swiss medical weekly

Original article | Published 15 May 2023 | doi:https://doi.org/10.57187/smw.2023.40072
Cite this as: Swiss Med Wkly. 2023;153:00000

Combined use of intraoperative MRI and awake tailored microsurgical resection to respect functional neural networks: preliminary experience

Constantin Tuleasca[abcd*], Henri-Arthur Leroy[a*], Ondine Strachowski[a], Benoit Derre[a], Claude-Alain Maurage[e], Iulia Peciu-Florianu[a], Nicolas Reyns[a**]**

[a] Centre Hospitalier Regional Universitaire de Lille, Roger Salengro Hospital, Neurosurgery and Neurooncology Service, Lille, France
[b] Department of Clinical Neurosciences, Neurosurgery Service and Gamma Knife Center, Lausanne University Hospital (CHUV), Lausanne, Switzerland
[c] Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland
[d] Signal Processing Laboratory (LTS 5), Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland
[e] Centre Hospitalier Regional Universitaire de Lille, Roger Salengro Hospital, Pôle de Biologie-Pathologie-Génétique, Lille, France
[*] Equal contribution as first authors
[**] Equal contribution as senior authors

Summary

INTRODUCTION: The combined use of intraoperative MRI and awake surgery is a tailored microsurgical resection to respect functional neural networks (mainly the language and motor ones). Intraoperative MRI has been classically considered to increase the extent of resection for gliomas, thereby reducing neurological deficits. Herein, we evaluated the combined technique of awake microsurgical resection and intraoperative MRI for primary brain tumours (gliomas, metastasis) and epilepsy (cortical dysplasia, non-lesional, cavernomas).

PATIENTS AND METHODS: Eighteen patients were treated with the commonly used “asleep awake asleep” (AAA) approach at Lille University Hospital, France, from November 2016 until May 2020. The exact anatomical location was insular with various extensions, frontal, temporal or fronto-temporal in 8 (44.4%), parietal in 3 (16.7%), fronto-opercular in 4 (22.2%), Rolandic in two (11.1%), and the supplementary motor area (SMA) in one (5.6%).

RESULTS: The patients had a mean age of 38.4 years (median 37.1, range 20.8−66.9). The mean surgical duration was 4.1 hours (median 4.2, range 2.6−6.4) with a mean duration of intraoperative MRI of 28.8 minutes (median 25, range 13−55). Overall, 61% (11/18) of patients underwent further resection, while 39% had no additional resection after intraoperative MRI. The mean preoperative and postoperative tumour volumes of the primary brain tumours were 34.7 cc (median 10.7, range 0.534−130.25) and 3.5 cc (median 0.5, range 0−17.4), respectively. More-over, the proportion of the initially resected tumour volume at the time of intraoperative MRI (expressed as 100% from preoperative volume) and the final resected tumour vol-ume were statistically significant (p= 0.01, Mann-Whitney test). The tumour remnants were commonly found pos-terior (5/9) or anterior (2/9) insular and in proximity with the motor strip (1/9) or language areas (e.g. Broca, 1/9). Further resection was not required in seven patients because there were no remnants (3/7), cortical stimulation approaching eloquent areas (3/7) and non-lesional epilepsy (1/7). The mean overall follow-up period was 15.8 months (median 12, range 3−36).

CONCLUSION: The intraoperative MRI and awake microsurgical resection approach is feasible with extensive planning and multidisciplinary collaboration, as these methods are complementary and synergic rather than competitive to improve patient oncological outcomes and quality of life.

Constantin Tuleasca, MD-PhD
University of Lausanne
Faculty of Biology and Medicine and Centre Hospitalier Universitaire Vaudois (CHUV)
Department of Clinical Neurosciences
Neurosurgery Service and Gamma Knife Center
CH-1011 Lausanne
constantin.tuleas-ca[at]chuv.ch

Introduction

Primary central nervous system (CNS) tumours are heterogeneous and derived from cells within the CNS. They can be benign or malignant, while the most malignant tumours are gliomas with a 5-year overall survival (OS) not greater than 35% [1]. The resection extent is associated with OS [2–4], with a larger resection reducing tumour recurrence and further malignant transformation of low-grade gliomas [5, 6]. The introduction of fluorescence-guided microsurgical resection further improved the extent of resection [7, 8]. Initially, intraoperative MRI was considered to lead to a 20% increase in resection extent [9, 10], particularly for low-grade gliomas, but more recent series indicate that this benefit is much higher [11, 12].

CNS pathologies located within eloquent areas pose a specific challenge, particularly to their gross-total microsurgical resection. The primary goal remains neurological function preservation while maximising the extent of resection to optimise long-term neurooncological outcomes and neurological function. In such instances, intraoperative electrical stimulation helps to define cortical areas underlying eloquent function [13−15].

Conscious or awake craniotomy has a long neurosurgical track record and was initially recommended for patients at risk of language function and intractable epilepsy [16]. The current goal of awake craniotomy is to preserve motor, language and cognitive neurological functions for patients with any type of pathology anatomically located near or within eloquent areas of the brain [17]. Consequently, there is a need for the combined use of intraoperative MRI and awake microsurgical resection for both primary brain tumours and epilepsy of various origins to achieve a tailored microsurgical resection to respect functional neural networks [18].

In most of the available literature with regards to the combined management using awake intraoperative MRI and awake microsurgical resection for primary brain tumours, there is heterogeneity in terms of complete initial tumour resection, further resection, no further resection, or complete resection post-surgery [17, 19−25]. Complete initial resection was reported between 10 to 58.3%, while further resection after intraoperative MRI was 36.7% and the final rate of complete resection was between 40.5% and 70% [17, 19−25]. There is also heterogeneity in terms of final results, as some authors describe this as resection to an eloquent margin, subtotal, gross total, near-total or complete resection [17, 19−25], which may confuse the interpretation of the published data.

Our hospital has benefited from the first intraoperative MRI installation in France in 2014, so we sought to review our experience as a referral centre for the operative techniques of combined awake craniotomy and intraoperative MRI. Herein, we present a detailed overview of our data using standardised scales and complete patient information to provide a broader view of combined management awake microsurgical resection and intraoperative MRI in patients with gliomas as well as other pathologies. Moreover, we illustrate some of the indications also covering various eloquent anatomical areas and describe our asleep-awake-asleep technique.

Methods

Study design

The study was a retrospective, non-randomised, case series. The case report form for each patient was retrospectively analysed. All patients provided informed consent and this historical case series review was approved by the Lille University Hospital Ethical Committee. Initially, we published a series of 56 cases with lesions adjacent to eloquent areas managed by intraoperative MRI [26] but herein, we focus on those benefiting from the combined management of awake microsurgical resection and intraoperative MRI. The CNIL number was 791.

Inclusion and exclusion criteria

The inclusion criteria were patients aged more than 18 years, able to provide written informed consent, with either a primary brain tumour or epileptic focus anatomically located within a motor and/or language area (table 1; the illustrative cases are shown in figures 1 and 2). Exclusion criteria were patients aged less than 18 years at the time of surgery, unable to provide written informed consent, minimal residual motor function, pronounced aphasia, a score under 23 on the Mini Mental Status examination, and those with an apathic/disorganised comportment, large vascular lesions or potential airway difficulties [27].

Patient population

Eighteen patients were treated with this approach at Lille University Hospital, France, from November 2016 until the end of May 2020 (see table 1 for patient details) and all procedures were performed by the senior neurosurgeon (NR). The mean patient age was 38.4 years (median 37.1, range 20.8−66.9) and the male-to-female ratio was 7:11. The mean overall follow-up period was 15.8 months (median 12, range 3−36) and the preoperative symptoms included partial seizure in 11 patients (61.1%), generalized seizure in 4 patients (22.2%), a motor deficit in 1 patient (5.6%), headaches in 1 patient (5.6%) and incidental in 1 patient (5.6%). In terms of preoperative neurological deficits, one patient had a right superior upper limb deficit. The exact anatomical location was insular with various extensions, frontal, temporal or fronto-temporal in 8 patients (44.4%), parietal in 3 patients (16.7%), fronto-opercular in 4 patients (22.2%), Rolandic in two patients (11.1%), and the supplementary motor area (SMA) in 1 patient (5.6%).

Pre- and postoperative clinical assessment

Clinical assessment was performed by a board-certified neurosurgeon preoperatively and at 3, 6, and 12 months postoperatively using the Karnofsky performance score (KPS). The neuropsychological exam was performed by a specialized neuropsychologist (co-author OS) for patients' task-based functional MRI (fMRI) to check for their dominant hemisphere. Complementary diffusion tensor imaging by fibre tracking (DTI) was performed to evaluate the position of major fascicles including, but not limited to, the corticospinal tract, arcuate fasciculus, inferior fronto-occipital fasciculus (IFOF), and arcuate fasciculus (AF) [28]. Postoperative MRI was usually performed within the first 48 hours after surgery and at 3 and 6 months.

The awake surgery technique

The most common procedure performed in our institution is the combination of general anaesthesia and an awake technique, referred to as “asleep awake asleep” (AAA). During this approach, the patient is placed under general anaesthesia before and after brain mapping and/or finalised resection. Usually, there is an initial phase of general anaesthesia, followed by intraoperative awakening and then back to general anaesthesia.

All patients in this case series underwent craniotomy under general anaesthesia. The opening of the dura was performed in the awake condition after local anaesthesia with Lidocaine (without noradrenaline). The intraoperative MRI was generally performed in the awake condition with patients remaining awake during the second resection if required. They were placed back to sleep if no further resection was performed for their comfort, except for in three cases who expressed the desire to remain awake.

The electrical stimulation mapping was performed using a bipolar electrical stimulator probe (5 mm between tips) connected to a pulse generator (Ojemann Cortical Stim-

ulator, Integra LifeSciences), which was placed outside the 5-gauss field to further prevent electrical interference. Typically, stimulation was performed over the entire exposed cortical surface using biphasic square wave pulses (0.5 msec per pulse, 50 Hz, 2-second duration) starting at 2.5 mA. The identification of eloquent areas during cortical stimulation was as follows: somatosensory cortex – paresthesia appeared, receptive language cortex (Wernicke area) - speech arrest and anomia, motor language cortex (Broca area) – speech arrest during number counting. Cortex points that did not elicit an effect on stimulation were deemed non-eloquent. Identification sterile tags were not

Table 1:
Basic demographic data.

Pts	Sex	Age (yrs)	Side	Anatomical location	Preoperative symptom	Preoperative deficit	Histological type	Further treatment	Follow-up (months)
#1 intraoperative MRI	F	36.4	L	Anterior insular	Partial seizures	None	Cortical dysplasia type IIb	Surgery 30 months later (epilepsy)	36
	F	38.9	L	Anterior insular	Partial seizures	None	Cortical dysplasia type IIb	None	12
#2 intraoperative MRI	M	37.7	L	Fronto-temporo-insular	Partial seizures	None	Oligoastrocytoma WHO II (diagnosed on biopsy 7 y before with further chemotherapy)	Surgery 21.6 months later (epilepsy & volumetric progression)	36
	M	39.4	L	Temporo-polar; insular;	Partial seizures	None	Anaplastic astrocytoma, IDH-1 mutated (WHO III, WHO IV foci)	Chemo (6 cycles of Temodal)- plus radiotherapy	24
#3	M	23.4	L	Frontal, precentral (SMA)	Generalised seizures	None	Cortical dysplasia, schizencephaly	None	12
#4	F	37	L	Temporo-insular	Partial seizure with language arrest	None	Anaplastic astrocytoma, IDH 1 mutated, WHO III	Chemo (6 cycles of Temodal) - plus radiotherapy	29 (remnant stability)
#5	F	37.1	L	Rolandic and parietal	Headache (incidental discovery, Chiari type I surveillance)	None	Oligodendroglioma, WHO II on a previous biopsy (4 months before surgery); astrocytoma IDH 1 mutated, WHO II, with anaplastic foci, Chr 7, no 1p19q codelation	Chemo (6 cycles of Temodal) - plus radiotherapy	24 (no remnant)
#6	F	36.7	L	Fronto-temporo-insular	Generalised seizure	None	Astrocytoma WHO II, IDH 1 mutated, absence chr 13,19, no codelation 1p 19q	Chemo (6 cycles of Temodal) - plus radiotherapy	21 (remnant stability)
#7	F	38.9	L	Parietal	Partial motor seizure	None	Oligodendroglioma WHO II, IDH 1 mutated, 1p 19q codelation	None	18 months(no remnant)
#8	F	20.8	L	Frontal	Headaches	None	Oligoastrocytoma WHO II IDH 1 mutated, 1p19q codelated(previously operated 5 y before)	None	20 (no remnant)
#9	F	66.6	L	Rolandic area	Headaches	Right superior upper limb deficit	Metastasis, breast adenocarcinoma(previously 2 Gamma Knife, 1 Cyber Knife and 4 surgeries, including 1 awake without intraoperative MRI)	Further Gamma Knife on remnant	12 (remnant stability)
	F	66.94	L	Rolandic area	Right superior upper limb deficit	Right superior upper limb deficit	Metastasis, breast adenocarcinoma(previously 2 Gamma Knife, 1 Cyber Knife and 4 surgeries, including 1 awake with intraoperative MRI)	None	Stability
#10	F	26.4	L	Inferior parietal	Drug-resistant epilepsy (SEEG previously performed, with thermocoagulation on relevant electrodes)	None	Discrete gliosis/ dysplasia without further details being possible	None	12
#11	F	59.1	L	Fronto-temporo-insular	Partial seizures	NoneCognitive decline	Oligodendroglioma WHO II, IDH 1 mutated (also by biopsy 5 years before awake surgery)	Chemo (6 cycles of Temodal) - plus radiotherapy	24 (remnant stability)
#12	M	27.7	L	Temporo-insular	Generalised seizures	None	Astrocytoma WHO II (majority, some foci of III), IDH 1 mutated	Chemo (6 cycles of Temodal) - plus radiotherapy	12 (remnant stability)
#13	M	20.8	L	Opercula	Generalised seizures (recurrence)	None	Pleomorphic xanthoastrocytoma WHO II (previously operated twice in another country, no details)	None	6 (remnant stability)
#14	M	46.4	L	Fronto-opercular	Partial seizures	None	Glioblastoma WHO IV (previously biopsy- anaplastic gangliogliomas without further details)	EORTC 1709 (Stupp protocol plus Marizomib)	6 (remnant stability)
#15	F	31.1	L	Fronto-opercular	Partial seizures	None	Astrocytoma WHO II, IDH 1 mutated	Chemo (6 cycles of Temodal) - plus radiotherapy	3 months (remnant stability)
#16	F	46.9	L	Anterior insular	Partial seizures	None	Astrocytoma WHO II, IDH 1 mutated	Chemo (6 cycles of Temodal) - plus radiotherapy	3 months (remnant stability)
#17	M	41.6	L	Fronto-opercular	Partial and generalised seizures	None	Non-lesional epilepsy	None	3 months
#18	M	27.5	L	Inferior parietal	Partial seizures	None	Cavernoma	None	3 months

routinely placed over the brain area, only in selected cases as presented in the literature.

Intraoperative evaluation of microsurgical resection

For primary brain tumours, tumour removal was performed by dissecting circumferentially around the tumour border, as determined by the registered preoperative MR images displayed on the neuronavigation system. Microsurgical resection was guided by the surgeon's intraoperative observation and assessment of tumour margins. An intraoperative MRI was performed as described below.

Intraoperative MRI: general considerations and specific sequences

A new intraoperative MRI was performed when the neuronavigation became insufficiently accurate and/or to assess the presence of a residual tumour.

Before translating the patient into the MRI, a checklist was completed to ensure the absence of metallic material in the surgical site that could interfere with the magnetic field.

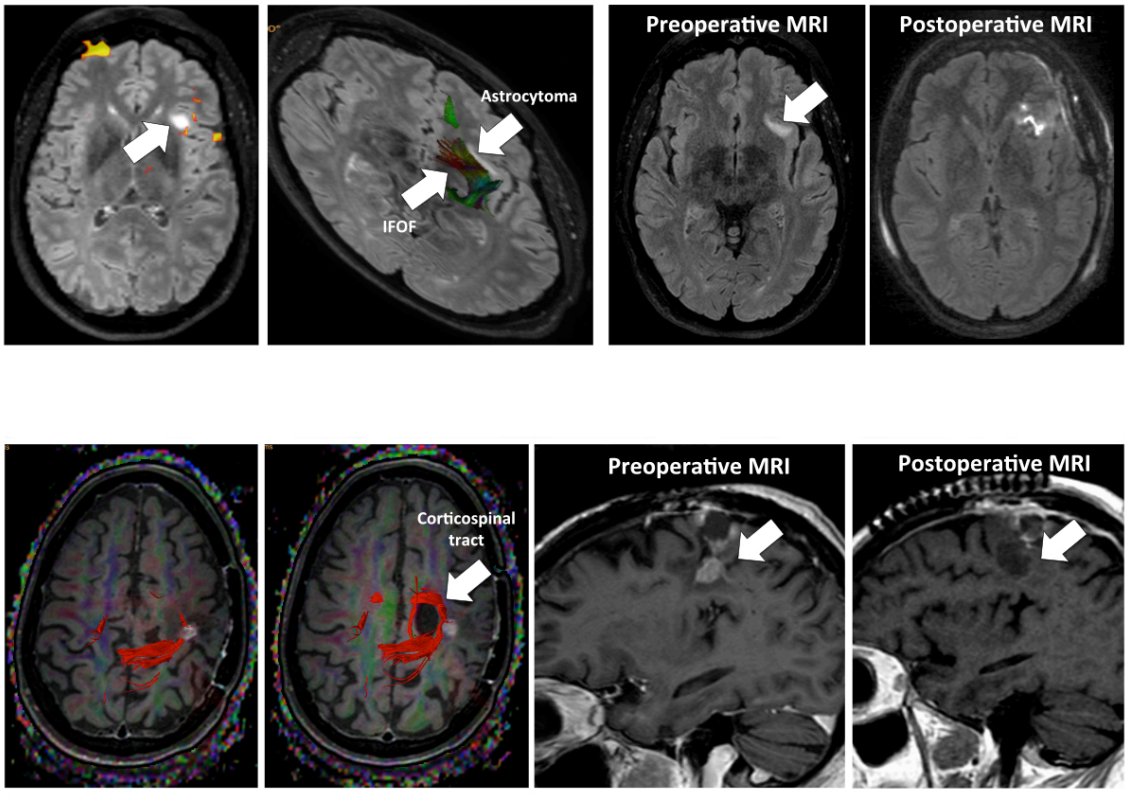
Before performing the intraoperative MRI evaluation to assess the extent of resection, the dura mater and skin were approximated. A sterile field was placed over the operative field and the head was held using a Mayfield MR/X-Ray Skull clamp with Excite 3.0T Adaptor (Integra Lifescience, New Jersey, USA). All patients benefitted from an intraoperative 1.5 Tesla MRI (General Electric®, Boston, MA) and the imaging sequences for neuronavigation were 3D T1 after gadolinium injection with 1-mm slice thickness. Additional sequences, such as 3D FLAIR (especially for low-grade gliomas), diffusion (B1000 and ADC), and T2 with gradient echo, were also performed if required. An intraoperative tractography was performed when the gliomas were close to functional areas (e.g., corticospinal tract). The neuronavigation data update procedure was performed using the automatic coregistration provided by Brainlab® Munich, Germany, with the quality and accuracy of the coregistration double-checked by an imaging engineer and the board-certified neurosurgeon [28]. The MRI was discussed with the neuroradiologist to evaluate the extent of resection.

The surgical microscope (OPMI Pentero® Zeiss, Germany) was connected to the imaging network and could be used for neuronavigation.

Volumetric assessment of primary brain tumours

Two independent neurosurgeons measured all volumetric primary brain tumour volumes using the Intellispace Portal (Philips®, Amsterdam, Netherlands) module BTumour tracking software.The lesions without contrast enhancement or slightly enhanced after gadolinium infusion were contoured using the T2/FLAIR hypersignal MR sequences and highly contrast-taking tumours were segmented using the T1 hypersignal after gadolinium infusion sequences. After segmentation, volumes were calculated in cubic centimetres (cc). For a discrepancy > 10% between the two observers, both segmentations were compared to achieve a consensus volume. The extent of resection was reported in both cc and percentages.

Figure 1: Illustrative cases benefiting from the combined use of awake surgery and intraoperative MRI. Case 1: Preoperative evolutive primary brain tumor (insular astrocytoma IDH 1 mutated) WHO II, in contact on its medium pole with the inferior fronto-occipital fasciculus (IFOF). Case 2: Recurrent (multioperated and irritiated) brain metastasis, localized in the central area, in contact with the corticospinal tract (in red, interrupted by the tumor).



Histological analysis of primary brain tumours

For each patient, the definitive histologic subtype was reviewed by a senior neuropathologist based on the 2016 WHO classification.

The diagnosis in the present series (n= 13, primary brain tumours, table 1) included astrocytoma WHO grade II in 5 patients (27.8%), oligoastrocytoma WHO grade II in 1 patient (5.6%), oligodendroglioma WHO grade II in 2 patients (11.1%), pleomorphic xantoastrocytoma WHO grade II in 1 patient (5.6%), anaplastic astrocytoma WHO grade III in 2 patients (11.1%), glioblastoma WHO grade IV and brain metastasis in 1 patient (5.6%) each, respectively.

Short review of the literature

A short review of the literature is presented in table 2 and further detailed in the *results* section [11, 17, 20–25, 29–31].

Figure 2: Illustrative cases benefiting from the combined use of awake surgery and intraoperative MRI. Case 3: Cortical dysplasia, with structural T1 preoperative MRI (left), functional task-based fMRI showing that the lesion is in contact with premotor and motor areas of the hand (center) and diffusion tensor imaging showing the motor tract (in blue, left). Case 4: cavernous malformation, located at the junction between the inferior parietal and the posterior temporal lobe (Wernicke area).

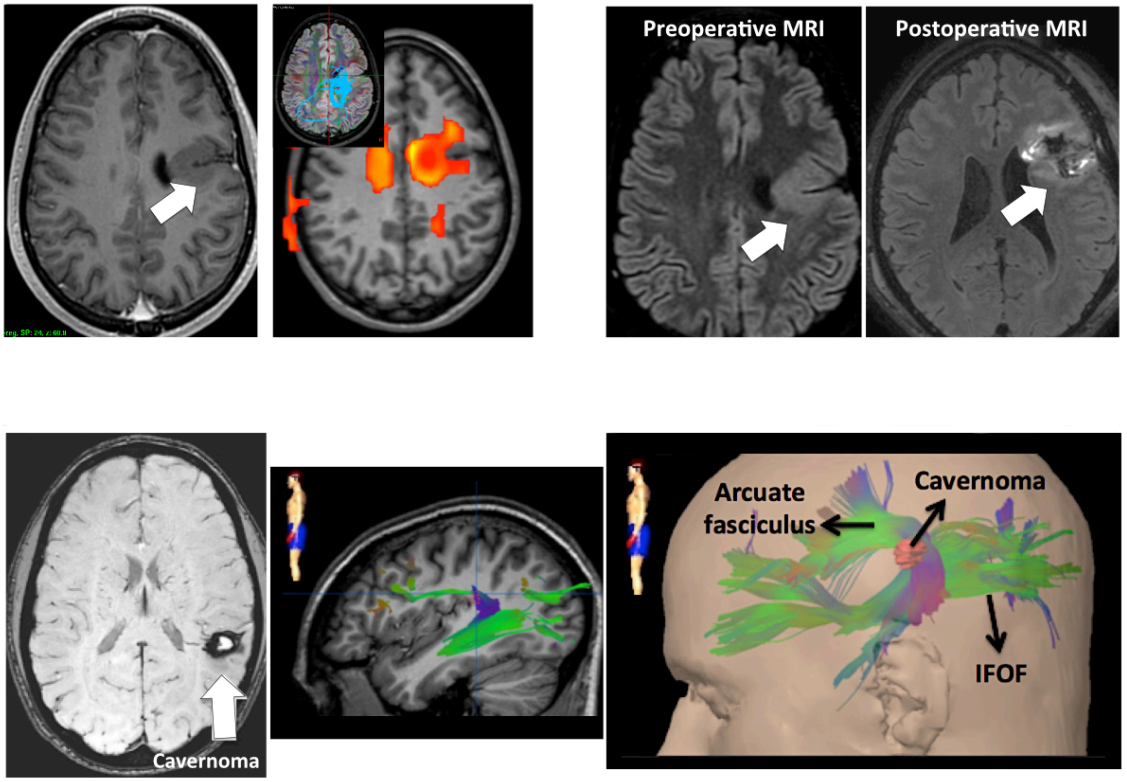


Table 2:
Short review of the literature for the use of awake surgery and intraoperative MRI for primary brain tumours.

Series	Intraoperative MRI complete resection	Further resection	No further resection (n, percentage)	Complete resection (details)
Whiting et al. (2020)	14/62 (22.6%)	41/48 (85.4%)	7/48 (14.6%)	27/63 (42.8%)
White et al. (2018)	12/36 (33%)	18/36 (50%)	16/24 (66.7%)	–
Motomura et al. (2017)	9/25 (36%)	7/16 (43.8%)	9/16 (56.2%)	–
Mehdorn et al. (2017)	–	–	–	–
Zhuang et al. (2016)	16/30 (53%) GTR	–	–	23/30 (77%)
Ghinda et al. (2016)	44/106 (41.5%)	30/62 (48.4%)	32/62 (51.6%)	64/106 (60.4%)
Coburger et al. (2015)	–		–	17/26 (65.4%)
Maldaun et al. (2014)	–	17/42 (40.5%)	25/42 (59.5%)	17/42 gross total (40.5%) (grace to intraoperative MRI 7/17 [41%])
Tuominen et al. (2013)	–		–	10/20 (50%) complete
Lu et al. (2012)	11/30 (36.7%)	11/30 (36.7%)	19/30 (63.3%)	18/30 (60%) complete (grace to intraoperative MRI 7/18 [60%])
Leuthardt et al. (2011)	7/12 (58.3%)	6/12 (50%)	5/12 (41.7%)	5/12 (41.7%) complete
				2/12 (16.7%) nearly total
				5/12 (41.7%) subtotal
Weingarten et al. (2009)	1/10 (10%)	7/9 (77.8%)	2/9 (22.2%)	7/10 (70%) complete 3/10 (30%) to an eloquent margin

Intractable epilepsy: a multidisciplinary assessment using SEEG

For patients with intractable epilepsy or unknown or doubtful origin, SEEG was used before any microsurgical resection is performed, even in the case of an identified structural lesion on preoperative MRI. This is the standard approach together with the specialised team in our hospital.

The histological diagnosis for cases with intractable epilepsy (n= 5) in the present series was cortical dysplasia in 3 (16.7%), gliosis and cavernoma in 1 (5.6%) each, respectively.

Results

The mean operative time and duration of intraoperative MRI, lesion remnant, pre- and postoperative deficits are presented in table 3, showing a mean duration of microsurgery of 4.1 hours (median 4.2, range 2.6−6.4) and intraoperative MRI of 28.8 minutes (median 25, range 13−55; figure 3). The tumour remnants were most commonly located posterior (5/9) or anterior (2/9) insular and in proximity with the motor strip (1/9) or language areas (e.g. Broca, 1/9).

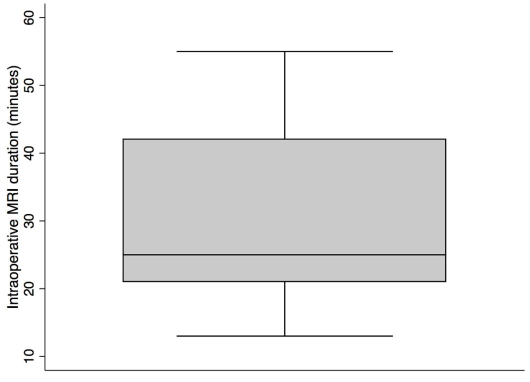
Microsurgery for primary brain tumours: further resection after the first intraoperative MRI and potential adjuvant therapies

The mean preoperative tumour volume of the primary brain tumours was 34.7 cc (median 10.7, range 0.534−130.25; standard deviation 41.2 cc).

Overall, 61% (11/18) of cases underwent further resection, with no further resection in seven patients because there were no remnants (3/7), cortical stimulation approaching eloquent areas (3/7) and non-lesional epilepsy (1/7).

The mean postoperative volume was 3.8 cc (median 0.5, range 0−17.4; standard deviation 5.6 cc; figure 4, upper level, absolute values, in cc; lower level, in percentages, according to the reference preoperative volume of 100%). A Mann-Whitney test was performed to compare the mean perioperative tumour volumes (in cc) resected at the time of intraoperative MRI and the final resected tumour volumes showing that they were not statistically significant (p= 0.6, figure 4, upper part). However, the total tumour volumes resected at the time of intraoperative MRI (as by 100% tumour volumes preoperatively) compared to the final results were statistically significant (p= 0.01, figure 4, lower part).

Figure 3: Intraoperative MRI duration (minutes).



After multidisciplinary discussion, 8 (8/13, 61.5%) cases benefitted from a standard protocol of combined radiotherapy (50.4 Gy) and six cycles of Temozolomide, 1 patient (1/13, 7.7%) was involved in the EORTC 1709 (the Stupp protocol plus Marizomib) and two (2/13, 15.4%) cases were subsequently followed-up.

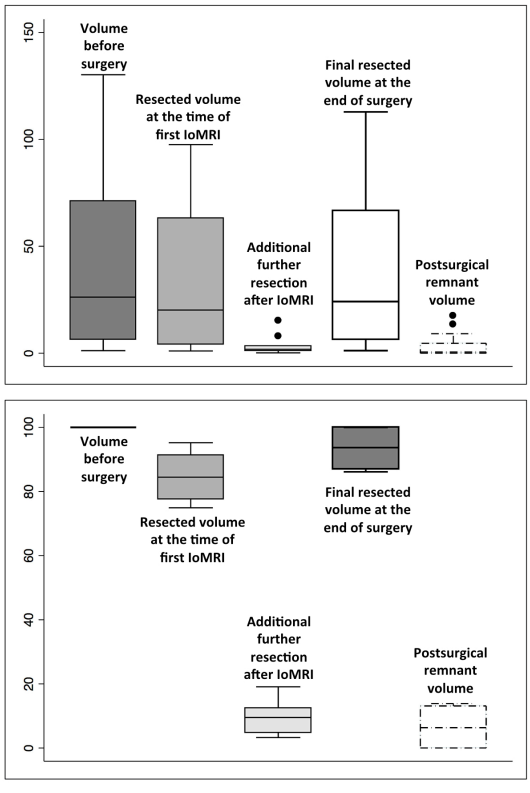
At the last follow-up, 12 (12/13, 92.3%) patients had volumetric tumour stability or a decreased volume. One (7.7%) patient with oligoastrocytoma WHO II required further surgery at 21.6 months after the first resection due to volumetric progression and drug-resistant epilepsy, with LPFS achieved (see figure 5).

A short review of the literature on this topic is provided in table 2, presenting the initial complete resection rates, as well as those at the end of the surgery. The mean initial resection rate at the time of the first intraoperative MRI was 36.4% (median 36.3, range 10−58.3) and at the end of surgery was 56.4% (median 60, range 40.5−77).

Microsurgery for epilepsy: further resection after the first intraoperative MRI and clinical outcome

One case with cortical dysplasia type IIb underwent further surgery after the initial procedure. The patients with cortical dysplasia had, among the epilepsy cases, the longest follow-up in the present series and all experienced a major decrease in seizure frequency and duration (see table 3 for the Engel classes).

Figure 4: The impact of intraoperative MRI on the microsurgical resection in terms of volumes (as cc, upper side; as percentages, lower side).



The patient with non-lesional epilepsy (number 17) experienced no crisis to date (3-month follow-up, previously several crises per week) and the patient with cavernoma had no seizures after 3 months of follow-up.

Neurological complications

Transient neurological complications were encountered in 3/18 (16.7%) cases, each one with transient hemiparesis, ataxia and dysgraphia, and right-hand hypoesthesia.

Definitive neurological complications occurred in 2/18 (11.1%) patients, each with neuropathic pain and partial motor seizures and right-hand hypoesthesia, respectively.

Neuropsychological exam and Karnofsky performance status

A neuropsychological exam was performed in 5 cases with no statistically significant difference between the pre-and postoperative assessment (table 4). Also, there was no sta-

Table 3:
Operative time and duration of intraoperative MRI, lesion remnants, pre- and postoperative deficits.

Pts	Total operative time (hours)	Scanning time for intraoperative MRI (min)	Remnant anatomical location during intraoperative MRI	Further surgery after intraoperative MRI	Remnant at the end of the surgery	Preoperative deficit	Postoperative deficit
#1	3h:23	0h:42	Left frontal, in contact with the lenticular nucleus	Yes, approaching the intraoperative MRI residual part	Insular, anterior and superior	None	None
#2	5h:48	0h:32	Insular and frontal internal	Yes, approaching the internal part	Insular posterior and temporo-polar	None	Transient right hemiparesis
#3	3h:05	0h:28	Posterior, at the interface with the motor cortex	Yes, optimizing the resection	Posterior, at the interface with the motor cortex	None	Transient supplementary motor area syndrome
#4	5h:16	0h:19	-	Yes, optimising the extent of resection	Insular, behind the superior temporal gyrus	None	None. No postoperative partial seizures (under Vimpat 400 mg/day) (Engel IA)
#5	4h:14	0h:25	Anterior, within the inferior part of the intraparietal sulcus area where paresthesias were encountered during cortical stimulation	Yes, optimising the extent of resection	None	Right upper limb ataxia	Preexistent right upper limb ataxia became more important. Profound sensibility problems. Neuropathic pain (left lower limb). Partial motor seizures (Engel IIB)
#6	4h:29	0h:18	Insular and fronto-basal	Yes, approaching the fronto-basal part	Insular	None	None. Seizure disappearance (Engel IA)
#7	4h:04	0h:21	Minimal, between postcentral&cingulate sulcus	Yes, approaching the remnant part	None	None	Ataxia, well alleviated. Dysgraphia, disappeared
#8	-	0h:21	None	Not applicable (no remnant)	None	None	None. Emotional issues due to the awake surgery
#9	4h:40	0h:43	Anterior and inferior at the level of the surgical cavity	Not possible as per intraoperative cortical stimulation	Anterior and inferior at the level of the surgical cavity	Right superior upper limb deficit	Worsening of right superior upper limb deficit
	3h:31		Anterior and inferior at the level of the surgical cavity	Not possible as per intraoperative cortical stimulation	Anterior and inferior at the level of the surgical cavity	Right superior upper limb deficit	Stability
#10	4h:04	0h:13	Left inferior parietal	Yes, approaching the remnant part	None	None	Postoperative stability of neuropsychological exam
#11	5h:16	0h:55	Left frontal superior and temporoinsular	Yes, approaching the left frontal superior	Temporo-insular	None	None
#12	6h:38	0h:25	Left posterior T1 and insular	Yes, approaching both parts	Temporo-insular	None	None
#13	4h:50	0h:25	None	Not applicable	Not applicable	None	Transient right-hand hypoesthesia. Decrease in seizure frequency (Engel IIB)
#14	5h:30	0h:52	Intraventricular (plus Flair remnant, left untouched due to its anatomical location)	Yes, approaching the intraventricular part	Flair remnant in functional areas (Broca); contrast-enhancing part completely resected)	None	None
#15	2h:58	0h: 32	Minimal left fronto-opercular remnant due to transient language arrest	Not possible as per intraoperative cortical stimulation	Left fronto-opercular due to transient language arrest	None	None
#16	4h:29	0h:19	The vast majority of the lesion (microsurgical resection just at the anterior pole of it)	Yes, approaching the lesion	None	None	None
#17	3h:13	0h:26	Non-lesional epilepsy	No, unnecessary	Not applicable	None	None
#18	2h:56	0h:22	None	Not applicable	Not applicable	None	None

* The only left-handed patient was number 6 with bilateral language areas on fMRI

tistically significant difference between the pre-and post-operative Karnofsky performance status (table 4).

Discussion

The present study evaluated our preliminary results of the combined technique of awake microsurgical resection and

Figure 5: Illustrative case of an oligodendroglioma WHO II, 1p19q co-deleted.

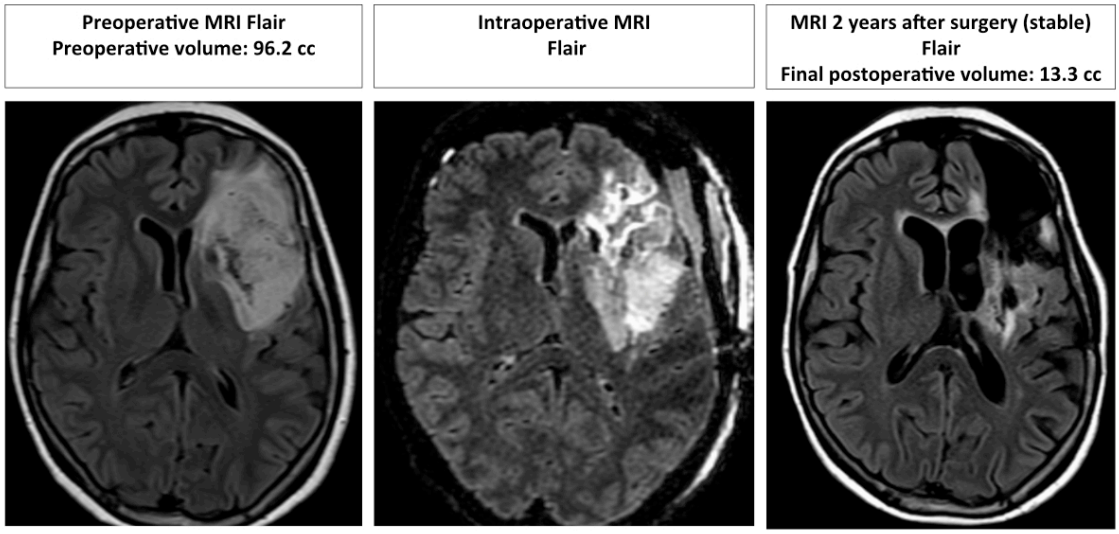


Table 4:
Pre- and postoperative neuropsychological exam and pre- and postoperative OMS and Karnofsky performed depending on the pathology.

Pts	Preoperative neuropsychological exam	Postoperative neuropsychological exam	Pre- and postoperative OMS (when relevant)	Pre- and postoperative Karnofsky (when relevant)
#1	IQ = 91, VIQ = 86, PIQ = 100	IQ = 94, VIQ = 81, PIQ = 114	–	–
	–: verbal LTM, verbal WM, VA, PS	–: verbal LTM, verbal WM, PS		
#2	–: verbal WM	–	1–1	100–90
#3	IQ = 89, VIQ = 102, PIQ = 72	IQ = 86, VIQ = 92, PIQ = 81	–	–
	–: VC, VF, PS	–: VC, VF, PS		
#4	–	–	0–0	100–100
#5	MoCA: 27/30	MoCA: 26/30	0–0	100–100
	–: verbal WM	–: IC, PS		
#6	MoCA: 27/30	MoCA: 25/30	0–0	100–100
	–: verbal WM, IC, VF, PS	–: verbal WM, IC, PS		
#7	MoCA: 29/30	MoCA: 28/30	0–0	100–90
	Normal	–: DA		
#8	MoCA: 28/30	MoCA: 27/30	0–0	100–90
	–: verbal WM, IC, VF	–: verbal WM, VF, PS		
#9	–	–		
#10	IQ = 80, VIQ = 78, PIQ = 83	IQ = 85, VIQ = 76, PIQ = 100	–	–
	–: verbal WM, IC, VF	–: verbal WM, VF		
#11	MoCA: 28/30	–	0–1	100–80
	–: verbal LTM			
#12	MoCA: 22/30	–	0–0	90–90
	–: VC, LTM, IC, VF, PS			
#13	–	–	1–1	90–90
#14	MoCA: 26/30	MMSE: 26/30	0–0	100–100
	–: verbal LTM, verbal WM, IC, VF	–		
#15	–: VC, verbal WM, S, IC, DA	–	0–0	90–90
#16	MoCA: 26/30	–	0–0	100–100
	normal			
#17	IQ = 76, VIQ = 76, PIQ = 82	–		
	–: verbal LTM, verbal WM, IC, VF, PS			
#18	MoCA: 30/30	MoCA: 28/30		
	Normal	Normal		

DA: divided attention, IC: inhibitory control, LTM: long-term memory, PIQ: P IQ, PS: processing speed, S: shifting, VA: visual attention, VC: visuo construction, VF: verbal fluency, VIQ: verbal IQ, WM: working memory

intraoperative MRI for primary brain tumours (including gliomas and brain metastasis) and epilepsy surgery (including cortical dysplasia, non-lesional epilepsy, and cavernoma). The combined intraoperative MRI and awake microsurgical resection is a challenging approach and the patient needs to be cooperative and motivated to participate in all language and/or motor tasks. The role of the anesthesiologist is crucial, both preoperatively (determining if the patient is a suitable candidate, medically and emotionally) and intraoperatively, while maintaining anT appropriate level of anaesthesia and analgesia. There is also much real-time information for the surgeon to process, so this approach requires a skilled and cohesive operative team and a compliant patient.

The anaesthetic technique in an awake brain surgical procedure varies from light or deep sedation [32] to general anaesthesia with an endotracheal tube [33] or laryngeal mask [34]. The anaesthetic goals are mainly to maintain an awake and cooperative patient during cortical mapping while ensuring the safety of the airway, and providing adequate cerebral perfusion and brain relaxation [35]. Inherent challenges are desaturation or hypercapnia during surgery and it is possible that this awake-asleep-awake (AAA) paradigm would potentially interfere with intra-operative testing of the respective eloquent areas due to anaesthesia remnants. Therefore, to avoid such interference, we use a laryngeal mask and Remifentanil, a short-acting synthetic opioid analgesic. The advantage of such a drug is that the context-sensitive half-life remains at 4 minutes after, for example, 4 hours of administration [36] and it is also associated with fewer seizures compared with other opioids. In general, factors that might potentially modulate the effects of anaesthetic agents include but are not limited to, patient age, physical and medical conditions, and pharmacogenetics. Also, dural local anaesthetics are used once the patient is awake. To date, no randomised trials comparing our approach with the awake tumour resection under local anaesthetic [37] have been performed but it is acknowledged that awake tumour resection can be completed using only local anaesthesia [38]. Nevertheless, in our experience, using sedative drugs can be particularly helpful for craniotomy and closure. Due to a lack of comparative studies, there is no evidence showing the superiority of one technique over the other [39].

Of note, the craniotomy is performed when the patient is asleep and the dura mater is not opened during this first step. Once the patient is awake, completely stable and calm, the dura mater is infiltrated to further proceed to its opening, thereby avoiding increased intraoperative intracranial pressure in the transition from asleep to awake with its potential inherent consequences.

The entry cortical point is always selected using the neuronavigation system and if this point is formally contraindicated after cortical stimulation, we proceed to further changes. Indeed, the response of the cortical stimulation provides multiple possibilities for cortical routes and the cranial flap is designed to provide enough room. Naropein-immersed cottonwoods are not used on the dura for local anaesthesia [40], rather the dura is indirectly infiltrated [41]. Importantly, the brain is not pain sensitive, while the basal dura and larger vessel manipulation could potentially engender pain [42].

Cortical stimulation can generate seizures, with an incidence of 5−20% [43]. In our centre, these episodes can be managed by cold Ringer's lactate solution irrigation of the cortex and patience without the need for intravenous antiepileptic medication [44].

The interruption time due to the intraoperative MRI is usually small, around 30 minutes (15 minutes couch in, 15 minutes couch out).

With regards to the use of such an approach for primary brain tumours and particularly for gliomas, the literature review [11, 17, 20−25, 29−31] shows a clear benefit, increasing the mean extent of resection by approximately 20% for primary brain tumours. Tuominen et al. [24] showed that this approach reduces the risk of postoperative impairment following resection of tumours located in or near speech and motor areas, whilst Mehdorn et al. [23] suggested that there was a slight preponderance in redo surgeries for tumour remnants in the first (11.2%, before the use of intraoperative MRI) compared to the second period (7.4%, after the use of intraoperative MRI). Moreover, interestingly, patients with low-grade gliomas in the second series (using intraoperative MRI) did not experience recurrences as frequently as those in the first series.

The aim of epilepsy surgery is either complete excision or disconnection of the epileptic network while conserving the structure and function of the eloquent cortex [45]; we consider that presurgical correct diagnosis is mandatory for this. Modern epileptologists can use multimodal diagnostic tools, including semiology analysis, electrophysiological recordings, functional testing and complex neuroimaging techniques [45], complementary modalities that define the location and boundaries of the epileptic zone. In challenging cases, stereo-electroencephalography (SEEG) by depth electrodes is considered [46]. The existence of a lesion does not automatically relate to an epileptogenic network solely driven by that specific lesion. Moreover, a lesion can recruit and further drive other epileptogenic zones in the brain, making diagnosis even more challenging [47, 48]. In our experience, SEEG is used when necessary to establish a preoperative project, which proposes an area of microsurgical resection including the electrodes for which intraoperative MRI can refine the pre-planned resection area and evaluate the extent of resection. Together with subcortical mapping and other aiding tools, the surgeon can determine whether further resection is required. The awake component remains crucial for function preservation, thus complete resection becomes strictly related to an SEEG preoperative project.

The infection rate in these particular procedures involving intraoperative MRI and additional staff is approximately 1.2%, which is similar to our overall cohort in classical brain surgeries.

The present study has several inherent limitations. First, the retrospective nature of this study with all the inherent bias. Second, there may be small variations in the volumetric analysis depending on the slice thickness etc. A third limitation is the inclusion of multiple pathologies such as gliomas, brain metastasis, cavernomas, cortical dysplasia etc. However, they all share the same goal, which is for infiltrative brain tumours, the gross-total resection and for others, microsurgical resection while respecting functional neural networks present at their boundaries.

Conclusion

Intraoperative MRI and awake microsurgical resection is a feasible approach with extensive planning and multidisciplinary collaboration. These two methods can be considered complementary and synergic rather than competitive, aimed at improving patient oncological outcomes and quality of life. This case series shows a statistical significance when comparing the percentage initially resected at the time of intraoperative MRI and the final extent of resection for primary brain tumours and although the series is small, these results might translate to a clear neurooncological benefit if extended to a large population of patients.

Funding

Constantin Tuleasca gratefully acknowledges receipt of a "Young Researcher in Clinical Research Grant" (Jeune Chercheur en Recherche Clinique) from the University of Lausanne (UNIL), Faculty of Biology and Medicine (FBM) and the Lausanne University Hospital (CHUV). Lausanne University Hospital and University of Lausanne.

Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

References

1. Lapointe S , Perry A , Butowski NA . Primary brain tumours in adults. Lancet. 2018 Aug;392(10145):432–46. http://dx.doi.org/10.1016/S0140-6736(18)30990-5.
2. Berger MS , Rostomily RC . Low grade gliomas: functional mapping resection strategies, extent of resection, and outcome. J Neurooncol. 1997 Aug;34(1):85–101. http://dx.doi.org/10.1023/A:1005715405413.
3. Laws ER , Parney IF , Huang W , Anderson F , Morris AM , Asher A , et al.; Glioma Outcomes Investigators . Survival following surgery and prognostic factors for recently diagnosed malignant glioma: data from the Glioma Outcomes Project. J Neurosurg. 2003 Sep;99(3):467–73. http://dx.doi.org/10.3171/jns.2003.99.3.0467.
4. Sanai N , Berger MS . Glioma extent of resection and its impact on patient outcome. Neurosurgery. 2008 Apr;62(4):753–64. http://dx.doi.org/10.1227/01.neu.0000318159.21731.cf.
5. Berger MS , Deliganis AV , Dobbins J , Keles GE . The effect of extent of resection on recurrence in patients with low grade cerebral hemisphere gliomas. Cancer. 1994 Sep;74(6):1784–91. http://dx.doi.org/10.1002/1097-0142(19940915)74:6<1784::AID-CNCR2820740622>3.0.CO;2-D.
6. Martin C , Alexander E 3rd , Wong T , Schwartz R , Jolesz F , Black PM . Surgical treatment of low-grade gliomas in the intraoperative magnetic resonance imager. Neurosurg Focus. 1998 Apr;4(4):e8. http://dx.doi.org/10.3171/foc.1998.4.4.11.
7. Stummer W , Novotny A , Stepp H , Goetz C , Bise K , Reulen HJ . Fluorescence-guided resection of glioblastoma multiforme by using 5-aminolevulinic acid-induced porphyrins: a prospective study in 52 consecutive patients. J Neurosurg. 2000 Dec;93(6):1003–13. http://dx.doi.org/10.3171/jns.2000.93.6.1003.
8. Stummer W , Pichlmeier U , Meinel T , Wiestler OD , Zanella F , Reulen HJ ; ALA-Glioma Study Group . Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. Lancet Oncol. 2006 May;7(5):392–401. http://dx.doi.org/10.1016/S1470-2045(06)70665-9.
9. Oh DS , Black PM . A low-field intraoperative MRI system for glioma surgery: is it worthwhile? Neurosurg Clin N Am. 2005 Jan;16(1):135–41. http://dx.doi.org/10.1016/j.nec.2004.07.010.
10. Schulder M , Carmel PW . Intraoperative magnetic resonance imaging: impact on brain tumor surgery. Cancer Contr. 2003;10(2):115–24. http://dx.doi.org/10.1177/107327480301000203.
11. Coburger J , Merkel A , Scherer M , Schwartz F , Gessler F , Roder C , et al. Low-grade Glioma Surgery in Intraoperative Magnetic Resonance Imaging: Results of a Multicenter Retrospective Assessment of the German Study Group for Intraoperative Magnetic Resonance Imaging. Neurosurgery. 2016 Jun;78(6):775–86. http://dx.doi.org/10.1227/NEU.0000000000001081.
12. Coburger J , Wirtz CR . Fluorescence guided surgery by 5-ALA and intraoperative MRI in high grade glioma: a systematic review. J Neurooncol. 2019 Feb;141(3):533–46. http://dx.doi.org/10.1007/s11060-018-03052-4.
13. Berger MS , Kincaid J , Ojemann GA , Lettich E . Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. Neurosurgery. 1989 Nov;25(5):786–92. http://dx.doi.org/10.1227/00006123-198911000-00015.
14. Duffau H . Intraoperative cortico-subcortical stimulations in surgery of low-grade gliomas. Expert Rev Neurother. 2005 Jul;5(4):473–85. http://dx.doi.org/10.1586/14737175.5.4.473.
15. Ojemann G , Ojemann J , Lettich E , Berger M . Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurg. 1989 Sep;71(3):316–26. http://dx.doi.org/10.3171/jns.1989.71.3.0316.
16. Zanello M , Meyer B , Still M , Goodden JR , Colle H , Schichor C , et al. Surgical resection of cavernous angioma located within eloquent brain areas: international survey of the practical management among 19 specialized centers. Seizure. 2019 Jul;69:31–40. http://dx.doi.org/10.1016/j.seizure.2019.03.022.
17. Motomura K , Natsume A , Iijima K , Kuramitsu S , Fujii M , Yamamoto T , et al. Surgical benefits of combined awake craniotomy and intraoperative magnetic resonance imaging for gliomas associated with eloquent areas. J Neurosurg. 2017 Oct;127(4):790–7. http://dx.doi.org/10.3171/2016.9.JNS16152.
18. Tuleasca C , Leroy HA , Peciu-Florianu I , Strachowski O , Derre B , Levivier M , et al. Impact of combined use of intraoperative MRI and awake microsurgical resection on patients with gliomas: a systematic review and meta-analysis. Neurosurg Rev. 2021 Dec;44(6):2977–90. http://dx.doi.org/10.1007/s10143-021-01488-3.
19. Ghinda D , Zhang N , Lu J , Yao CJ , Yuan S , Wu JS . Contribution of combined intraoperative electrophysiological investigation with 3-T intraoperative MRI for awake cerebral glioma surgery: comprehensive review of the clinical implications and radiological outcomes. Neurosurg Focus. 2016 Mar;40(3):E14. http://dx.doi.org/10.3171/2015.12.FOCUS15572.
20. Leuthardt EC , Lim CC , Shah MN , Evans JA , Rich KM , Dacey RG , et al. Use of movable high-field-strength intraoperative magnetic resonance imaging with awake craniotomies for resection of gliomas: preliminary experience. Neurosurgery. 2011;69(1):194-205; discussion -6. http://dx.doi.org/10.1227/NEU.0b013e31821d0e4c.
21. Lu J , Wu J , Yao C , Zhuang D , Qiu T , Hu X , et al. Awake language mapping and 3-Tesla intraoperative MRI-guided volumetric resection for gliomas in language areas. J Clin Neurosci. 2013 Sep;20(9):1280–7. http://dx.doi.org/10.1016/j.jocn.2012.10.042.
22. Maldaun MV , Khawja SN , Levine NB , Rao G , Lang FF , Weinberg JS , et al. Awake craniotomy for gliomas in a high-field intraoperative magnetic resonance imaging suite: analysis of 42 cases. J Neurosurg. 2014 Oct;121(4):810–7. http://dx.doi.org/10.3171/2014.6.JNS132285.
23. Mehdorn HM , Schwartz F , Becker J . Awake Craniotomy for Tumor Resection: Further Optimizing Therapy of Brain Tumors. Acta Neurochir Suppl (Wien). 2017;124:309–13. http://dx.doi.org/10.1007/978-3-319-39546-3_45.
24. Tuominen J , Yrjänä S , Ukkonen A , Koivukangas J . Awake craniotomy may further improve neurological outcome of intraoperative MRI-guided brain tumor surgery. Acta Neurochir (Wien). 2013 Oct;155(10):1805–12. http://dx.doi.org/10.1007/s00701-013-1837-3.
25. Whiting BB , Lee BS , Mahadev V , Borghei-Razavi H , Ahuja S , Jia X , et al. Combined use of minimal access craniotomy, intraoperative magnetic resonance imaging, and awake functional mapping for the resection of gliomas in 61 patients. J Neurosurg. 2019:1–9.
26. Reyns N , Leroy HA , Delmaire C , Derre B , Le-Rhun E , Lejeune JP . Intraoperative MRI for the management of brain lesions adjacent to eloquent areas. Neurochirurgie. 2017 Jun;63(3):181–8. http://dx.doi.org/10.1016/j.neuchi.2016.12.006.
27. Nabavi A , Goebel S , Doerner L , Warneke N , Ulmer S , Mehdorn M . Awake craniotomy and intraoperative magnetic resonance imaging: patient selection, preparation, and technique. Top Magn Reson Imaging. 2009 Jan;19(4):191–6. http://dx.doi.org/10.1097/RMR.0b013e3181963b46.
28. Leroy HA , Delmaire C , Le Rhun E , Drumez E , Lejeune JP , Reyns N . High-field intraoperative MRI and glioma surgery: results after the first 100 consecutive patients. Acta Neurochir (Wien). 2019 Jul;161(7):1467–74. http://dx.doi.org/10.1007/s00701-019-03920-6.
29. Weingarten DM , Asthagiri AR , Butman JA , Sato S , Wiggs EA , Damaska B , et al. Cortical mapping and frameless stereotactic navigation in the high-field intraoperative magnetic resonance imaging suite. J

Neurosurg. 2009 Dec;111(6):1185–90. http://dx.doi.org/10.3171/2009.5.JNS09164.

30. White T , Zavarella S , Jarchin L , Nardi D , Schaffer S , Schulder M . Combined Brain Mapping and Compact Intraoperative MRI for Brain Tumor Resection. Stereotact Funct Neurosurg. 2018;96(3):172–81. http://dx.doi.org/10.1159/000488991.
31. Zhuang DX , Wu JS , Yao CJ , Qiu TM , Lu JF , Zhu FP , et al. Intraoperative Multi-Information-Guided Resection of Dominant-Sided Insular Gliomas in a 3-T Intraoperative Magnetic Resonance Imaging Integrated Neurosurgical Suite. World Neurosurg. 2016 May;89:84–92. http://dx.doi.org/10.1016/j.wneu.2016.01.067.
32. Hervey-Jumper SL , Li J , Lau D , Molinaro AM , Perry DW , Meng L , et al. Awake craniotomy to maximize glioma resection: methods and technical nuances over a 27-year period. J Neurosurg. 2015 Aug;123(2):325–39. http://dx.doi.org/10.3171/2014.10.JNS141520.
33. Huncke K , Van de Wiele B , Fried I , Rubinstein EH . The asleep-awake-asleep anesthetic technique for intraoperative language mapping. Neurosurgery. 1998 Jun;42(6):1312–6. http://dx.doi.org/10.1097/00006123-199806000-00069.
34. Piccioni F , Fanzio M . Management of anesthesia in awake craniotomy. Minerva Anestesiol. 2008;74(7-8):393–408.
35. Meng L , Berger MS , Gelb AW . The Potential Benefits of Awake Craniotomy for Brain Tumor Resection: An Anesthesiologist's Perspective. J Neurosurg Anesthesiol. 2015 Oct;27(4):310–7. http://dx.doi.org/10.1097/ANA.0000000000000179.
36. Komatsu R , Turan AM , Orhan-Sungur M , McGuire J , Radke OC , Apfel CC . Remifentanil for general anaesthesia: a systematic review. Anaesthesia. 2007 Dec;62(12):1266–80. http://dx.doi.org/10.1111/j.1365-2044.2007.05221.x.
37. Potters JW , Klimek M . Local anesthetics for brain tumor resection: current perspectives. Local Reg Anesth. 2018 Feb;11:1–8. http://dx.doi.org/10.2147/LRA.S135413.
38. Danks RA , Rogers M , Aglio LS , Gugino LD , Black PM . Patient tolerance of craniotomy performed with the patient under local anesthesia and monitored conscious sedation. Neurosurgery. 1998;42(1):28-34; discussion -6. http://dx.doi.org/10.1097/00006123-199801000-00006.
39. Danks RA , Aglio LS , Gugino LD , Black PM . Craniotomy under local anesthesia and monitored conscious sedation for the resection of tumors involving eloquent cortex. J Neurooncol. 2000 Sep;49(2):131–9. http://dx.doi.org/10.1023/A:1026577518902.
40. Chowdhury T , Singh GP , Zeiler FA , Hailu A , Loewen H , Schaller B , et al. Anesthesia for Awake Craniotomy for Brain Tumors in an Intraoperative MRI Suite: challenges and Evidence. Front Oncol. 2018 Nov;8:519. http://dx.doi.org/10.3389/fonc.2018.00519.
41. Duffau H . Awake surgery for nonlanguage mapping. Neurosurgery. 2010 Mar;66(3):523–8. http://dx.doi.org/10.1227/01.NEU.0000364996.97762.73.
42. Fontaine D , Almairac F , Santucci S , Fernandez C , Dallel R , Pallud J , et al. Dural and pial pain-sensitive structures in humans: new inputs from awake craniotomies. Brain. 2018 Apr;141(4):1040–8. http://dx.doi.org/10.1093/brain/awy005.
43. Sartorius CJ , Wright G . Intraoperative brain mapping in a community setting—technical considerations. Surg Neurol. 1997 Apr;47(4):380–8. http://dx.doi.org/10.1016/S0090-3019(96)00340-0.
44. Sartorius CJ , Berger MS . Rapid termination of intraoperative stimulation-evoked seizures with application of cold Ringer's lactate to the cortex. Technical note. J Neurosurg. 1998 Feb;88(2):349–51. http://dx.doi.org/10.3171/jns.1998.88.2.0349.
45. Rosenow F , Lüders H . Presurgical evaluation of epilepsy. Brain. 2001 Sep;124(Pt 9):1683–700. http://dx.doi.org/10.1093/brain/124.9.1683.
46. Thorsteinsdottir J , Vollmar C , Tonn JC , Kreth FW , Noachtar S , Peraud A . Outcome after individualized stereoelectroencephalography (sEEG) implantation and navigated resection in patients with lesional and non-lesional focal epilepsy. J Neurol. 2019 Apr;266(4):910–20. http://dx.doi.org/10.1007/s00415-019-09213-3.
47. Luders HO , Najm I , Nair D , Widdess-Walsh P , Bingman W . The epileptogenic zone: general principles. Epileptic disorders : international epilepsy journal with videotape. 2006;8 Suppl 2:S1-9.
48. Abel TJ , Woodroffe RW , Nourski KV , Moritani T , Capizzano AA , Kirby P , et al. Role of the temporal pole in temporal lobe epilepsy seizure networks: an intracranial electrode investigation. J Neurosurg. 2018 Jul;129(1):165–73. http://dx.doi.org/10.3171/2017.3.JNS162821.