GTR), subtotal resection (STR) and partial resection (PR), when software-estimated resected volumes were >99%, 90-99% and <90%, respectively.

Patient Preparation, Head Coils, Disinfection and Sterilization. After cranial fixation, the head of each patient is covered by sterile plastic sheath, in which the operating area is opened. Before every iMRI, the head of the patient was placed in a sterile plastic bag and further covered by sterile surgical drape. Two types of coils (flexible and rigid) were used, according to the tumor localization. The flexible coil was placed directly on the patient's head, while the head is inserted into the rigid coil after being wrapped in a sterile plastic bag and covered with a sterile surgical drape. After the surgery, the flexible coil is cleaned with water, soap, and alcohol antiseptic solution (SoluPrep) and then sterilized with ethylene oxide (6-hour exposure). The rigid coil is cleaned with water, soap and SoluPrep[20].

Pre- and post-surgical assessment of the patient. Karnofsky performance status (KPS)[21] and neurological clinical status were evaluated before surgery and 30 days after it. Early postoperative complications were also assessed.

Statistical analysis. Descriptive analysis was carried out. Due to the small sample size and skewed distribution of variables, the median and range was used to assess the age of the patients and the volumes of the tumor. Wilcoxon test was applied to evaluate changes in pre/ post KPS; a value of $P<0.05$ was considered statistically significant.

Results

The characteristics of the study population are reported in Figure 3. Median age of the patients was 50 years. More frequent tumor localizations were temporal and frontal areas (53%). According WHO classification, 18 (64%) and 10 (36%) were high- and low-grade gliomas, respectively.

Figure 3: Characteristics of Study Population

		Median (range) n (%)
N		28
Sex (male:female)		19 (68) : 9 (32)
Age median (years)		50 (6 – 75)
Low-grade glioma (WHO I, II)		18 (64)
High-grade glioma (WHO III, IV)		10 (36)
Dominant Tumor localization	Frontal	8 (28)
	Temporal	7 (25)
	Parietal	2 (7)
	Thalamus	3 (11)
	Insular	2 (7)
	Mesencephalus	2 (7)
	Cerebellum	2 (7)
	Intraventricular	1 (4)
	Corpus callosum	1 (4)

From the 26 patients in whom a complete tumor resection was considered, a GTR was achieved in 22 (84.6 %) and STR in 4 (15.3 %) patients. The larger the tumor volume, the lower GRT rate: tumors in which GTR was achieved (median volume: 46.6 cm^3; range: 4.1 to 207.76 cm^3) were significant smaller than tumors in which only STR could be completed (median volume: 70.8 cm^3; range: 36.5 to 249.6 cm^3; P=0.040). In those 4 patients we performed STR, the residual tumor volume ranged between 0.5 and 8.2 cm^3; they were not individually analyzed, considering that those cases not making a statistical difference or impact on the final postoperative clinical evolution of the patients.

The 2 patients in which an incomplete resection was considered, only PR were underwent; that decision was taken before surgery, on basis of preoperative MRI, showing in one patient a left tumor involving three brain lobes (frontal, temporal, insular), and a frontal insular speech area involvement in the other.

In all patients, from 1 to 4 iMRI scans were performed. All tumors could be reliably visualized on intraoperative imaging. In 2/28 patients (7%), GTR was achieved already before the first iMRI. In resting 26 patients (93%), iMRI revealed residual tumor tissue, leading to further tumor resection. Extended resection did not translate into a higher rate of neurological deficits (Figure 4 A-D and Figure 5 A-D).

From the moment the surgeon stops the surgery and orders the sequence for obtaining adequate iMRI images, the minimum time required was 12 minutes and the maximum was 41 minutes. The time required to cover the patient's head and place it in the isocenter of the magnet ranged from 30 to 90 seconds.

The rate of post-operative neurological deficit was evaluated using clinical neurological examination and KPS thirty days after surgery in all cases. 24 patients (85.7%) had no signs of new neurological deficit, 3 patients (10.7%) showed worsening of previous neurological symptoms (2 were temporary and the other persistent deficits) and 1 patient (3.6%) had new neurological symptoms (right hemiparesis). Those data are consistent with those reported in patients participating on the Glioma Outcome Project[22].

Figure 4: Preoperative and intraoperative images of low-grade glioma in right insular region. A: preoperative images obtained with high-field MRI system. B: first intraoperative control with low-field MRI system in FLAIR sequences with tumor remnant (arrows). C: second intraoperative control with low-field MRI system in FLAIR sequences with small tumor remnant (arrows). D: last intraoperative control with low-field MRI system in T1 sequences with complete tumor removal.

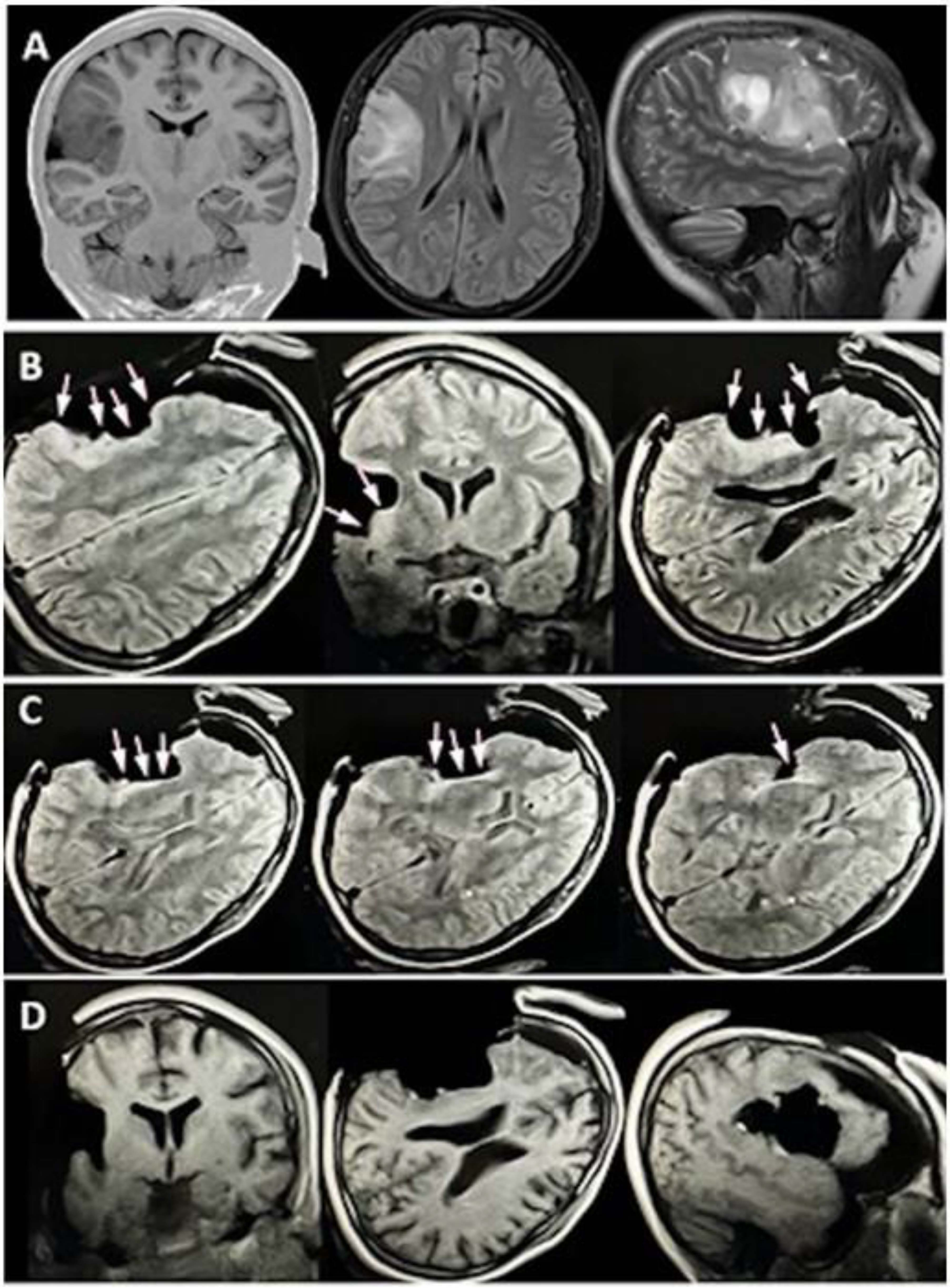
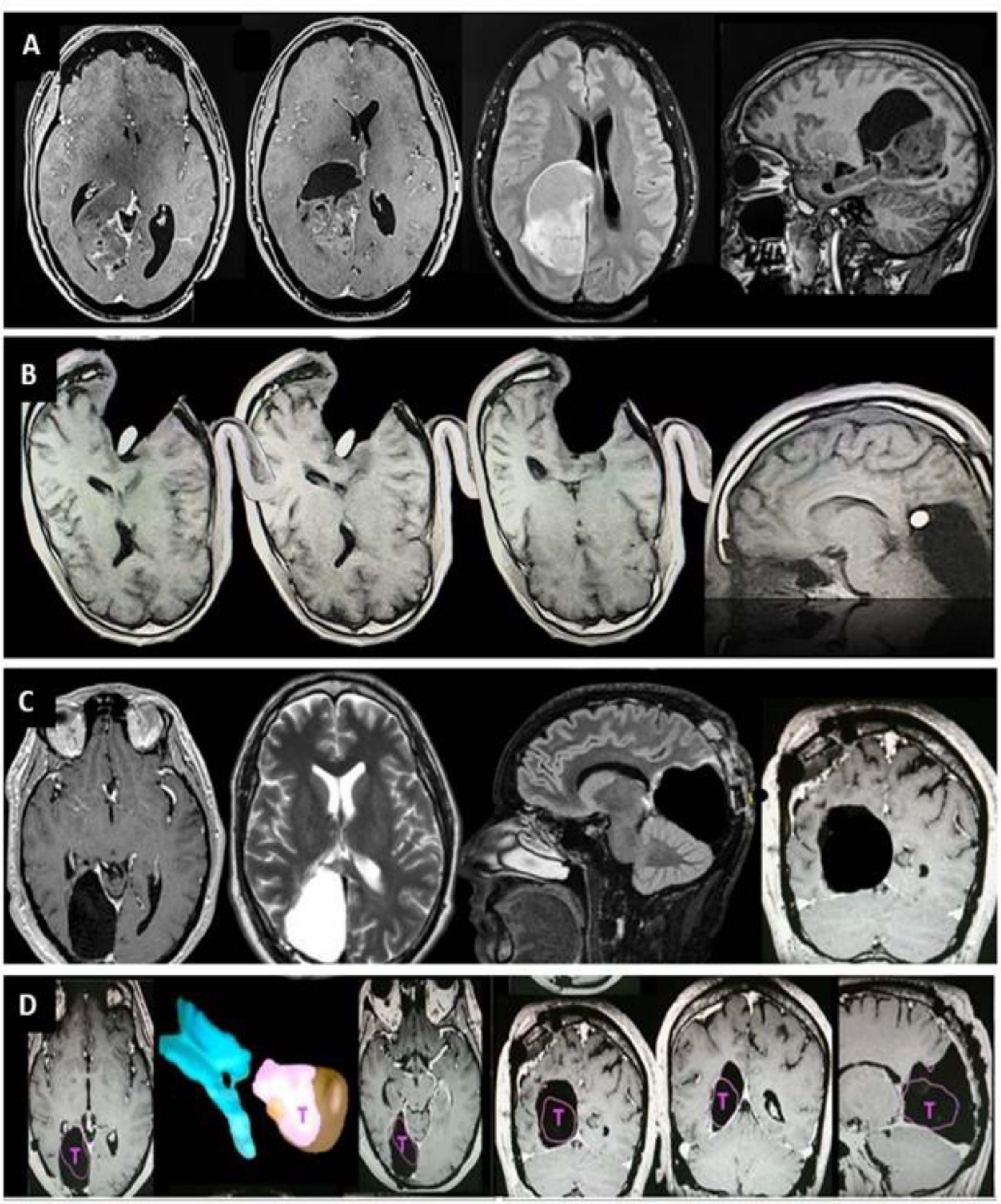


Figure 5: A: Preoperative 3-T MRI in high-grade glioma in right parietal-occipital region. **B:** Intrasurgery image with low-field MRI as surgical guided; a vitamin E capsule placed in a finger of sterile surgical glove is positioned into the surgical cavity to localize accurately the residual tumor in the operating field. **C:** Postsurgical 3-T MRI images, showing the gross total resection of brain glioma. **D:** "T" and pink line represents the presurgical location and volume of tumor.



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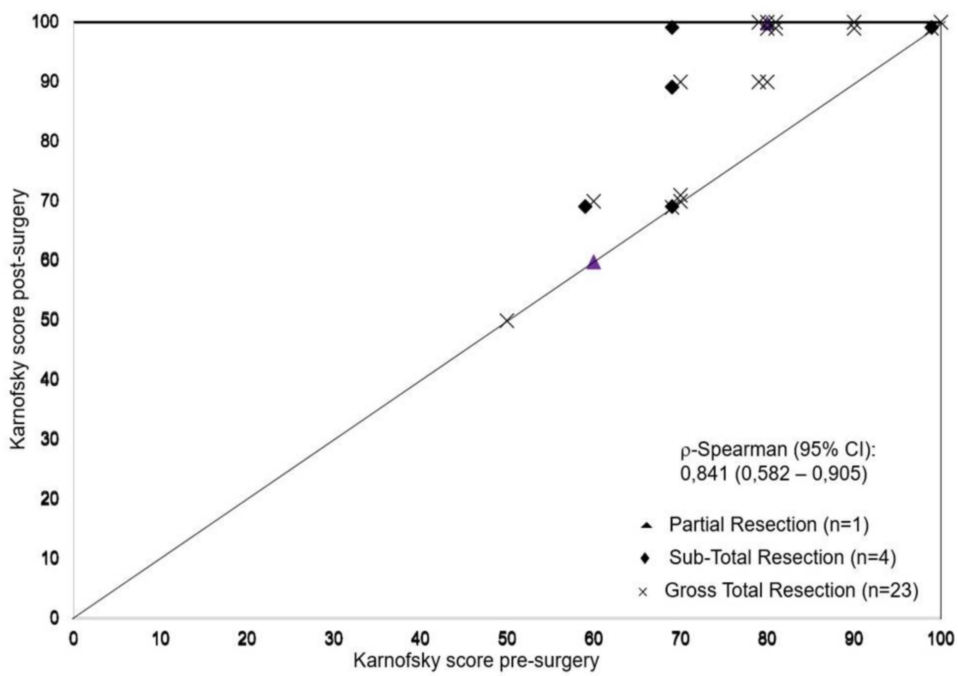
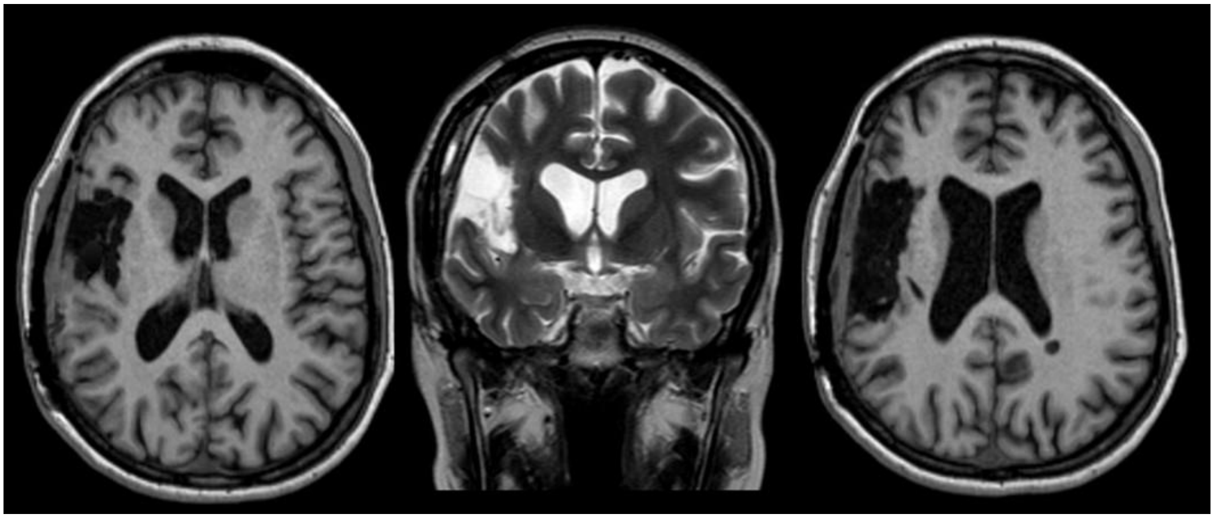
KPS ≥70 was preoperatively evident in 24 patients (86%) and postoperatively in 26 patients (93%) (*P*=0.00003). The changes in KPS after surgery are reported in Figure 6.

Figure 6: Relationship between Karnofsky score before and after glioma surgery according to EOR. Cross indicates patients with GTR, rhombus patients with STR and triangle patients with PR.



During the postoperative period, 1 patient (3.6%) experienced nosocomial pneumonia and another patient (3.6%) had surgical site infections attributed to *Staphylococcus aureus*. Both cases did not require toilette or bone plaque removal; they were successfully treated with antibiotics, without consequences to the patients. There was no perioperative mortality reported within 30 days after surgery (Figure 7).

Figure 7: Same patient of Figure 4. Postsurgical 3-T MRI at 3 months from surgery.



Discussion

Argentina was the fifth country around the world to start operating with iMRI, after the USA, Germany, Finland, and Canada. In July 2000, we operated the first patient using a low-field 0.23T Picker™ system. Twenty-three years after, more than 700 surgical interventions in high- and low-grade gliomas were performed. In all that time, the benefits of using iMRI in the surgery of the most common brain tumor (glioma) were well recognized, particularly in comparative studies with awake surgery, stereotaxy, neuronavigation, and conventional neurosurgery.

However, considering the 662 million of people who live only in Latin America and the Caribbean, there are less than half a dozen operating rooms equipped with iMRI for them showing that iMRI accessibility is low and extremely inhomogeneous.

We believe that the scarce and delayed development of iMRI in global neurosurgery is due to two fundamental problems (that they were not the focus of our work, but they are nonetheless very important): One, the magnitude of investments and amazing building modifications that its installation requires. Two, high-field iMRI equipment significantly alters conventional neurosurgery (timing, methodology, movement of anesthetized patient with an exposed brain 7 to 10 meters or moving the magnet towards the patient -depending on the different systems-); making it difficult and complex to perform more than one iMRI image control per surgery. That why, even in centers where these systems are available, they are underutilized.

The compact mobile models of 0.10, 0.15, and 0.20T, specifically designed to offer flexibility and mobility, have failed when implemented in neurosurgical practice. The discontinuation of these models four years ago was due to multiple factors, including poor quality of intraoperative images, an insufficient field of view for effective anatomical correlations and difficulties in the neurosurgical positioning of patients. These challenges are exacerbated by the physical variations of patients and the specific location of the pathology being treated, often resulting in inadequate or sometimes directly impossible surgical positioning.

Ultra Low-field MRI, which are in a very early stage of development, face critical challenges in their application within the field of neurosurgery, especially in complex procedures such as the resection of brain gliomas. These systems are characterized by an ultra-low-field magnetic intensity, which results in significantly reduced image quality. This limitation is evident in images with lower resolution and less detail, which is a considerable disadvantage in interventions that require precise visualization of small and complex brain structures. Moreover, these systems require a prolonged acquisition time to compensate for the low signal and achieve a moderately acceptable image quality. This increase in acquisition time not only prolongs the duration of surgical procedures but also increases the risks associated with longer operations, which is particularly problematic in a surgical environment where efficiency and speed are crucial for the success and safety of the patient.

The goal of iMRI in brain surgery is to eliminate as much of the tumor as possible, without excessive prolongation of the intervention and without important interferences with surgical and anesthesiologic procedures. To have an iMRI in glioma surgeries keeps to increase the likelihood of performing complete resections of this kind of tumors, highlighted in several studies: Senft et al (2011) carried out a randomized controlled trial of patients with contrast enhancing gliomas, a GTR was achieved in 96% of patients in the iMRI group compared to 68% in the control group[14]. Wirtz et al (2000) could reduce the STR of high-grade gliomas from 62% intrasurgery to 33% postoperatively thanks to iMRI[23]. In patients with glioblastoma, Roder et al (2014) showed that GTR was more frequent with iMRI (74%) than conventional surgery (13%), and GTR increased 6-month progression-free survival from 32 to 45%[24]. In our experience, using a low-field MRI system located directly inside the operating room, we were able to achieve GTR of gliomas in 82% and STR in 14%, in which it is often difficult to distinguish the tumor from the adjacent healthy tissue; although the residual tissue in STR was small, ranging between 0.5 and 8.2 cm^3; those results were similar to outcomes of Lacroix et al (2001) that included 416 patients with glioblastoma in which the resection of ≥89% of tumor volume significantly improved patient survival, and GTR was an independent predictor of survival[4].

An important feature of the iMRI system is the feasibility and speed with which intraoperative images can be obtained directly in the operating room. The combination of a low-field MRI system and the rotating table, which serves both as a surgical table and as a support base for the patient in the iMRI, made it possible in this experience to acquire 1 to 4 intraoperative scans in 12 to 41 minutes. The possibility of repeated intraoperative imaging is useful also in patients who are not suitable for GTR. For example, in our patient with low-grade glioma located in the insular lobe with extension towards Broca's area in the left frontal lobe, iMRI was essential for an accurate resection that left intact the frontal-basal eloquent zone.

We attempted to evaluate the risk of peri- and postoperative complications attributable to iMRI, although this was difficult because there are no standardized definitions for the degrees and types of complications from magnetic field exposure. However, there were no unforeseen situations or accidents due to magnetic field.

Regarding the postoperative neurological status, monitoring with real-time intraoperative MRI images the progress of surgical resections minimizes the risks and improves the possibilities of preserving healthy brain tissue. No patient decreased the KPS, and except for 2 patients who maintained the score, all of them registered a score above 70 points. In a series of predominantly critical cases with limited follow-up time, we thought it is important to emphasize the relevance of favorable results in the evolution and post-operative recovery of patients at 30 days using the KPS.

The main objective of our study was to show the feasibility of glioma tumor resections with low-field iMRI and how this technology keeps us optimal resections, to avoid future tumor recurrences. Neither neurosurgeons nor patients who need a complete and safe removal of a brain glioma can afford to move from the failure represented by the lack of universal proliferation of high-field intraoperative magnetic resonance in neurosurgical operating rooms to waiting another 30 years for the development of ultra-low field systems when low-field systems today prove to be an excellent neurosurgical tool.

Comment of authors. Low-field MR systems have shown a remarkable renaissance and evolution thanks to technological advances in hardware and software. These systems now offer features comparable to high-field systems (1.5T and 3T), with the advantage of fewer artifacts from magnetic susceptibility and better management of T1 relaxation times. Recent innovations in high-performance gradients and advanced imaging techniques have enabled low-field systems to provide high-quality images without the need for high field intensities. These technological advances have transformed low-field MR systems into valuable and practical tools for neurosurgery, providing superior quality images with easier integration into established surgical procedures. Moreover, improvements in image quality and reductions in acquisition times contribute to more efficient and safer surgery, enhancing compatibility with the needs of the surgeon and the patient during neurosurgery.

Conclusion

While ultra-low field systems still struggle to find their place in clinical applications, low-field systems are proving to be a superior and viable alternative, suggesting a reconsideration of their use in neurosurgery to improve both surgical outcomes and accessibility and economy in operating rooms. These systems represent an ideal convergence of efficacy, cost, and functionality, positioning them as a preferred option for the future of neurosurgical interventions.

Having a low-field MRI system situated directly in the operating room can facilitate brain tumor resection to a maximum safe extent without significant interference with surgical and anesthesiologic procedures and without excessive prolongation of the procedure.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

Authors Contribution:

RRF: Conceptualization, Writing - Original Draft Preparation, Supervision. JLL: Methodology, Writing – Review & Editing. HPR: Methodology, Writing - Review & Editing. FS: Validation, Writing - Review & Editing. JMH: Methodology, Writing - Review & Editing. AE: Validation, Writing - Review & Editing.

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