



DOI: 10.5137/1019-5149.JTN.18346-16.1

Received: 31.05.2016 / Accepted: 23.08.2016

Published Online: 20.09.2016

Original Investigation

Optimizing the Extent of Resection and Minimizing the Morbidity in Insular High-Grade Glioma Surgery by High-Field Intraoperative MRI Guidance

Li-feng CHEN^{1,*}, Yang YANG^{2,*}, Xiao-dong MA¹, Xin-guang YU¹, Qiu-ping GUI³, Bai-nan XU¹, Ding-biao ZHOU¹

¹The Chinese PLA General Hospital, Department of Neurosurgery, Beijing, China

²The Chinese PLA General Hospital, Department of Geriatric Neurology, Beijing, China

³The Chinese PLA General Hospital, Department of Pathology, Beijing, China

*Drs. CHEN and YANG contributed equally to the manuscript.

ABSTRACT

AIM: The result of surgical resection for insular high-grade glioma (HGG) is disappointing due to the complex anatomy of insula and aggressive growth of HGG. The use of intraoperative magnetic resonance imaging (iMRI) was reported to improve the results of glioma surgery. The authors aimed to evaluate the impact of high-field iMRI and functional neuronavigation on the surgical resection of insular HGG.

MATERIAL and METHODS: Between July 2010 and July 2014, 51 insular HGG patients underwent operations guided by combined high-field iMRI and functional neuronavigation. Twenty-two insular HGG patients underwent conventional neuronavigation operations were assessed as the control group. Preoperative and postoperative tumor volumetric scan analysis, Karnofsky performance score (KPS) and follow-up results were reviewed retrospectively.

RESULTS: Residual tumor was detected by the iMRI in 42 patients, and residual tumor of 37 patients was further resected in the iMRI-assisted group. The median extent of resection (EOR) increased significantly from 79% (58%–100%) to [96% (86%–100%), $p < 0.001$]. The median EOR of iMRI-assisted group [96% (86%–100%)] was significantly higher than that of conventional neuronavigation group [84% (69%–100%); $p = 0.031$]. Mean residual tumor volume of iMRI-assisted group [0.6 (0.0–5.2) cm^3] was significantly smaller than that of conventional neuronavigation group [3.8 (0.0–12.1) cm^3 ; $p = 0.003$]. KPS within 3 days after surgery reduced and KPS at 3 months after surgery improved for both groups. KPS of iMRI-assisted group [90(70–100)] was significantly higher than that of control group [80(60–100); $p = 0.021$] at 3 months after surgery. The median progression-free survival (PFS) of iMRI-assisted group [18(9–42) months] was better than that of control group [15(3–32) months; $p = 0.010$]. The median overall survival (OS) of iMRI-assisted group [28(14–49) months] was better than that of control group [18 (7–38) months; $p = 0.035$].

CONCLUSION: Combined high-field iMRI and functional neuronavigation optimize the extent of resection and minimize the morbidity in insular HGG surgery. Aggressive resection of insular HGG is predictive of improved OS and PFS.

KEYWORDS: Intraoperative MRI, Extent of resection, Neuronavigation, Glioma, Surgery



Corresponding author: Xiao-Dong MA

E-mail: maxiaodong301@126.com

■ INTRODUCTION

Insula is a deep and complex anatomical region. Insular gliomas are not rare, making up more than 25% of all low grade gliomas (LGGs) and 10% of all high grade gliomas (HGGs) (7). Treatment options of insular gliomas remain controversial. The proximity of insular gliomas to critical eloquent cortices and tracts affecting motor, sensory, and language functions, as well as the microvasculature around the tumor serving important language and motor systems carry the high risk of surgical treatment (22).

Resecting insular gliomas is a challenging procedure for most neurosurgeons. The cost-benefit balance of insular HGGs surgery is even more unfavorable than in any other tumors due to short life expectancy of the HGG patient and high risk of insular tumor surgery in the past.

Yasargil and other authors (8-10,13,15,24,35,39,42,44,45) have reported resecting some groups of insular gliomas is possible with substantial but acceptable morbidity. In recent years, some surgical techniques including awake surgery, intraoperative monitoring, 5-aminolevulinic acid (5-ALA) and intraoperative magnetic resonance imaging (iMRI)-assisted surgery are evolving continuously (14,17,19,32). Although some studies have demonstrated the value of these techniques, their impact on clinical practice remains controversial (3,11,25).

Combined iMRI and functional neuronavigation has been shown to be helpful in achieving maximal tumor resection and minimal postoperative functional impairment in patients with various intra-axial tumors and pituitary adenomas, and glioma resection was frequently reported as an indication for iMRI-guided surgery (1,5,20,26-30). However, there are few reports describing the resection of insular HGGs guided by the iMRI system.

The goal of this retrospective study is to evaluate the additional value and superiority of high-field iMRI-guided insular HGG surgery over conventional neuronavigation surgery by comparing the extent of resection (EOR), neurological deficit, Karnofsky performance score (KPS), progression-free survival (PFS) and overall survival (OS).

■ MATERIAL and METHODS

Subjects

During a 4-year period between July 2010 and July 2014, 51 consecutive patients with histologically verified insular primary glioblastoma (GBM, glioma grade IV) or anaplastic astrocytoma (grade III) were treated using combined high-field iMRI and functional neuronavigation in the Department of Neurosurgery of our hospital. Twenty-two insular primary GBM (grade IV) or anaplastic astrocytoma (grade III) patients underwent conventional neuronavigation. All the patients gave informed consent. The study was approved by the Ethics Committee of the Chinese People's Liberation Army (PLA) General Hospital. The clinical information was reviewed by hospital charts, clinic notes, and operative reports.

Evaluation Methods

Gender, age, the neurological function, KPS, and neuroimaging evaluations of the patients were recorded preoperatively, within 3 days, and then every 3 months after surgery. The tumor volume of pre- and postoperative magnetic resonance (MR) imaging was analyzed by the same neurosurgeon. Manual segmentation was performed with region-of-interest analysis to measure tumor volumes (cm³) on the basis of contrast-enhancing tissue seen on post-contrast T1-weighted MR images or T2 fluid-attenuated inversion recovery sequence images. The EOR was classified as <80%, 80-89%, 90-99% and 100%. PFS was defined as the time from initial surgery and demonstration of an increase in tumor size on follow-up MR imaging. OS was defined as the time from initial surgery to death.

Image Acquisition

A dual-room high-field iMRI suite with a scanner of a movable 1.5T magnet (Siemens Espree, Erlangen, Germany) was installed at our hospital in February 2009 (4). Preoperative and intraoperative images were acquired, including 3D T1-weighted and postcontrast 3D T1-weighted magnetization-prepared rapid-acquisition gradient echo sequences, T2-weighted sequences, 3D T2 fluid-attenuated inversion recovery sequences and diffusion tensor images. The parameters of the scans have been reported in our previous publications (4,31,40,41,46).

Image Processing

The imaging data was processed by the neuronavigation planning software iPlan 2.6 (BrainLab, Feldkirchen, Germany). Details of the process are the same as our previous reports (4,31,40,41,46). The first step of image processing was conducting format conversion of the data and infusion of the different image sets. 3D reconstruction image of the tumor (40) was obtained by the object creation module of iPlan 2.6. Tumor segmentation was performed based on the postcontrast 3D T1-weighted anatomical dataset or 3D T2 fluid-attenuated inversion recovery sequence images dataset. The outermost rim of postcontrast 3D T1-weighted sequences or 3D T2 fluid-attenuated inversion recovery sequence images were defined as the border for segmentation. The tumor was outlined after segmentation was performed on a slice-by-slice basis in the 3D anatomical data mode. Then the tumor was reconstructed into a 3D object and the computer calculates the volume of the tumor.

The fiber tracking module of iPlan 2.6 based on a tensor deflection algorithm was used to reconstruct the pyramidal tract and the arcuate fasciculus. Seeds were placed on Broca's and Wernicke's areas to reconstruct the arcuate fasciculus. The first region of interest (ROI) and the second ROI were placed on the subcortical white matter in the precentral gyrus and the cerebral peduncle to reconstruct the motor tract, respectively. The first ROI and the second ROI were placed on the subcortical white matter in the postcentral gyrus and the cerebral peduncle to reconstruct the sensory tract, respectively.

Surgical Techniques

The surgery was performed under general anesthesia. Patients are positioned in a semilateral position with the head turned parallel to the floor. The surgical approaches include the transcortical approach and transsylvian approach. The neuronavigation microscope (Pentero; CarlZeiss, Oberkochen, Germany) could display the contour of the tumor and the functional data during surgery. All the processed image data were integrated for surgical planning and intraoperative neuronavigation (Figure 1A,B). After a conventional fronto-temporal craniotomy, cortical language area, arcuate fasciculus, and the pyramidal tract were identified using functional neuronavigation. The transcortical windows above and below the sylvian fissure were created through non-functional cortex, taking care to maintain at least a 0.5 cm margin from any functional site. All resections were continued until eloquent pathways and the lenticulostriate arteries were encountered around the surgical cavity, and then followed according to functional boundaries.

Statistical Methods

All descriptive and statistical analysis was performed using the Statistical Package for the Social Sciences version 19.0 (SPSS, Chicago, IL, USA). PFS, OS, and the efficacy of two treatment modalities were analyzed using the Kaplan-Meier Method.

We applied 100%, 90-99, 80-89, and < 80% EOR cutoffs to maintain consistency across this study for Kaplan-Meier curves plotting the EOR and OS or PFS.

Postoperative neurological complications at 3 days and 3 months after surgery were assessed and compared in the 2 groups. Categorical data was analyzed by Fisher's exact test. Parametric data was analyzed by t-test for unpaired samples. Nonparametric data was analyzed using the Mann-Whitney-U test. Statistical significance was declared at $p < 0.05$.

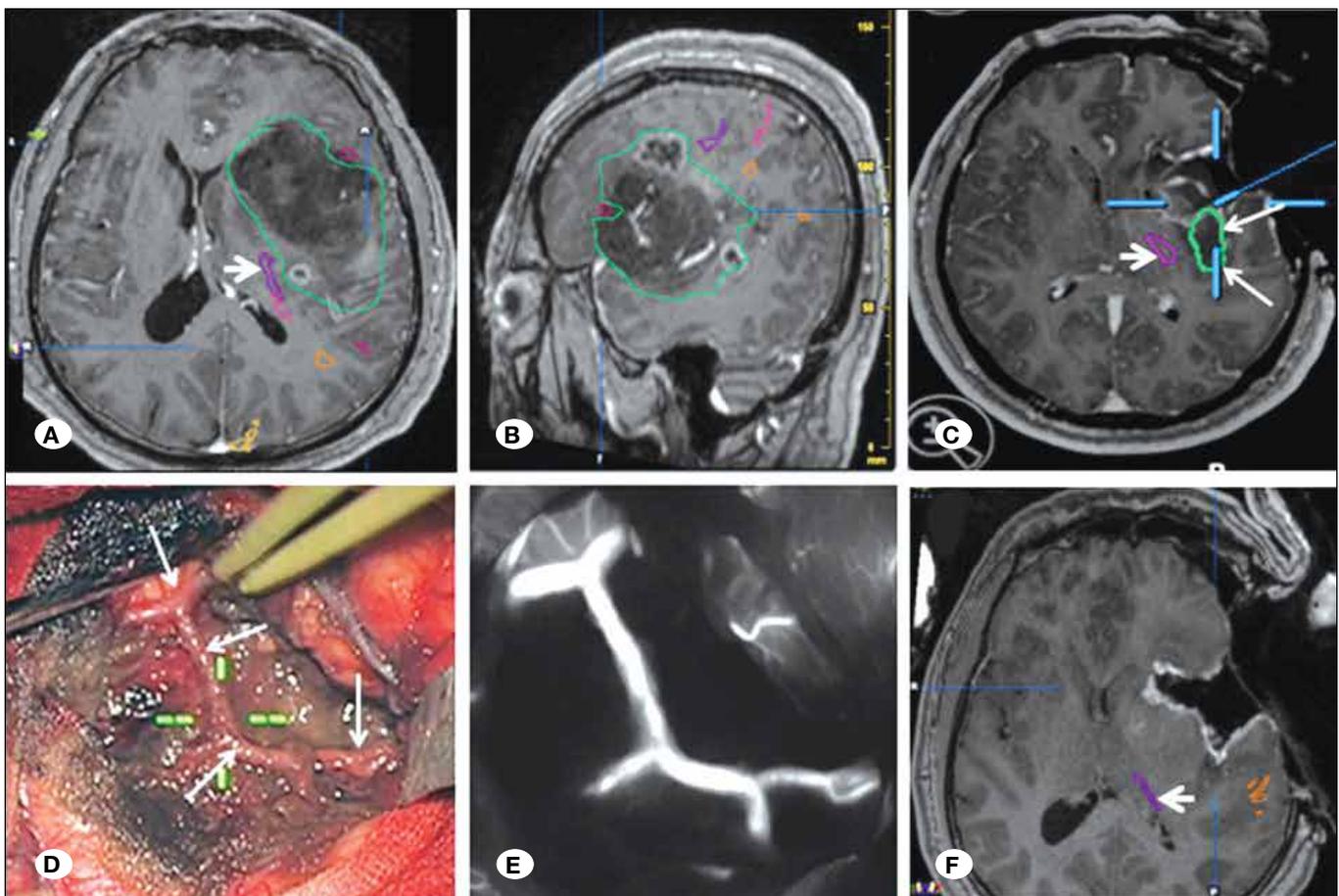


Figure 1: Illustrative case of a 51-year-old man with a giant left insular astrocytoma (grade III-IV), which was successfully removed. Preoperative axial (A) and sagittal (B) T1-weighted contrast-enhanced magnetic resonance imaging (MRI) scan showing a giant left insular glioma. First intraoperative axial T1-weighted contrast-enhanced MRI scan showing a residual mass (thin white arrows, C; 3.2 cm³) adjacent to the resection cavity (C). Middle cerebral artery (MCA) and its branches were seen and protected during resection (thin white arrows, D). Intraoperative fluorescent angiography demonstrated MCA and its branches were intact (E). Final intraoperative axial T1-weighted contrast-enhanced MRI scan after additional tumor removal was performed showing complete tumor removal (F). The pyramidal tract was intact during surgery (thick white arrows; A, C and F).

RESULTS

Preoperative Characteristics

The patients' demographics, the presenting symptoms, tumor location and volume were shown in Table I. The most common presenting symptom was seizure (50 cases, 68.5%). Preoperative neuroimaging studies showed glioma hypointense on T1-weighted image and hyperintense on T2-weighted image. Sixty-two GBMs showed enhancement on contrast-enhanced MRI in this series (Figure 2A,B).

Intraoperative MRI and Extent of Resection

The surgical approach, surgical time and postoperative hospital stay are shown in Table I. Residual tumor was detected by the iMRI in 42 patients (Figure 1C), and residual tumor of 37 patients was further resected in the iMRI-assisted group (Figure 1F). The median EOR increased significantly from 79% (58%–100%) to 96% (86%–100%) ($p < 0.001$) (Figure 3). The median EOR of iMRI-assisted group [96% (86%–100%)] was significantly higher than that of conventional neuronavigation group [84% (69%–100%); $p = 0.031$] (Table I).

Mean residual tumor volume of iMRI-assisted group [0.6 (0.0–5.2) cm^3] was significantly smaller than that of conventional neuronavigation group [3.8 (0.0–12.1) cm^3 ; $p = 0.003$] (Table I). The major impediment to gross-total resection (GTR) was the difficulty in dissection from the perforating vessels (Figure 1D,E).

Postoperative Course

There was no perioperative mortality. Table II and Figure 4 show that there is indeed a reduction of KPS at 3 days and improvement at 3 months after surgery for both groups of patients. KPS of iMRI-assisted group 90 (70–100) was significantly higher than that of control group [80 (60–100); $p = 0.021$] at 3 months after surgery (Table II, Figure 4). The other surgical outcome at 3 days and 3 months after surgery were summarized in Table II. The senior neuropathologist verified the histological examinations of all the tumors. The histology of tumors according to the World Health Organization (WHO) classification is shown in Table I. All patients received adjuvant conventional radiotherapy and chemotherapy with temozolamide (TMZ) after the initial resection.

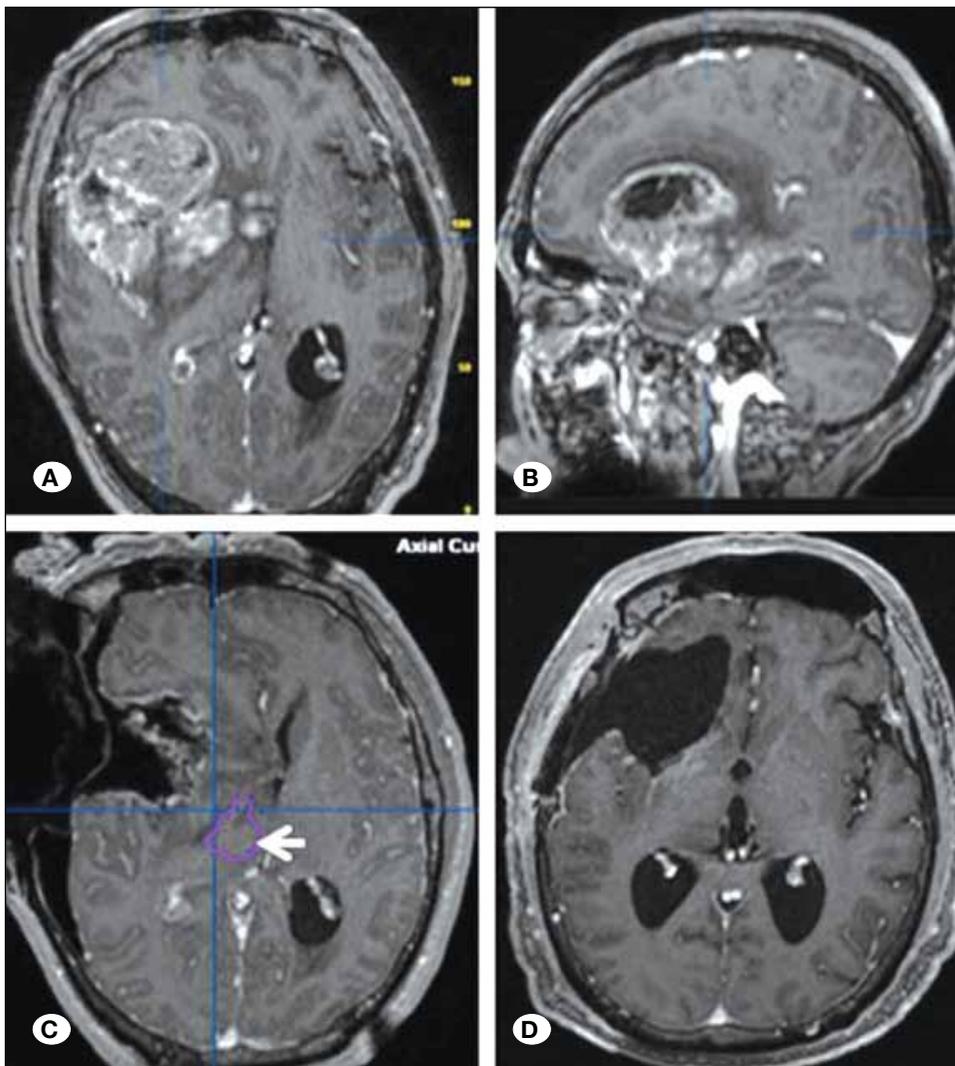


Figure 2: Illustrative case of a 45-year-old woman with a giant right insular glioblastoma (grade IV), which was successfully removed. Preoperative axial (A) and sagittal (B) T1-weighted contrast-enhanced MRI scan showing a giant right insular glioma. Intraoperative axial T1-weighted contrast-enhanced MRI scan showing complete tumor removal and the pyramidal tract was intact during surgery (though white arrow), (C). Axial T1-weighted contrast-enhanced MRI scan at 36 months after surgery showing complete tumor removal (D).

Overall Survival and Progression-Free Survival

The mean duration of follow-up period is shown in Table I. The re-growth was clinically and radiologically observed in 68 patients (93.2%) after the initial resection. Thirty nine patients (53.4%) underwent re-operation, whereas 12 received adjuvant chemotherapy. Fifty seven patients (78.1%) died during the

follow-up period due to tumor progression. The median OS of iMRI-assisted group [28(14-49) months] is better than that of control group [18 (7-38) months; $p=0.035$] (Figure 5A). The median PFS of iMRI-assisted group [18(9-42) months] is better than that of control group [15(3-32) months; $p=0.010$] (Figure 5B). Figure 6A, B shows that aggressive resection of insular HGG is predictive of improved OS and PFS.

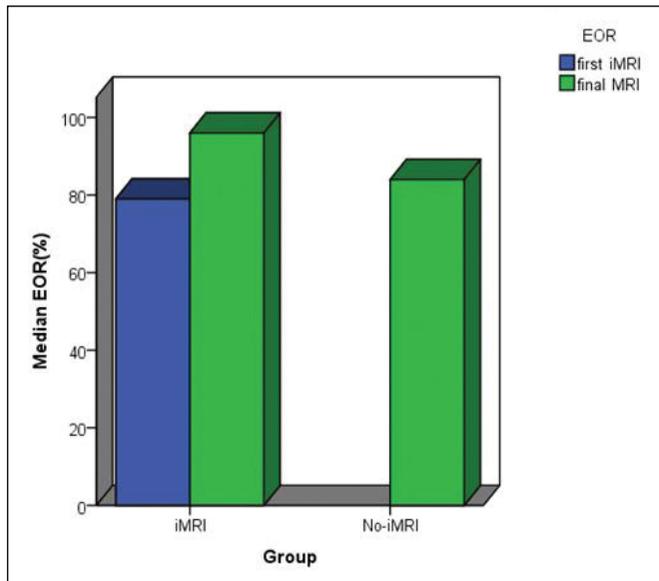


Figure 3: Bar graph showing the extent of resection (EOR, as percentage) in patients undergoing surgery with iMRI guidance and no-iMRI guidance. The percentage of tumor removed with iMRI guidance was determined from the intraoperative initial iMRI (EOR- first iMRI) and from the final MRI (EOR- final iMRI).

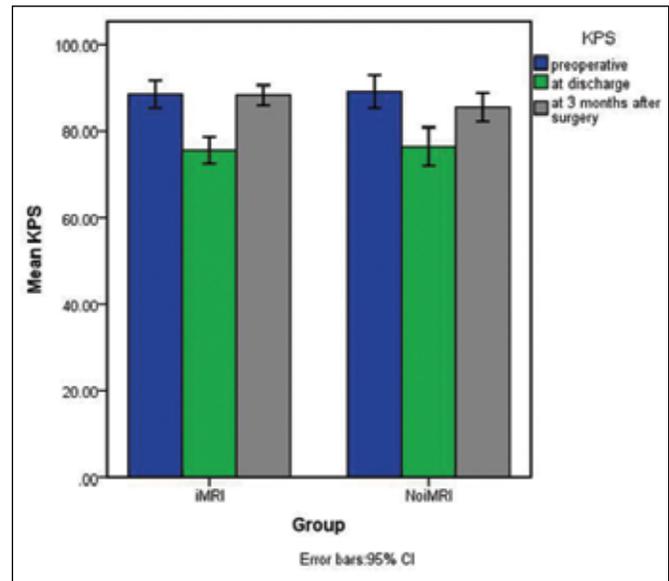


Figure 4: Bar graph showing Karnofsky performance score (KPS) of insular high-grade glioma patients undergoing surgery with iMRI guidance and no-iMRI guidance.

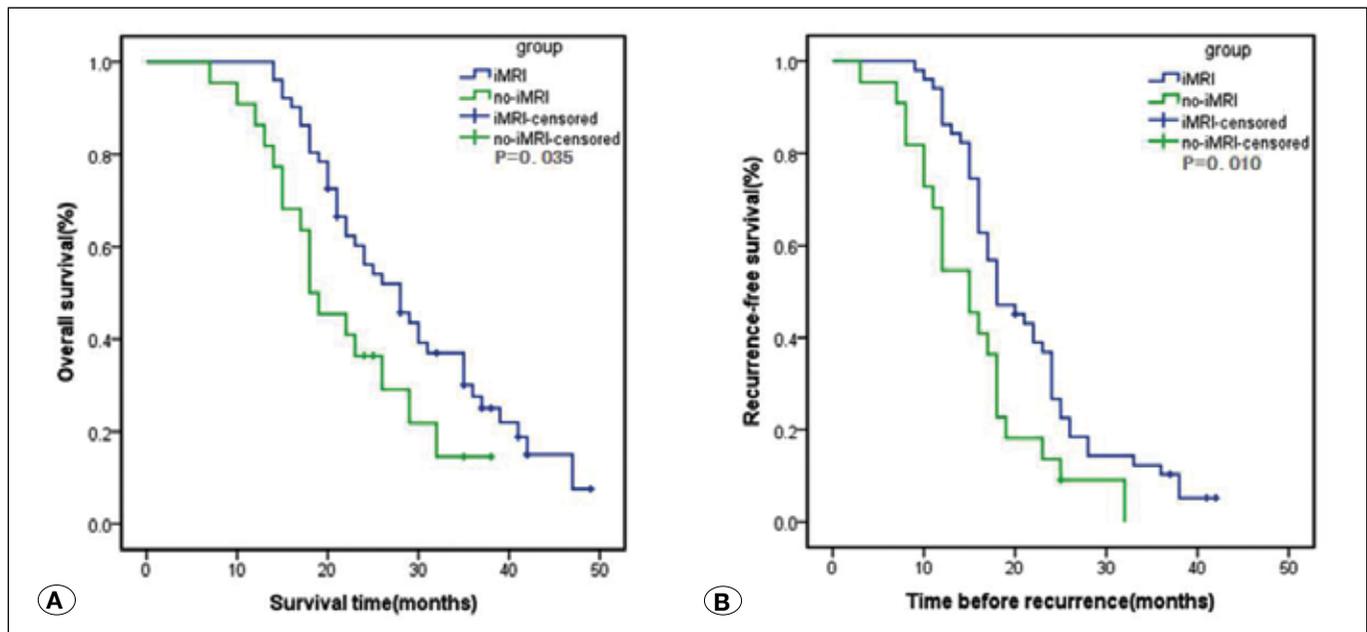


Figure 5: Kaplan-Meier curves showing that combined iMRI and functional neuronavigation operations appeared to extend overall survival (A), and recurrence-free survival (B) compared with conventional neuronavigation operations.

Table I: Characteristics of 73 Patients Who Underwent Surgical Treatment for Insular HGG from 2010 to 2014

Characteristics/ No. of cases	iMRI-assisted group (n=51, 69.9%)	No iMRI-assisted group (n=22, 30.1%)	Results (p)
Male: Female	32:19	14:8	0.942 ^a
Mean age (years)	54.2 (23-69)	51.8 (25-72)	0.798 ^b
Major presenting complaints			
Seizure	36 (70.6%)	14 (63.6%)	-
Headache and dizziness	18 (35.3%)	6 (27.3%)	-
Motor deficits	6 (11.8%)	3 (13.6%)	-
Sensory deficits	4 (7.8%)	2 (9.1%)	-
Language deficit	3 (5.9%)	2 (9.1%)	-
Incidental	2 (3.9%)	1 (4.5%)	-
Median pre-operative KPS	90 (50-100)	90 (70-100)	0.928 ^b
Side of tumor in patients (lt/rt)	21/30	9/13	0.983 ^a
Insular GBM location by zone*			
all (giant)	18 (35.3%)	7 (31.8%)	-
I+IV	11 (21.6%)	4 (18.2%)	-
III+IV	8 (15.7%)	3 (13.6%)	-
II+III	7 (13.7%)	4 (18.2%)	-
I+II	4 (7.8%)	2 (9.1%)	-
I	2 (3.9%)	0 (0)	-
IV	1 (2.0%)	2 (9.1%)	-
Mean preoperative tumor volume (cm ³)	74.5 (25.5-180.6)	69.2(21.4-174.0)	0.062 ^b
Surgical approach (TCO/TSY)	47/4	21/1	0.994 ^c
Surgical time (hours)	6.5±0.7	6.3±0.6	0.716 ^d
Postoperative hospital stay (days)	11.5±2.7	12.1±3.7	0.892 ^d
Continued resection after iMRI	37 (72.5%)	-	-
Mean residual tumor volume (cm ³)	0.6 (0.0-5.2)	3.8 (0.0-12.1)	0.003 ^b
EOR (extent of resection)			
100%	16 (31.4%)	1 (4.5%)	0.013 ^a
90-99%	23 (45.1%)	7 (31.8%)	0.357 ^a
80-89%	12 (23.5%)	9 (40.9%)	0.132 ^a
<80% [#]	0	5 (22.7%)	-
Median	96% (86%–100%)	84% (69%–100%)	0.031 ^b
Tumor histology (WHO grade)			
Anaplastic astrocytoma (III)	7	4	
GBM (IV)	44	18	0.895 ^c

TCO: Transcortical, **TSY:** Transsylvian, **KPS:** Karnofsky performance score, **HGG:** High grade glioma, **GBM:** Glioblastoma, **WHO:** World Health Organization, **iMRI:** intraoperative magnetic resonance imaging, **lt:** left, **rt:** right.

*Berger-Sanai insular glioma classification system (33-35).

[#]Because of low event numbers, statistical significance was not reached.

^aPearson Chi-square Test was used.

^bTwo-Independent-samples Tests (Mann-Whitney) was used.

^cContinuity Correction Chi-square Test was used.

^dIndependent-samples T Test was used.

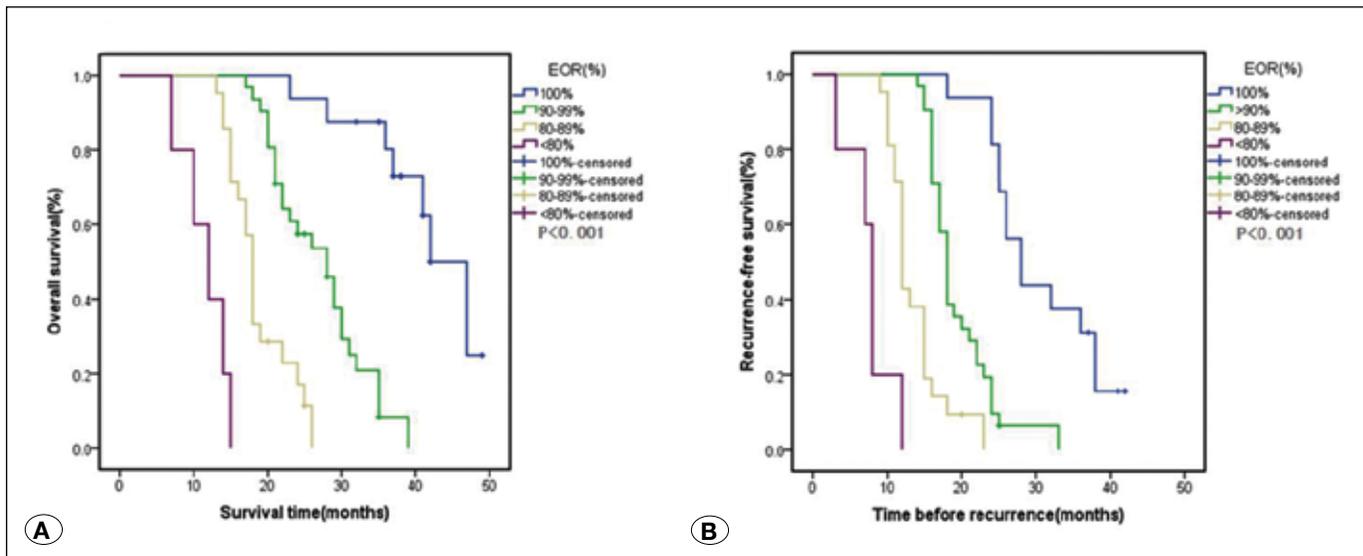


Figure 6: Kaplan-Meier curves revealing the overall survival (A), and recurrence-free survival (B) of patients with insular high-grade glioma, stratified by EOR. More extensive resections may provide overall and recurrence-free survival advantage.

DISCUSSION

Extent of Resection

The prognosis of patients with HGG is poor. The goal of glioma surgery is to maximize EOR while minimizing surgical co-morbidities. GTR is desired for the treatment of insular glioma. However, GTR can sometimes be limited by adhesions which the insular glioma may have with surrounding eloquent anatomy and vessels. With improvements in microsurgical techniques, neurological imaging, and electrophysiological monitoring, nervous and vascular structures can be safely identified and manipulated. The complication rates of insular glioma surgery are still significant. The potential benefits of a glioma surgery should be balanced against postoperative neurological complication rates. Significant neurological complication rates of insular HGGs surgery may detract from the patient's quality of life, which will well outweigh any prolongation of survival. So, optimal treatment for insular HGGs remains controversial due to the morbidity inherent to the operation and short life expectancy of the HGG patients.

Although the lack of Class I evidence, data from several studies demonstrated that a maximum safe EOR as a positive predictor for extended OS and PFS for HGG patients (2,12,23,33,34,36,38,39,43). Sanai and Berger (34) also reviewed the major clinical literatures and concluded that more extensive surgical resection is associated with longer life expectancy for patients with glioma. We observed that a better OS and PFS for patients, in whom a 100% and 90–99% resection was achieved, but much of the statistical effect was due to the relatively unfavorable prognosis of patients with a 80–89% and < 80% tumor resection (Figure 6A,B). Our analysis provides further evidence that greater EOR leads to improved OS and PFS significantly.

Insular HGGs located in the deep region characterized by the lack of anatomical landmarks, paucity of functional information,

and risk of overlooking hidden tumor portions. Furthermore, HGGs have infiltrative behavior and intimate co-habitation with brain vascular supply. These factors carry a limitation as regards EOR. Sanai et al.(35) reported the median EOR was 81% (range 47–100%) for insular HGGs. In our series, the median EOR of iMRI-assisted group [96% (86%–100%)] was significantly higher than that of conventional neuronavigation group [84% (69%–100%); $p=0.031$]. Mean residual tumor volume of iMRI-assisted group [0.6 (0.0–5.2) cm^3] was significantly smaller than that of conventional neuronavigation group [3.8 (0.0–12.1) cm^3 ; $p=0.003$]. The better EOR (Table I) in the iMRI-assisted group of our series seemed to be attributed to the combined iMRI and neuronavigation system. Kawaguchi et al.(18) reported that the clear tumor boundaries is one of the indicators for radical resection of insulo-opercular gliomas.

Insular HGGs may invade and compress the surrounding structures, and the borders of the tumor may be difficult to distinguish during surgery. In iMRI-assisted group of our series, iMRI is recommended to update the neuronavigation after brain shift, increase its usefulness for distinguishing tumor borders and avoidance of important structures after resection of the main part of large insular gliomas. The combined iMRI and neuronavigation system is also very helpful when the residual tumor is too small for easy detection. In the iMRI-assisted group of our series, residual tumor was detected by the iMRI in 42 patients, and residual tumor of 37 patients was further resected. The median EOR increased significantly from 79% (58%–100%) to [96% (86%–100%), $p<0.001$](Figure 3). If iMRI had not been used to detect the residual tumor, the median EOR would only have been 79%. It showed that iMRI increased the EOR of insular HGG surgery (Figure 2D).

The mid-posterior part of the superior temporal gyrus and the posterior dominant insula are usually both essential for speech function. Furthermore, the posterior insula is very close to the posterior limb of the internal capsule. The posterior part

Table II: Operative Outcome of 73 Patients Who Underwent Surgical Treatment for Insular HGG

Parameters/ Group	iMRI-assisted group (n=51)	No iMRI-assisted group (n=22)	Results (p)
Hemiparesis			
Immediate ^a	1 (2.0%)	4 (18.2%)	0.044 ^c
Medium term ^b	0 (0)	3 (13.6%)	-
Monoparesis			
Immediate ^a	2 (3.9%)	4 (18.2%)	0.116 ^c
Medium term ^b	2 (3.9%)	3 (13.6%)	0.316 ^c
Facial droop			
Immediate ^a	2 (3.9%)	3 (13.6%)	0.316 ^c
Medium term ^b	0 (0)	0 (0)	-
Sensory deficits			
Immediate ^a	1 (2.0%)	3 (13.6%)	0.147 ^c
Medium term ^b	0 (0)	0 (0)	-
Seizure			
Immediate ^a	1 (2.0%)	1 (4.5%)	1.000 ^c
Medium term ^b	0 (0)	0 (0)	-
Motor aphasia			
Immediate ^a	0 (0)	1 (4.5%)	-
Medium term ^b	0	0	-
Sensory aphasia			
Immediate ^a	1 (5.9%)	4 (18.2%)	0.044 ^c
Medium term ^b	0 (0)	0 (0)	-
Hematoma			
Immediate ^a	0 (0)	1 (4.5%)	-
Medium term ^b	0 (0)	0 (0)	-
Infection			
Immediate ^a	1 (3.9%)	0 (0)	-
Medium term ^b	0 (0)	0 (0)	-
Postoperative death			
	0 (0)	0 (0)	
Total neurological deficits			
Immediate ^a	8 (15.7%)	12 (54.5%)	0.001 ^d
Medium term ^b	2 (3.9%)	6 (27.3%)	0.012 ^c
Median immediate ^a KPS	80 (50-90)	80 (50-90)	0.683 ^e
Median medium term ^b KPS	90 (70-100)	80 (60-100)	0.021 ^e
Mean follow-up duration, mo	29.3 (14-49)	21.9 (7-38)	-
Median OS, mo	28 (14-49)	18 (7-38)	0.035
Median PFS, mo	18 (9-42)	15 (3-32)	0.010

OS: overall survival, **PFS:** progressive-free survival, **KPS:** Karnofsky performance score, **HGG:** High grade glioma, **mo:** months, **iMRI:** intraoperative magnetic resonance imaging

^anew neurological deficits or worsening of pre-existing deficits at discharge.

^bnew neurological deficits or worsening of pre-existing deficits at 3 months after surgery.

^cContinuity Correction Chi-square Test was used.

^dPearson Chi-square Test was used.

^eTwo-Independent-samples Tests (Mann-Whitney) was used.

of the dominant insula limits total removal of insular glioma, and many studies (6,24,45) reported examples of residual glioma in the posterior insular region. To avoid this problem, we usually performed an anterotemporal lobectomy or the superior temporal gyrus lobectomy. Because most of insular HGGs have temporal or frontal extensions, additional cortical resection of superior temporal gyrus maximizes surgical space to provide a better exposure of the residual tumor in the posterior insular region. iMRI and neuronavigation can give the surgeon information about the exact locations of speech function area and the arcuate fasciculus, which help to guide the location of the safe cortical incision in the frontal or temporal gyrus. In iMRI-assisted group of our series, 47 cases were approached through one or more transcortical corridors. Integrating intraoperative functional MRI data and diffusion-tensor imaging-based fiber tracking (DTI-ft) into the neuronavigation system can also help to visualize major white-matter tracts and avoid damage to the pyramidal tract (Figure 1A,C,F and Figure 2C). In iMRI-assisted group of our series, the residual tumor of 3 patients was very close to the pyramidal tract in the posterior limb of the internal capsule, and the surgeon did not continue to resect the residual tumor. The transylvian approach often requires the sacrifice of some veins, and leads to inferior frontal gyrus and superior temporal gyrus retraction, which may also cause postoperative neurological deficits. In our series, the transylvian approach was performed in only 5 small volume tumors of early period.

Morbidity

Aggressive EOR should be weighed against postoperative quality of life, since lower postoperative neurological deficits might be more important with regard to OS than increasing the EOR (21). Postoperative clinical condition of the patient is one of the important prognostic factors, and the patient's quality of life and tumor control should be the ultimate strategies of treatment. Sanai et al.(35) reported the median EOR was 81% (range 47–100%) for insular HGGs, permanent postoperative deficits were noted in 6 patients (6%). Simon et al.(39) reported a > 90% resection was achieved in 42% of cases, KPS scores deteriorated in 41% of patients at discharge. Our data confirm that in addition to improving the EOR, the combined iMRI and neuronavigation can increase the safety of tumor resection. We incurred a 96% median EOR with a permanent postoperative morbidity rate of 2.0% in the iMRI-assisted group (Table II). Although there was indeed a reduction of KPS at 3 days after surgery, improvement was observed at 3 months after surgery. KPS of iMRI-assisted group [90(70-100)] was significantly higher than that of control group [80(60-100); $p=0.021$] at 3 months after surgery (Table II, Figure 4). It may imply advantage of the iMRI in enhancing quality of life after resection of insular HGGs.

Duffau (6) reported that almost all severe complications were related to injury of the perforating vessels. Similar to Duffau's report, 2 of 3 patients had postoperative hemiparesis due to injury of perforating vessels in the conventional neuronavigation group of our series.

Intraoperative anatomical alterations and shift of the brain will often cause wrong neuronavigation which is set-up based on preoperative MR imaging. The usual anatomical landmarks and some techniques included intraoperative neurophysiological monitoring and real-time ultrasonography cannot provide the exact location of the perforating arteries to the surgeon. The combined iMRI and neuronavigation can guide the surgeon to identify the location of perforating arteries (Figure 1 D,E). When a HGG encases the important perforating artery, the surgeon should leave a small amount of residual tumor. In iMRI-assisted group of our series, the residual tumor of 2 patients involves the important perforating artery in the anterior perforating substance, and the surgeon left a layer of residual tumor tissue along these vessels in the deep insular region.

Survival and Progression-Free Survival

The OS and PFS after HGGs surgery depends on many variables, including histological features, age, EOR, and preoperative KPS scores (39). Since the introduction of iMRI, some studies reported that low-field-strength iMRI affected negatively OS of HGG patients. Senft et al.(37) reported 41 GBM patients on a 0.15 T scanner, and median OS was 88 weeks for the iMRI-group compared with 68 weeks for the conventional neuronavigation group ($p=0.07$). Hirschberg et al.(16) analyzed 32 patients of GBM on a 0.5 T iMRI scanner. The result showed mean OS of the iMRI-group and control group without iMRI were 14.5 months and 12.1 months respectively ($p=0.14$). The high-field iMRI added some benefits compared with low-field iMRI in our study. In our series, 62 of 73 patients had GBMs. No patient has suffered from adverse events during high-field iMRI scanning. Surgical time and postoperative hospital stay time are not different between the iMRI-group and conventional neuronavigation group (Table I). The median PFS of iMRI-assisted group [18(9-42) months] is better than that of the control group [15(3-32); $p=0.010$]. The median OS of iMRI assisted group [28(14-49)] is better than that of conventional neuronavigation group [18(7-38); $p=0.035$]. The OS and PFS in iMRI-assisted group of our series were generally quite good for HGGs patients. Our study demonstrated that high-field iMRI is more effective than conventional neuronavigation-guided surgery in prolonging OS and PFS of insular HGG patients.

CONCLUSION

Aggressive resection of insular HGG is predictive of improved OS and PFS. The techniques of resection guided by combined high-field iMRI and neuronavigation optimize the extent of resection and minimize the morbidity in insular HGG surgery.

ACKNOWLEDGEMENT

This work was supported by grants from the Sanya innovation fund (no. 2014YW36).

■ REFERENCES

- Berkmann S, Schlaffer S, Nimsky C, Fahlbusch R, Buchfelder M: Intraoperative high-field MRI for transsphenoidal reoperations of nonfunctioning pituitary adenoma. *J Neurosurg* 121:1166-1175, 2014
- Bloch O, Han SJ, Cha S, Sun MZ, Aghi MK, McDermott MW, Berger MS, Parsa AT: Impact of extent of resection for recurrent glioblastoma on overall survival. *Clinical article. J Neurosurg* 117:1032-1038, 2012
- Cedzich C, Taniguchi M, Schäfer S, Schramm J: Somatosensory evoked potential phase reversal and direct motor cortex stimulation during surgery in and around the central region. *Neurosurgery* 38:962-970, 1996
- Chen X, Xu BN, Meng X, Zhang J, Yu X, Zhou D: Dual room 1.5 T intraoperative magnetic resonance imaging suite with a movable magnet: Implementation and preliminary experience. *Neurosurg Rev* 35:95-109, 2012
- Claus EB, Horlacher A, Hsu L, Schwartz RB, Dello-Iacono D, Talos F, Jolesz FA, Black PM: Survival rates in patients with low-grade glioma after intraoperative magnetic resonance image guidance. *Cancer* 103: 1227-1233, 2005
- Duffau H: A personal consecutive series of surgically treated 51 cases of insular WHO Grade II glioma: Advances and limitations. *J Neurosurg* 110:696-708, 2009
- Duffau H, Capelle L: Preferential brain locations of low-grade gliomas. *Cancer* 100:2622-2626, 2004
- Duffau H, Capelle L, Lopes M, Faillot T, Sichez JP, Fohanno D: The insular lobe: Physiopathological and surgical considerations. *Neurosurgery* 47:801-810, 2000
- Duffau H, Taillandier L, Gatignol P, Capelle L: The insular lobe and brain plasticity: Lessons from tumor surgery. *Clin Neurol Neurosurg* 108:543-548, 2006
- Ebeling U, Kothbauer K: Circumscribed low grade astrocytomas in the dominant opercular and insular region: A pilot study. *Acta Neurochir (Wien)* 132:66-74, 1995
- Fadul C, Wood J, Thaler H, Galicich J, Patterson RH Jr, Posner JB: Morbidity and mortality of craniotomy for excision of supratentorial gliomas. *Neurology* 38:1374-1379, 1988
- Grabowski MM, Recinos PF, Nowacki AS, Schroeder JL, Angelov L, Barnett GH, Vogelbaum MA: Residual tumor volume versus extent of resection: Predictors of survival after surgery for glioblastoma. *J Neurosurg* 121:1115-1123, 2014
- Guenot M, Isnard J, Sindou M: Surgical anatomy of the insula. *Adv Tech Stand Neurosurg* 29:265-288, 2004
- Gumprecht H, Ebel GK, Auer DP, Lumenta CB: Neuronavigation and functional MRI for surgery in patients with lesion in eloquent brain areas. *Minim Invasive Neurosurg* 45:151-153, 2002
- Hentschel SJ, Lang FF: Surgical resection of intrinsic insular tumors. *Neurosurgery* 57:176-183, 2005
- Hirschberg H, Samset E, Hol PK, Tillung T, Lote K: Impact of intraoperative MRI on the surgical results for high-grade gliomas. *Minim Invasive Neurosurg* 48:77-84, 2005
- Kamada K, Todo T, Masutani Y, Aoki S, Ino K, Takano T, Kirino T, Kawahara N, Morita A: Combined use of tractography-integrated functional neuronavigation and direct fiber stimulation. *J Neurosurg* 102:664-672, 2005
- Kawaguchi T, Kumabe T, Saito R, Kanamori M, Iwasaki M, Yamashita Y, Sonoda Y, Tominaga T: Practical surgical indicators to identify candidates for radical resection of insulo-opercular gliomas. *J Neurosurg* 121:1124-1132, 2014
- King RB, Schell GR: Cortical localization and monitoring during cerebral operations. *J Neurosurg* 67:210-219, 1987
- Knauth M, Wirtz CR, Tronnier VM, Aras N, Kunze S, Sartor K: Intraoperative MR imaging increases the extent of tumor resection in patients with high-grade gliomas. *AJNR Am J Neuroradiol* 20:1642-1646, 1999
- Kubben PL, ter Meulen KJ, Schijns OE, ter Laak-Poort MP, van Overbeeke JJ, van Santbrink H: Intraoperative MRI-guided resection of glioblastoma multiforme: A systematic review. *Lancet Oncol* 12:1062-1070, 2011
- Kumabe T, Higano S, Takahashi S, Tominaga T: Ischemic complications associated with resection of opercular glioma. *J Neurosurg* 106:263-269, 2007
- Lacroix M, Abi-Said D, Fournay DR, Gokaslan ZL, Shi W, DeMonte F, Lang FF, McCutcheon IE, Hassenbusch SJ, Holland E, Hess K, Michael C, Miller D, Sawaya R: A multivariate analysis of 416 patients with glioblastoma multiforme: Prognosis, extent of resection, and survival. *J Neurosurg* 95:190-198, 2001
- Lang FF, Olansen NE, DeMonte F, Gokaslan ZL, Holland EC, Kalhorn C, Sawaya R: Surgical resection of intrinsic insular tumors: Complication avoidance. *J Neurosurg* 95:638-650, 2001
- Lehéricy S, Duffau H, Cornu P, Capelle L, Pidoux B, Carpentier A, Auliac S, Clemenceau S, Sichez JP, Bitar A, Valery CA, Van Effenterre R, Faillot T, Srouf A, Fohanno D, Philippon J, Le Bihan D, Marsault C: Correspondence between functional magnetic resonance imaging somatotopic and individual brain anatomy of the central region: Comparison with intraoperative stimulation in patients with brain tumors. *J Neurosurg* 92:589-598, 2000
- Nimsky C, Fujita A, Ganslandt O, Von Keller B, Fahlbusch R, Fahlbusch R: Volumetric assessment of glioma removal by intraoperative high-field magnetic resonance imaging. *Neurosurgery* 55:358-370, 2004
- Nimsky C, Ganslandt O, Tomandl B, Buchfelder M, Fahlbusch R: Low-field magnetic resonance imaging for intraoperative use in neurosurgery: A 5-year experience. *Eur Radiol* 12: 2690-2703, 2002
- Nimsky C, Ganslandt O, Von Keller B, Romstöck J, Fahlbusch R: Intraoperative high-field-strength MR imaging: Implementation and experience in 200 patients. *Radiology* 233: 67-78, 2004
- Nimsky C, von Keller B, Ganslandt O, Fahlbusch R: Intraoperative high-field magnetic resonance imaging in transsphenoidal surgery of hormonally inactive pituitary macroadenomas. *Neurosurgery* 59: 105-114, 2006
- Ntoukas V, Krishnan R, Seifert V: The new generation polestar n20 for conventional neurosurgical operating rooms: A preliminary report. *Neurosurgery* 62: 82-89, 2008
- Ren H, Chen X, Sun G, Hu S, Zheng G, Li F, Li J, Xu B: Resection of subependymal giant cell astrocytoma guided by intraoperative magnetic resonance imaging and neuronavigation. *Childs Nerv Syst* 29:1113-1121, 2013

32. Roessler K, Donat M, Lanzenberger R, Novak K, Geissler A, Gartus A, Tahamtan AR, Milakara D, Czech T, Barth M, Knosp E, Beisteiner R: Evaluation of preoperative high magnetic field motor functional MRI (3 Tesla) in glioma patients by navigated electrocortical stimulation and postoperative outcome. *J Neurol Neurosurg Psychiatry* 76:1152–1157, 2005
33. Ryken TC, Frankel B, Julien T, Olson JJ: Surgical management of newly diagnosed glioblastoma in adults: Role of cytoreductive surgery. *J Neurooncol* 89:271–286, 2008
34. Sanai N, Berger MS: Glioma extent of resection and its impact on patient outcome. *Neurosurgery* 62:753–764, 2008
35. Sanai N, Polley MY, Berger MS: Insular glioma resection: Assessment of patient morbidity, survival, and tumor progression. *J Neurosurg* 112:1–9, 2010
36. Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS: An extent of resection threshold for newly diagnosed glioblastomas. Clinical article. *J Neurosurg* 115:3–8, 2011
37. Senft C, Franz K, Blasel S, Oszvald A, Rathert J, Seifert V, Gasser T: Influence of iMRI-guidance on the extent of resection and survival of patients with glioblastoma multiforme. *Technol Cancer Res Treat* 9: 339–346, 2010
38. Shelley BP, Trimble MR: The insular lobe of Reil—its anatomico-functional, behavioural and neuropsychiatric attributes in humans—a review. *World J Biol Psychiatry* 5:176–200, 2004
39. Simon M, Neuloh G, von Lehe M, Meyer B, Schramm J: Insular gliomas: The case for surgical management. Clinical article. *J Neurosurg* 110:685–695, 2009
40. Sun GC, Chen XL, Zhao Y, Wang F, Hou BK, Wang YB, Song ZJ, Wang D, Xu BN: Intraoperative high-field magnetic resonance imaging combined with fiber tract neuronavigation-guided resection of cerebral lesions involving optic radiation. *Neurosurgery* 69:1070–1084, 2011
41. Sun GC, Chen XL, Zhao Y, Wang F, Song ZJ, Wang YB, Wang D, Xu BN: Intraoperative MRI with integrated functional neuronavigation-guided resection of supratentorial cavernous malformations in eloquent brain areas. *J Clin Neurosci* 18:1350–1354, 2011
42. Vanaclocha V, Sáiz-Sapena N, García-Casasola C: Surgical treatment of insular gliomas. *Acta Neurochir* 139:1126–1135, 1997
43. Wrensch M, Rice T, Miike R, McMillan A, Lamborn KR, Aldape K, Prados MD: Diagnostic, treatment, and demographic factors influencing survival in a population-based study of adult glioma patients in the San Francisco Bay Area. *Neuro Oncol* 8:12–26, 2006
44. Yasargil MG, von Ammon K, Cavazos E, Doczi T, Reeves JD, Roth P: Tumours of the limbic and paralimbic systems. *Acta Neurochir (Wien)* 118:40–52, 1992
45. Zentner J, Meyer B, Stangl A, Schramm J: Intrinsic tumors of the insula: A prospective surgical study of 30 patients. *J Neurosurg* 85:263–271, 1996
46. Zhao Y, Chen X, Wang F, Sun G, Wang Y, Song Z, Xu B: Integration of diffusion tensor-based arcuate fasciculus fibre navigation and intraoperative MRI into glioma surgery. *J Clin Neurosci* 19:255–261, 2012