ROLE OF FUNCTIONAL MAGNETIC RESONANCE IMAGING IN MAKING BRAIN TUMOR SURGERY SAFER

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Abstract:
OBJECTIVE: To plan neurosurgery that preserves brain function, it is crucial to obtain accurate images of the areas surrounding the eloquent tumor. The study's objective was to compare the diagnostic capabilities of preoperative functional magnetic resonance imaging (fMRI) to a comprehensive evaluation of morphological magnetic resonance imaging (MRI) data. The objective was to assess the relative usefulness of both techniques in the preoperative diagnostic process.

METHODS: A thorough examination of the neurological system was performed on 77 individuals who had Rolandic lesions, utilizing a magnetic field strength of 1.5 Tesla. The examination was standardized and included both functional and structural components. The central part of each hemisphere was precisely located through the use of six morphological markers and three functional markers.

RESULTS: The localization of the motor hand region by fMRI was successful in 76 out of 77 patients, greatly exceeding structural MRI analysis, which was successful in only 66 out of 77 patients (p-value < 0.002). Furthermore, 96% of patients had extra diagnostic data about tongue representation from fMRI, and 97% had additional diagnostic data regarding foot representation from fMRI. The preoperative risk assessment using fMRI and the postoperative clinical outcome was shown to be positively correlated in 88% of cases.

CONCLUSIONS: The research findings suggest that using preoperative functional magnetic resonance imaging (fMRI) can provide a more accurate assessment of the location of the motor cortex in relation to the brain tumor compared to traditional 3D MRI scans. This can simplify the preoperative evaluation of the potential risks and benefits of surgery, and make it easier to plan for a surgery that preserves neurological function. Although the study did require a longer imaging time, the results also indicate that fMRI may help to reduce hospital stays and minimize surgical complications.

Keywords: FMRI, tumor, surgery

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INTRODUCTION:

The major motor (M1, Brodmann area 4) and somatosensory (S1, Brodmann areas 1-3) cortices are located in the central region of the brain, which also includes the pre- and postcentral gyri. Therefore, central nervous system surgery, such as that used to remove tumors, may result in both motor and sensorial abnormalities. Even though severe brain tumor resection results in greater survival rates, it is regrettably linked to higher postoperative morbidity [1]. It is especially crucial to prevent surgery-related impairments in patients who have aggressive and infiltrative tumor development and, as a result, a poor chance of receiving curative therapy. Instead, the focus should be on maintaining brain function to ensure the quality of life. In these situations, stringent justification for neurosurgery procedures must be assessed against less invasive and alternative treatment options. To carefully examine and organize neurosurgical operations, more information about the anatomy and functions of the afflicted brain areas is also required.

Due to its better capabilities in creating high-resolution pictures with great soft tissue contrast and the fact that it does not employ ionizing radiation, MRI is largely acknowledged as the preferred imaging tool for the detection of brain tumors with these advantages, MRI offers a clear and non-invasive way to see the brain and reliably identify brain tumors. Various morphological cues are utilized to locate the central portion of the brain, however, even in healthy participants, considerable anatomical variations between people might impair the accuracy of these signals. The motor hand area is thought to be the most accurate morphological marker. It is also known as the "hand knob" on transverse planes and the "hook sign" on sagittal planes. It is readily recognized by its physical characteristics and is situated in the precentral gyrus. Other parts of the body can only be somewhat identified based on the somatotopic anatomy of the primary motor and somatosensory cortices since they lack such distinct anatomical markers. It is difficult to pinpoint these areas precisely due to the absence of distinct indicators. Additionally, pathological signal modifications affecting the pre- or postcentral gyrus, which may result in substantial changes in anatomical proportions and partly or obstruct pre-surgical neuroimaging, often cause diagnostic erroneous results. Brain tumors may also move functional regions away from standard markers [4]. Identification of eloquent cortical regions is essential in the pre-surgical planning of tumor removal to prevent irreversible harm to neurological function [5]. ECoG, sometimes referred to as electrocorticography, is a popular technique for evaluating brain function during surgical operations. However, compared to functional magnetic resonance imaging, it is seen as an invasive and pricey alternative (fMRI). As a less intrusive alternative to ECoG, fMRI is becoming more and more popular as a potential substitute for it. In contrast to invasive treatments, fMRI offers non-invasive diagnostic data prior to surgery. The method detects regional hemodynamic changes that correspond to real neuronal activity in functional areas, which serves as an indirect measure of brain activity. The lower concentration of deoxyhemoglobin in active brain areas is measured using the blood-oxygen-level-dependent (BOLD) technique on T2*-weighted images, offering a thorough picture of brain activity. The accuracy of pre-surgical localization of the main motor cortex was confirmed by several investigations comparing BOLD-fMRI with well-known reference techniques like ECoG [9]. Although pre-surgical localization of the motor cortex is now the most well-established clinical use of fMRI, it is still not governed by universal standards for data collection, processing, and interpretation by physicians. Additionally, very few authors have made an effort to evaluate the diagnostic utility of pre-surgical fMRI, and the available studies are mostly based on non-standardized research in limited patient populations [10]. There haven't been many thorough studies done in this field, despite the potential advantages of using fMRI in preoperative diagnostic setting before neurosurgery. This has made it harder for people to employ this non-invasive technique in therapeutic settings. However, it is essential to thoroughly and uniformly assess the diagnostic capability and therapeutic advantages of pre-surgical fMRI. In a large patient group with central brain tumours, the diagnostic efficacy of pre-operative fMRI and morphological MRI was examined in this research. This study objective is to get a better comprehension of the diagnostic benefits of fMRI and how it may be used in a preoperative setting to aid in the surgical procedure.

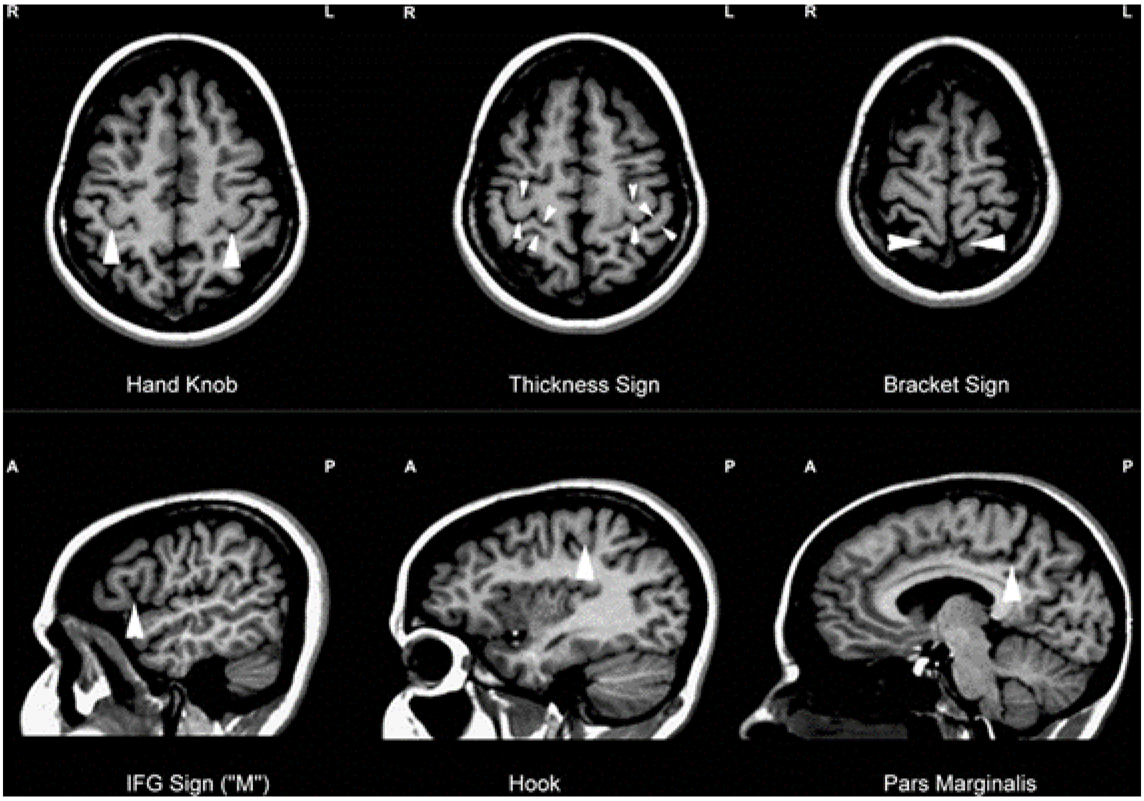

Figure 1: Landmarks in the central region's anatomy

METHODS: In the current research, 77 consecutive patients with central brain tumors (average age of 51 and range of 16–80 years) were examined using morphological and functional MRI by established presurgical investigational guidelines before a prospective neurosurgical procedure. Before the experiment, each patient provided their informed permission. Clinical information was retroactively gleaned from operating procedures and clinical records. The underlying causes of the mass lesions were varied, with the majority being of a malignant nature (as shown in Table 1). In 38 cases, the tumors were found to be located in the left hemisphere, while in 37 patients, the tumors impacted both hemispheres in multiple instances. At the time of imaging, the mass lesion affected 10 patients with mixed motor and somatosensory impairments, 21 patients with somatosensory deficits, and 29 patients with motor deficits. In addition, 37 individuals showed signs of focal and generalized seizures, speech and language impairments, difficulties with word searching, and/or personality changes. Only minor impairments, such as headaches and vertigo, were observed by some individuals. Retrospectively, there were no trustworthy clinical data available for the 2 individuals. In three instances, the patients were not exhibiting any symptoms, and it was only through coincidence that the mass lesions were discovered (1 case of a cavernoma and 2 meningiomas). These findings were incidental in nature.

Table 1: Classification of brain mass lesions in the central region of the study participants.

Type of Tumor	WHO Grades	N
Brain abscess		2
Angioma/Cavernoma		7
Metastasis		17
Malignant histiocytoma		1
Atypical meningioma	II	1
Meningioma	I	4
Oligoastrocytoma	II	2
Oligodendroglioma	Unknown	1
Oligodendroglioma\	III	1
Oligodendroglioma	II	2
Gliosarcoma		2
Glioblastoma		19
Astrocytoma (unknown grade)	Unknown	3
Astrocytoma	III	7
Astrocytoma	II	7
Astrocytoma	I	1
Total		77

Using a typical birdcage head coil, all patients were examined. By placing the individual in a relaxed posture and securing the head with foam cushions that have already been made, movement artifacts were minimized. The patients had an imaging technique in which a contrast agent containing gadolinium was administered intravenously. A T1-weighted 3-dimensional anatomical data set was created during this process, and it was then utilized to navigate the surgical site and superimpose functional data. The data set demonstrated that the peri-rolandic mass lesions that were encircled by the contrast enhancement ranged in size from 4 to 24 millimeters on axial images.

Six well-established morphological markers in both hemispheres were used to identify the core area on T1-weighted structural images [12]. The patients' unaffected hemisphere served as a guide for locating the core region of the damaged hemisphere. A number of morphological indicators were used to pinpoint the position of the centre region. The procedure entailed contrasting the changes and anatomical variances between the landmarks employed in the afflicted and unaffected hemispheres. Figure 1 shows the morphological traits that were employed for this.

In this study, the central area of the brain was identified in patients with central brain tumours using a wide variety of morphological markers. These markings made it easier to precisely and accurately locate the impacted region. In order to distinguish the central area of the brain in patients with central brain tumours, many morphological indications were used in the study. The "thickness sign," which refers to the distinctive trait of the precentral gyrus having a thicker cortical layer than the postcentral gyrus, was one of the markers employed. Another morphological signal was the "hand knob and hook," which, when examined on axial planes, showed as a dorsally directed "hook" or "omega" and, when viewed on sagittal scans, as a posteriorly directed "omega" or "epsilon"-shaped convexity. The "pars marginalised and bracket sign," which on parasagittal planes denotes the existence of both pars marginals of the cingulate sulci behind the central sulcus, was also used in the study. The "inferior frontal gyrus," which on parasagittal sections shows as an M-shaped structure made up of the partes orbitalis, triangularis, and opercular, was another marker. On axial sections, it creates fictitious "brackets" around the partes marginales of the cingulate sulci.

In the fMRI process, the T2*-weighted single-shot blipped gradient echo Echo-Planar-Imaging sequence was utilized. This sequence featured a TR/TE of 4,000/80 ms, a field of view of 256256 mm2, and a flip angle of 90°. The fMRI required an additional 7 minutes of imaging time for each measurement, which included 4 baseline periods, 3 stimulation periods, and 1 offset period of 20 seconds each. The subjects performed finger tapping, tongue movements, and toe flexions and extensions on the side opposite the lesion. When complicated finger opposition was impossible due to tumor-associated paralysis, repeated fist clenching was used as a substitute. BrainVoyager was used to evaluate the functional MRI data, which comprised motion correction, smoothing, and estimation of BOLD activation. Semi-automated data processing was used, superimposing structural and functional pictures. The functional activations were computed based on the correlation between the BOLD data and the hemodynamic reference function. A minimum cluster size of 36 mm3 was set as a requirement for data assessment, and a dynamic statistical threshold was used to constantly reduce the correlation threshold. As a consequence, the activation that was larger than the 36 mm3 clusters and had the strongest connection to the hrf was shown first. Further lowering the threshold allowed for the hierarchical presentation of activations in additional functional regions that had a lesser correlation between the observed BOLD signals and the hrf. This process was carried out repeatedly until activations were found throughout all interest areas (ROI). To guarantee that BOLD-signals could be distinguished from background noise, a highly conservative limit of $r = 0.4$ with p-value < 0.05 (Bonferroni adjusted) was imposed. This was classified as "no activation" if there was no BOLD activation seen in any ROIs that fell under this lower threshold. BOLD signals with a relative change of $S>5\%$ were also declared biassed and omitted from the evaluation since such high-level activations are likely to originate from draining veins [15]. The activations that were most strongly associated with the hrf were categorised as precentral and used as functional landmarks in accordance with our past study, as shown in (Figure 2):

- Cortical depiction of the foot
- Cortical depiction of the hand
- Cortical depiction of the tongue

The only part of the body represented by an anatomical landmark that allowed for comparison of the two diagnostic MRI instruments was the motor hand region. The Student's t-test was used in statistical analysis to compare the MRI and fMRI data. With the use of this test, the importance of any variations between the two sets of data was assessed, as well as the precision with which the motor hand area could be localized.

RESULTS: When it came to locating the unaffected hemisphere in normal anatomical conditions, the "thickness sign" and the "hand knob" proved to be the most reliable anatomical markers with a success rate of 99% (76 out of 77) and 97% (75 out of 77) respectively, as shown in

Table 2. However, in the tumor-affected hemisphere, only 49% (38/77) and 86% (66/77) of the patients were able to locate such landmarks. According to anatomical criteria, the motor hand region could not be distinguished in 14% (11/77) of patients. The precentral hook, a sagittal pendant to the hand knob, was less obvious and offered no further information in this group if the hand knob could not be detected clearly.

On the side with the tumour, the functional somatotopic mapping of the motor cortex was carried out (for contralateral movements). The findings revealed that 76 out of 77 cases—or 99% of cases—saw the motor hand area effectively detected. Even though up to 29 individuals had pareses due to tumors, localization of the hand's motor region was still achievable in all but one instance. As a result, supplementary functional MRI was considerably better at localizing the motor hand region than morphological MRI (p=0.002). When the motor regions of the tongue and foot were examined in 70 individuals, 97% (68/70) and 96% (67/70) of the patients could be convincingly recognized (Table 3). Since there are no reliable anatomical markers for the motor foot and tongue regions, only the fMRI approach could be used to pinpoint these representations.

In 67.5% (52/ 77) of patients, the choice to have neurosurgical intervention was taken after a thorough examination of the clinical situation, tumor origin, and fMRI data. fMRI was utilized to depict the centers of activation clusters but not to define the boundaries of resections. Three individuals only had partial resection, compared to the entire resection of 49 cases. Due to multiple metastases, arteriovenous angiomas, or poor clinical condition, 25 patients were not operated on; however, in 16 of these cases, the decision was significantly influenced by fMRI results because the imaging revealed a high likelihood of surgery-induced neurological impairments if the centre of activation was close to damaged or abnormal tissue. These 16 tumors were all malignant, with the majority being gliomas of various stages.

Table 2: Finding morphological features in both the damaged and healthy hemispheres

		Sagittal			**Axial**		
		Inferior frontal gyrus	**Pars marginalis**	**Hook**	**Bracket sign**	**Hand knob**	**Thickness sign**
Unaffected hemisphere	**Uncertain**	26	8	3	2	2	0
	Non-existent	0	0	1	1	0	1
	Existent	51	69	73	74	75	76
Affected hemisphere	**Uncertain**	22	2	11	2	0	0
	Non-existent	16	54	12	20	11	39
	Existent	39	21	54	55	66	38

When pre- and postoperative data for all patients undergoing neurosurgery were analysed, it was found that 12 patients' clinical conditions improved following surgery, 15 had a moderate or temporary impairment, and 4 patients had a substantial neurological impairment. The brain functioning of 19 persons did not alter in any way. In other words, preoperative fMRI-based risk assessment was highly correlated with the clinical result, and 88% (46 out of 52 postoperative patients) showed very minor impairments or even functional improvement.

Table 3: Identification of functional ipsilesional markers.

Functional landmarks	**Tongue**	**Toes contralateral**	**Fingers contralateral**
Technical error	3	0	0
Not investigated	7	7	0
Movement artefacts	0	1	0
Severe paresis	0	1	1
Existent	67	68	76

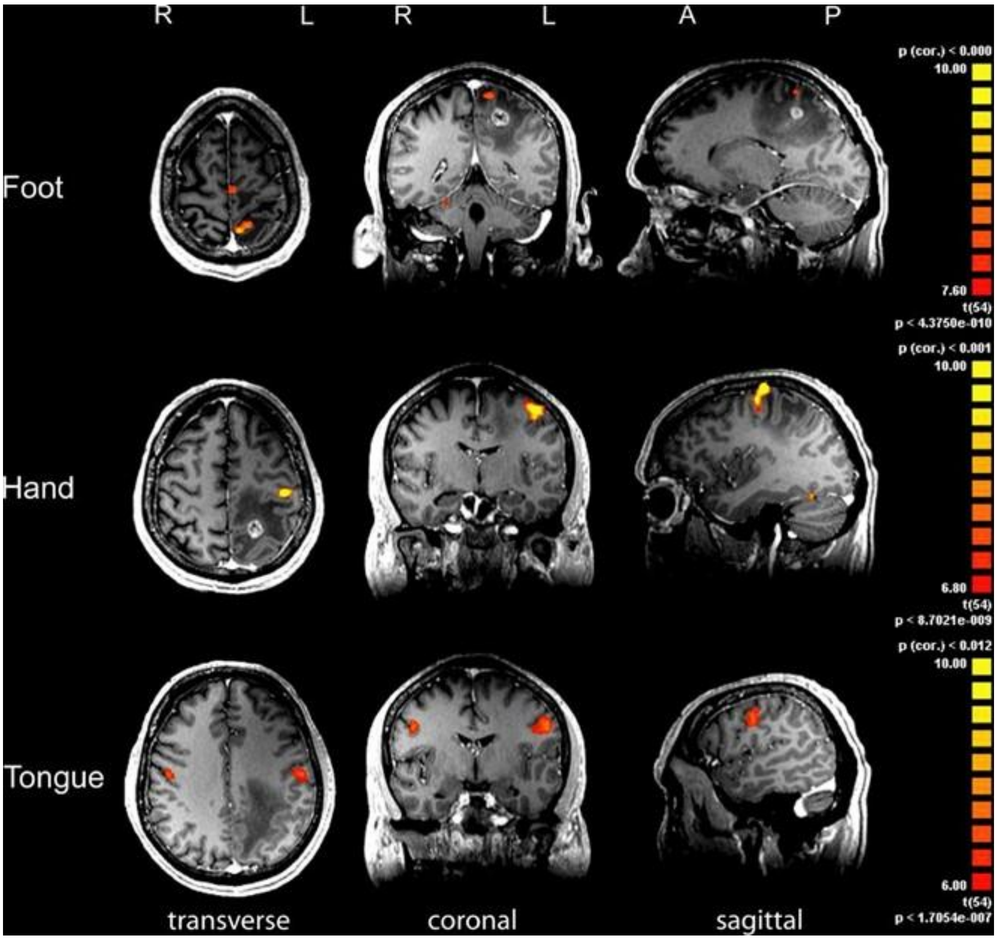

Figure 2: Central region landmarks that serve a purpose

DISCUSSIONS: The findings of preoperative imaging have a significant role in therapy choices for individuals with central brain tumors. It is crucial to determine if neurological abnormalities are possible after the excision of the tumor by neurosurgery and how much the tumor has damaged the eloquent brain regions. Progressive, infiltrative tumor development is often accompanied by alteration of anatomical lead structures, placing limitations on morphological imaging methods. When treating patients with aggressive tumors, preserving critical brain functions and maintaining a high quality of life is of utmost importance. This is because a cure through surgical resection is often not possible for the majority of these patients. Thus, it's crucial to consider these factors in the course of treatment.

Preoperative fMRI has seen a rise in use in pre-surgical neuro-imaging as a result of methodological and technical advancements, particularly in big medical facilities. It is still unknown to what degree presurgical fMRI may provide diagnostic advantages over traditional MR imaging. Only trials in small patient groups using irregular and varied procedures have been described so far. However, research [16] has offered a basic idea of the diagnostic advantages of fMRI over MRI. In the aforementioned research, only 3 individuals with brain tumors were included, and none of them had a mass effect lesion that was directly in the central area, which raised severe questions about the validity of their findings at the time. Numerous research have focused on the function of pre-surgical fMRI in precisely identifying key regions of the brain in patients with malignancies. [17] While others have looked at bigger groups with different outcomes, others have considered small patient populations and found encouraging findings. [18] The current research mainly explored the diagnostic value of fMRI in localising functional regions in patients with brain tumours, with a focus on 77 individuals. The results showed that the thickness sign and hand knob were the most precise anatomical signals for identifying the motor hand region, with identification rates of 99% and 97% in the healthy hemisphere, respectively. The motor hand area was unidentified in 14% of patients, and these landmarks were only reliably detected in 49% and 86% of tumor-affected hemispheres. This study emphasises the potential use of fMRI in pre-surgical neuroimaging, while more extensive, bigger investigations are still required to thoroughly evaluate its effectiveness. [19]

In individuals with no abnormalities, the fMRI mapping findings demonstrated a high degree of accuracy in identifying the motor representations of tongue, feet, and hands, feet, with success rates exceeding 100%. [20] In this research, 77 individuals with central area brain tumours were included. Even in patients with tumor-related muscular weakness, fMRI was 99% accurate in identifying the central region. The localization of the motor hand area using fMRI was shown to be considerably better than using conventional MRI ($p = 0.002$). Full somatotopic mapping using fMRI only needs an extra 7 minutes of imaging time, and post-acquisition analysis may be quickly included into clinical practises with the use of standardized methods and automated data processing tools. [21] Additionally, despite a decline in BOLD signal readings in situations of acute paralysis, sensory stimulation during fMRI may still provide extra data. [22]

Despite the benefits of pre-operative fMRI that our work has shown, methodological restrictions and possible concerns should not be ignored. These include altered BOLD responses in hypervascularized tumors or arteriovenous malformations, movement artifacts, possible superimposition, coregistration errors, and movement artifacts [23].

The length that should be retained between the resection border and functional representation is another question that neurosurgeons often ask, and we feel that fMRI cannot (yet) reliably address it [24]. The incidence of neurological abnormalities brought on by surgery is negatively correlated with the location of the brain tissue closest to the tumor.

The results of our analysis confirmed data from other patient groups and showed how useful pre-operative fMRI is for diagnosing medical conditions. The greatest benefit was shown in individuals whose surgery was postponed as a consequence of presurgical fMRI. 14 patients (or around 18%) made up this group in the current investigation.

CONCLUSIONS:

The extra diagnostic procedures needed to do an fMRI are seen to be justified and need to be a necessary component of pre-surgical examinations. This is due to the fact that the results of fMRI often play a vital role in the selection of a course of therapy. The link between the tumour and the adjacent sensorimotor cortex is also better understood with the use of fMRI, which improves the planning and execution of operations meant to protect brain function. Preoperative fMRI has the potential to greatly decrease therapy-related health issues and minimize hospital stays as a consequence of its inclusion in the preoperative procedure.

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