Presurgical fMRI Affecting the Extent of Resection and Outcome of the Supratentorial Gliomas; a Single-center Experience From a Developing Country

Abolghasem Mortazavi  
Tehran University of Medical Sciences (TUMS)

Mohammad Ali Suraki Azad  
Valiasr Teaching Hospital

Abbas Amirjamshidi  
Tehran University of Medical Sciences School of Medicine

Mohammad Shirani  
Tehran University of Medical Sciences School of Medicine

Seyed Ebrahim Ketabchi  
Tehran University of Medical Sciences School of Medicine

Kourosh Karimi Yarandi  
Tehran University of Medical Sciences School of Medicine

Ahmad Pour-Rashidi  
Tehran University of Medical Sciences School of Medicine  
ahmadpourrashidi89@gmail.com

Research Article

Keywords: Glioma, Functional MRI, Outcome, Extent of resection

DOI: https://doi.org/10.21203/rs.3.rs-528310/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background

Functional magnetic resonance imaging (fMRI) is one of the available non-invasive imaging to map the different brain areas, which has been used during the current years. In this study, we aimed to evaluate the effect of fMRI on decision-making, the extent of resection, and the outcome of the patients with supratentorial gliomas.

Methods

This prospective study conducted from 2014 through 2017 to investigate how presurgical fMRI can help the neurosurgeon during glioma surgery. Baseline demographic and clinical data were collected, and standard fMRI protocol was used for each patient.

Results

Forty-one patients with supratentorial gliomas met inclusion criteria, including 29 males and 12 females ranging in age from 21 to 72. Our results showed a significant association between eloquent areas tumor and the EOR. Eight out of 41 (19.5%) experienced higher EOR than what the neurosurgeon expected after adjusting the fMRI findings with the intraoperative situation. Among these patients, postoperative KPS and motor indices reflected dropped levels accompanied by an instant language index level in the short-term period, whereas all indices improved after long-term follow-up. There was a significant association between increasing EOR and all indices in the 1-year follow-up.

Conclusions

In conclusion, we postulate that preoperative fMRI should be considered preoperatively, especially in the eloquent areas gliomas disregarding tumor grade. Moreover, it can lead to a positive outcome in supratentorial gliomas via giving useful data about the relation of the tumor and vital centers of the brain, although it may result in an unfavorable short-term outcome.

Introduction

Intra-axial brain tumors like gliomas, especially slow-growing ones, are still challenging due to the higher postoperative morbidities and unacceptable consequences. The tumors close to or within the eloquent areas are more controversial in terms of operation, owing to various degrees of postoperative complications and decreased quality of life(1–3). In this regard, many neurosurgeons choose an observational approach until the neurologically deteriorated situation, or may prefer suboptimal resection that is accompanied by some other disadvantages such as wounded glioma(4).

During the last decades, advanced neuroimaging has helped neurosurgeons select the best approach to achieve the maximal extent of tumor resection, minimal postsurgical deficits, and improved survival(5–
Functional magnetic resonance imaging (fMRI) is one of the available imaging has been used during the current years. This modality identifies local hemodynamic changes in the brain tissues showing neuronal activities of the functional regions. In general, fMRI uses the blood oxygen level-dependent (BOLD) technique to detect the cerebral areas with a dropped deoxyhemoglobin level during the specific tasks(8). During the functional tasks, neuronal activities lead to raised regional cerebral blood flow causing increased oxygen saturation. Then, high deoxyhemoglobin levels have been detected in T2*-weighted imaging as hyperintensity, reflecting the eloquent regions(7).

It can map the cerebral regions non-invasively before and during the surgery. Hence, it may change the neurosurgeon's opinion in terms of the optimal approach, and when and where to stop(9). In this study, we aimed to evaluate the effect of fMRI on the extent of resection and the outcome of the patients with supratentorial gliomas.

**Materials And Methods**

**Patients**

The institutional review board approved the study, and each patient signed informed consent documents before we proceeded. Before surgery, patients underwent BOLD fMR imaging in a 3Tesla MR imager.

Forty-one consecutive patients (29 male and 12 female patients, mean age of 48.14 ± 22.1 years) with potentially resectable gliomas were evaluated prospectively from April 2014 to August 2017. All patients were operated by a neurosurgeon with more than 10 years experiences, and they were followed at least for a year. The tumor types were classified according to the World Health Organization (WHO) grading system resulted in 16 low-grade gliomas (LGG) and 25 high-grade gliomas (HGG) that all were newly diagnosed. All patients underwent postoperative conventional brain MRI within first 48 hours to estimate the EOR.

All the patients were cooperative and performed different essential functional tasks in association with the tumor location. There were not any confounded fMRI due to the artifact, because in patients with non-qualified fMRI, the imaging was repeated. Relevant Table 1 presented the anatomical and clinical data of the patients.
| Features                     | Findings                  |
|------------------------------|---------------------------|
| Age (years ± SD)             |                           |
| Male                         | 47.51 ± 15.51             |
| Female                       | 49.67 ± 10                |
| Sex (%)                      |                           |
| Male                         | 29 (70.7)                 |
| Female                       | 12 (20.3)                 |
| Tumor location (%)           |                           |
| Frontal                      | 13 (31.7)                 |
| Parietal                     | 12 (29.3)                 |
| Temporal                     | 10 (24.4)                 |
| Occipital                    | 5 (12.2)                  |
| Corpus callosum              | 1 (2.4)                   |
| Side (%)                     |                           |
| Right                        | 5 (12.2)                  |
| Left                         | 36 (87.8)                 |
| Eloquent area (%)            |                           |
| Yes                          | 24 (58.5)                 |
| No                           | 17 (41.5)                 |
| Tumor grade (%)              |                           |
| LGG                          | 16 (39)                   |
| HGG                          | 25 (61)                   |
| Preoperative KPS (%)         |                           |
| 70–90                        | 15 (36.5)                 |
| 90–100                       | 26 (63.5)                 |
| Handedness                   |                           |
| Right                        | 40 (97.6)                 |
| Left                         | 1 (2.4)                   |
| Symptoms                     |                           |
| Headache                     | 35 (85.3)                 |
| Seizure                      | 29 (70.7)                 |
| Neurological deficit         | 12 (29.2)                 |

*LGG: low grade glioma, HGG: high grade glioma, KPS: Karnofsky performance scale

**Functional MR Imaging**

Patients were asked to perform three different types of functional scans depending on the tumor location. Finger and toe-tapping were performed to show motor center activation and sponge squeezing for
assessing the sensory function. Besides, Language task was implemented using the previously developed task by neuroimaging and analysis group (NIAG)(10). For this case, due to the level of literacy and academic education, we run the reverse word reading task (RWR) to evaluate language functional area. The subject was presented with Persian word while letters were being presented in the left to right alignment and she was asked to read the word silently.

Imaging was performed using 3 Tesla MRI Scanner (Discovery MR 750, GE Healthcare) with a 24 channel head coil. For anatomical images, sagittal T1 fast spoiled gradient (FSPGR) BRAVO [repetition time (TR): 1800 ms, echo time (TE): 3.5 ms, matrix size: 256*256 and FOV: 256*256*160 mm3] was obtained. The echo planar imaging (EPI) of fMRI was obtained by TR: 3000 ms, TE: 30 ms, matrix size: 256*256, voxel spacing: 3.7*3.7*3 mm3, phase number: 96 and total scan time: 4 minutes and 48 seconds.

fMRI images were analyzed using FMRIB’s Software Library (FSL, www.fmrib.ox.ac.uk/fsl)(11). Preprocessing sections were applied firstly by brain extraction tool (BET) and continued by fMRI expert analysis tool (FEAT) for motion correction, slice timing correction, spatial smoothing, temporal filtering and intensity normalization.

For evaluating the effect of fMRI on decision making and the estimated extent of resection (EOR), we showed the conventional brain MRI to a group of four experienced neurosurgeons first, and ask them about their approach and estimated EOR. Then, we showed them conventional MRI along with fMRI, and ask them for same questions. Finally, we compared their opinions with postoperative EOR. Region of interest (ROI) was drawn by two different neurosurgeons (AA, and SEK) separately. Postoperative EOR was estimated after comparing the postoperative tumor cavity with preoperative tumor volume via FLAIR sequences in non-enhancing tumors and post-contrast images in enhancing lesions.

**Statistical analysis**

Statistical analysis was performed using SPPS (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp; 2016). The Student’s t-test and Fisher exact test were used to make inter-group comparisons for continuous and categorical data. Summary data were reported as frequency distribution for categorical variables and means and standard deviations for parametric variables. Comparisons between the categorical variables (e.g., fMRI and extent of resection) were performed by Pearson’s chi-square test and Fisher exact test. Mann Whitney and Kruskal Wallis tests were applied for inter-group comparison of continuous variables between 2 groups, respectively. Logistic regression analyses were used to identify independent associations with survival. Values with p < 0.05 in these analyses were considered statistically significant.

**Results**

A total of 41 patients with newly diagnosed supratentorial gliomas met inclusion criteria, including 29 males and 12 females ranging in age from 21 to 72. All patients, except one, were right-handed. The most
common presenting symptom was headache (85.3%), and seizure (70.7%). Only 29.2% of all cases reflected neurological deficits as presenting symptoms.

All patients had preoperative KPS of more than 70, and 63.5% had KPS more than 90 who were evaluated by the preoperative fMRI. HGG accounts for 61% of all, and the rest of them were LGG predominately in the left hemisphere. Table 1 shows all the patient features in detail.

Although presurgical fMRI led to a greater extent of resection (EOR) in 51.2% and decreased the EOR in 31.7% of patients, the differences between the estimated EOR before and after viewing fMRI were not significant statistically (p = 0.132).

The outcome was assessed in terms of three different indices, including language, motor, and KPS. In 11 out of 24 patients (45.83%) with eloquent areas tumors, the estimated EOR by the neurosurgeon utilizing only conventional images compared to conventional besides functional sequences changed according to the fMRI. In cases with non-eloquent tumors, fMRI did not affect the EOR.

Our results revealed a significant association between eloquent areas tumor and the EOR (p = 0.001 and Spearman's correlation coefficient = 0.51). Changes in the EOR after adjusting the fMRI were seen in 11 patients, including 5 LGG and 6 HGG, but there was no significant relationship between the EOR and tumor histology (p = 0.620).

According to our results, in patients that the neurosurgeon decided to increase the EOR after the fMRI evaluation, non-significant language deterioration in short-term follow-up (one month after surgery) occurred. However, ultimately they found normal language function in a 1-year follow-up (p < 0.05). The motor index had a similar situation to the language one as well. In 12 out of 24 (29.2%) presenting with motor deficits before admission, utilizing the fMRI by the neurosurgeon caused the EOR change. After one year, motor deficits improved in 6 out of 12, and in the other 6, deficits were constant.

For the patients in whom fMRI led to changed neurosurgeon’s mind about the EOR, postsurgical KPS dropped significantly till month one, whereas it reached out to the presurgical level or even better in a 1-year follow-up.

Patients who experienced the higher EOR by fMRI usage were analyzed independently. Eight out of 41 (19.5%) experienced higher EOR only after accessing the neurosurgeon to fMRI. Among these patients, postoperative KPS and motor indices reflected dropped levels accompanied by an fixed language index level in the short-term period, whereas all indices improved after a long-term follow-up. There was a significant association between increasing EOR and all indices in a 1-year follow-up.

After one year, four patients with HGG died, including one with non-eloquent gliomas and three with eloquent tumors. In two out of four, fMRI findings resulted in less EOR than what the neurosurgeon had estimated without the fMRI.
Discussion

In this prospective study, we assessed preoperative fMRI’s role as an advanced neuroimaging in surgery of supratentorial gliomas. Nowadays, advanced perioperative neuroimaging is used widely to help neurosurgeons minimize iatrogenic complications, postoperative neurological deficits, then increase the EOR and improve the overall survival (OS) of the patients as much as possible.

Although there was non-significant, presurgical fMRI changed the neurosurgeon’s mind about the EOR in our patients. Consistent with our results, Bartsch et al., Lorenzen et al., and Lau et al. have introduced fMRI as a supplement means affecting the neurosurgeon’s decision-making before the surgery(6,12,13).

EOR in gliomas has a prominent role in overall survival and progression-free survival(14). One of the preoperative fMRI goals is to help the surgeons increase the EOR as much as possible. Our results indicated a change in the EOR in more than 50% of all patients that statistically was significant in 45.83% of patients with eloquent areas gliomas. These data were in concordance with Lorenzen et al.(12) that the EOR diminished in 21.4% of all their patients, and 7.1% have been known as non-operable according to the fMRI. Moreover, there was no prominent relationship between the EOR and tumor histology similar to the Kapsalakis et al.(14).

Given the results mentioned above, patients in whom the neurosurgeon changed the EOR according to the fMRI findings showed worse short-term outcomes in terms of language, motor, and KPS, but all patients improved after a long-term period. Twenty-four patients presented with motor deficits and fMRI changed the EOR in half of them, led to the worst postoperative motor score. 50% of them reached the baseline score, and the other found motor improvement even better than the baseline within the first year after surgery. There was no report of permanent neurological deficits in our study, whereas Lorenzen et al. reported 28.5% postoperative deficits, in which 14.2% were permanent(12). Furthermore, Kapsalakis et al. reported 29.9% new postsurgical deficits and/or worsening of the presurgical deficits that were persistent in 13.8%(14). Similar to our results, Vysotski et al. revealed more improvement in postoperative neurological deficits in patients who underwent presurgical fMRI(9).

Parallel to Castellano et al., 19.5% of our patients found a higher EOR using the fMRI(15). In these cases, KPS and motor indices were aggravated in short-term follow-up along with unchanged language score (non-significant), whereas all three indices improved in the following year significantly. Our data were in concordance with Vysotski et al. and Castellano et al. findings [12, 13]. Short-term deterioration may result from relying on the fMRI findings leading to resection of the tumor as close as the eloquent regions. The fMRI limited the EOR in 31.7% that 15.3% of them diagnosing as HGG in eloquent cortex died after 1-year follow-up.

In future studies, a larger sample size with only eloquent areas gliomas as well as longer duration in the follow-up period is recommended. The findings of presurgical fMRI in association with intraoperative fMRI and intraoperative cortical and subcortical electrophysiological stimulation could provide more valuable results.
In conclusion, we postulate that preoperative fMRI should be considered preoperatively, especially in the eloquent areas gliomas disregarding the tumor grade. Moreover, it can lead to a positive outcome in patients with supratentorial gliomas via giving useful data about the relation of the tumor and vital centers of the brain, although it may result in an unfavorable short-term outcome.

**Declarations**

**Funding:**

Not applicable

**Conflicts of interest/Competing interests:**

Not applicable

**Ethics approval:**

The institutional review board approved the study, and the ethical number is IRSINA23041393.

**Consent to participate:**

Each patient signed informed consent documents before we proceeded.

**Contributions:**

SEK and AA conceived and designed research. AM and KKY conducted experiments. MASA contributed analytical tools. MS analyzed data. AP wrote the manuscript. All authors read and approved the manuscript.

**References**

1. Al-Okaili RN, Krejza J, Wang S, Woo JH, Melhem ER. Advanced MR imaging techniques in the diagnosis of intraaxial brain tumors in adults. Radiographics. 2006;26(suppl_1):S173–89.

2. Gupta A, Shah A, Young RJ, Holodny AI. Imaging of brain tumors: functional magnetic resonance imaging and diffusion tensor imaging. Neuroimaging Clin. 2010;20(3):379–400.

3. Gabriel M, Brennan NP, Peck KK, Holodny AI. Blood oxygen level dependent functional magnetic resonance imaging for presurgical planning. Neuroimaging Clin. 2014;24(4):557–71.

4. Alimohamadi M, Shirani M, Shariat Moharari R, Pour-Rashidi A, Ketabchi M, Khajavi M, et al. Application of Awake Craniotomy and Intraoperative Brain Mapping for Surgical Resection of Insular Gliomas of the Dominant Hemisphere. World Neurosurg. 2016;92.

5. Azad TD, Duffau H. Limitations of functional neuroimaging for patient selection and surgical planning in glioma surgery. Neurosurg Focus. 2020;48(2):E12.
6. Bartsch AJ, Homola G, Biller A, Solymosi L, Bendszus M. Diagnostic functional MRI: Illustrated clinical applications and decision-making. J Magn Reson Imaging An Off J Int Soc Magn Reson Med. 2006;23(6):921–32.

7. Brennan NMP, Holodny AI. Use of Advanced Neuroimaging (fMRI, DTI/Tractography) in the Treatment of Malignant Gliomas. In: Malignant Brain Tumors. Springer; 2017. p. 3–13.

8. Wengenroth M, Blatow M, Guenther J, Akbar M, Tronnier VM, Stippich C. Diagnostic benefits of presurgical fMRI in patients with brain tumours in the primary sensorimotor cortex. Eur Radiol. 2011;21(7):1517–25.

9. Vysotski S, Madura C, Swan B, Holdsworth R, Lin Y, Del Rio AM, et al. Preoperative FMRI associated with decreased mortality and morbidity in brain tumor patients. Interdiscip Neurosurg. 2018;13:40–5.

10. Mahdavi A, Houshmand S, Oghabian MA, Zarei M, Mahdavi A, Shoar MH, et al. Developing optimized fMRI protocol for clinical use: comparison of different language paradigms. J Magn Reson Imaging. 2011;34(2):413–9.

11. Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TEJ, Johansen-Berg H, et al. Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage. 2004;23:S208–19.

12. Lorenzen A, Groeschel S, Ernemann U, Wilke M, Schuhmann MU. Role of presurgical functional MRI and diffusion MR tractography in pediatric low-grade brain tumor surgery: a single-center study. Child's Nerv Syst. 2018;34(11):2241–8.

13. Lau JC, Kosteniuk SE, Bihari F, Megyesi JF. Functional magnetic resonance imaging for preoperative planning in brain tumour surgery. Can J Neurol Sci. 2017;44(1):59–68.

14. Kapsalakis IZ, Kapsalaki EZ, Gotsis ED, Verganelakis D, Toulas P, Hadjigeorgiou G, et al. Preoperative evaluation with FMRI of patients with intracranial gliomas. Radiol Res Pract. 2012;2012.

15. Castellano A, Cirillo S, Bello L, Riva M, Falini A. Functional MRI for surgery of gliomas. Curr Treat Options Neurol. 2017;19(10):1–23.