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Surgical Utility of Preoperative Combined Functional MR Imaging

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Abstract

Aim &objectives: *Preoperative imaging techniques that are increasingly being used to outline eloquent brain regions prior to resection include functional MR imaging and DTI. In this study we evaluate brain lesions in and around the eloquent cortex and find out whether there is significant difference in postoperative morbidity and successful outcome while using both BOLD functional MR technique &DTI instead of using BOLD technique alone.*

Materials & methods: *We have studied 46 patients with supratentorial space-occupying lesions either involving or adjacent to one or more eloquent WMTs or eloquent cortex using both BOLD imaging & DTI technique.*

Results: *Satisfactory postoperative outcome was 95% for patients evaluated with combined BOLD fMRI & DTI, as compared to 72% for the patients evaluated with fMRI alone. We find out significant statistical difference between fMRI and combined DTI-BOLD study with the chi -square test (P value of 0.03).Preoperative localization of eloquent cortex and white matter as well as detailed assessment of their relation to the brain lesions were feasible in the majority of patients using BOLD fMRI & DTI combined technique than patients evaluated with fMRI alone . Results provided by this combined technique modified the treatment strategy by avoiding damage to eloquent brain areas in significantnumber of patients.*

Conclusion: *Combined fMRI-3D DTI tractography technique helps the neurosurgeon to plan the surgical approach so as to avoid the major tract and eloquent cortex, and hence, patient to have no or minimal postoperative morbidity.*

Keywords*: Blood oxygen level dependent imaging, diffusion tensor imaging, white matter tract,Functional MR imaging.*

I. Introduction

Functional MR imaging includes DTI, BOLD imaging, perfusion imaging, MR spectroscopy and molecular imaging. BOLD -fMRI has been used to study functional activity of eloquent cortex like motor, language, visual and sensory cortex. Preoperative BOLD imaging study of this eloquent cortex provides information on the feasibility of surgery and allows adequate assessment of the risk of postoperative neurologic deficits[1,2,3].DTI is useful for depiction of eloquent white matter, because surgical severing of these white matter tracts can produce postoperative neurologic deficits[4]. So pre-operative BOLD imaging allows the neurosurgeon to decide whether to attempt a resection, a stereotactic biopsy or not to operate at all. fMRI also influence surgical approach, guide the intra-operative cortical stimulation during surgery and both shorten the surgical duration and the time under anaesthesia [3].

Prior to surgery, aims of every neurosurgeon are, a small and less invasive craniotomy, a resection as wide as possible, the preservation of eloquent areas and white matter major tracts and the minimization of postoperative morbidity. Therefore, it is important that the margin of resection should not affect functionally important white matter tracts and eloquent cortical areas. Mapping of these areas is traditionally achieved by invasive methods like intraoperative electrical stimulation[4]. These methods are not only invasive but also complicated and themselves need separate surgical procedures. The lack of proper knowledge of anatomical relation between lesion border and adjacent important fiber tract or eloquent cortex, it leads to blind decisions in neurosurgery. BOLD imaging precisely tells about eloquent cortex whereas DTI tells the relationship of lesion and eloquent white matter tracts. So, combining these various functional MR imaging (BOLD imaging, DTI and 3D tractography) provides most part of above mentioned information in a non-invasive manner and helps neurosurgeons to achieve their goal with satisfactory results.

In this study we evaluate brain lesions in and around the eloquent cortex and find out the usefulness of combined functional MR technique modalities over single BOLD- fMRI technique**.**

II. Materials And Methods

2.1Patient selection

After obtaining ethical clearance and informed consent, the study was commenced with 1.5 TESLA Siemens MRI system, from September one , 2014 to September one , 2015. 46 patients with supratentorial lesions who underwent morphological and functional MR imaging before neurosurgical procedure were followed up postoperatively.

Patients were clinically evaluated prior to surgery, to look for any neurological deficits, which may occur due to infiltration of the various tracts, displacement, edema or mass effect. In patients who had edema or mass effect in a particular tract, dominant cortex or plasticity on the contralateral cortex it was logical to assume that they would recover after surgery (provided there was no surgical destruction or damage to the tract).

Focal and generalised seizures, language and speech deficits, word finding deficits and/or change of personality were observed in 42 patients. Some patients reported only mild impairments such as headache and vertigo. In four patients mass lesions were detected incidentally (one-cavernoma, one -meningioma, two -AVM) .We have included both benign and malignant supratentorial brain lesions, gliosis that needs resection due to intractable epilepsy and single metastatic lesion with mass effect. We excluded deep grey matter and multiple metastatic lesions. Imaging results were compared with postoperative outcome subsequently.

2.2 MRI acquisition

The MRI studies were performed in a 1.5 T system (MagnetomAera; Siemens Medical Systems, Erlangen, Germany) using an 8 channel head coil. All patients underwent a conventional MRI protocol, including the following sequences: 3DAxial T2-weighed images (TR: 3200ms, TE: 381 ms, FOV: 250 mm, matrix: 256 × 256 and 1.5-mm section thickness , 3Dcoronal FLAIR images (TR: 5000 ms, TE: 333ms, FOV: 250 mm, matrix: 256 × 256 and 1.3-mm section thickness with 35% of interval), as well as pre and post contrast 3D sagittal T1-weighed images (TR: 1900ms,TE: 2.71 ms, FOV: 230 mm, matrix: 256 × 256 and 0.9-mm section thickness) after intravenous administration of 0.1 mmol/kg of gadolinium.

2.3 Functional MRI acquisition and post processing

The BOLD-weighted single-shot EPIs were obtained repeatedly at intervals defined by the repetition time for each patient during task performance. Technical parameters were as follows: field of view 220 mm, matrix 64 × 64, TR 3500 msec, TE 50 msec, fractional anisotropy 85°, 6-mm coronal plane sections, and 5mm axial plane sections. Spatial coverage was sufficient to provide mapping of the entire cortex. The number of images and the duration of imaging varied with the paradigm. Imaging duration ranged from 3 to 5 minutes. Additional high-resolution anatomical scans, including 3D volumetric T1- and T2-weighted sequences, were acquired as part of the preoperative assessment. All post processing was done using the work station.

2.4 DTI acquisition, post-processing and analysis

The DTI was performed using a single shot echo-planar sequence with acceleration factor of two and with the following parameters: TR: 3500 ms, TE: 83 ms, FOV: 224 mm, matrix: 148 × 148, section thickness: 4 mm, interval gap-1.5 mm, bandwidth: 1722 kHz, EPI factor: 148, echo-spacing: 0.83, flip angle: 90º, NEX: 3, diffusion encoding in 21 different directions and *b* values = zero and 1400 s/mm^2. Post processing was done in an offline workstation (EWS01 extended workstation). Fiber tracking was done by Fiber Assignment by Continuous Tracking method. FA values were calculated using free hand Region of Interest (ROI) method. For image analysis, white matter tracts adjacent to the tumour were compared with homologous tracts in contralateral control hemisphere both subjectively by visual comparison and quantitatively by comparing the FA and ADC values.

2.5 Imaging analysis

Our aim in the present study was to investigate whether preoperative combined BOLD FMRI&DTI technique provides satisfactory clinical outcome over BOLD -fMRI alone. Our series is based on 46 patients with supratentorial (both intra axial/ extra axial) space-occupying lesion either involving or adjacent to one or more eloquent WMTs (pyramidal tract, optic radiation, arcuate fasciculus ,SLF) or eloquent cortex (motor, sensory, Broca's area , Wernicke's area, visual cortex) using BOLD fMRI-DTI .

The case series included were gliomas (*n* =22), gliosis with intractable epilepsy (*n* =6), Focal cortical dysplasia (*n* = 3), cavernoma (n=3), single metastasis (*n* = 3), DNET (n=2), Meningioma (n=2), Arteriovenous malformation (n=4), extraventricular ependymoma (n=1). Case findings were read by two radiologists of more than ten years experience.

Many authors have described a "golden rule" that a minimal distance for feasible surgical resection is a distance of at least 10–15 mm between tumour margin and an essential structure [5,6,7]. So, we decided to have cut off value of 15 mm margin clearance for our study. Out of 46 patients, 18 lesions were away ($\geq$1 cm -which is essential for surgical clearance) from the eloquent cortex, 14 patients were within the eloquent cortex and 14 lesions were within <1cm of eloquent cortex.

Out of 46 patients, for 21 patients, DTI tractography was done in addition to bold imaging as suggested by neurosurgeon. Before doing the functional MR imaging, the following details were obtained from neurosurgeons: 1) Preoperative treatment plan 2) additional diagnostic testing like intra operative electrical stimulation testing that would be performed if functional MR imaging were not available. We included displacement and destruction of the white matter tract and feasible surgical approach in our DTI image analysis report. After discussing with the neurosurgeon, we have altered neurosurgical approach in most of the patients. Our neurosurgeons also were comfortable with those approach advised by us in most of the patients.

2.6 Statistical analysis

Of the 46 patients, three were patients were deferred surgery after explaining postoperative complications (Table 1&3). These three lesions were located inside the motor cortex, broca's area and eloquent white matter. In remaining 43 patients, eight patients developed postoperative symptoms inspite of perfect preoperative planning and limited resection. Of these eight patients, the lesion was located either within or closer (<1cm) to the eloquent cortex in seven patients and one lesion was away (>1 cm) from eloquent cortex. On postoperative follow up, 17/25 patients who have undergone BOLD- fMRI alone (Table 2) developed no significant postoperative symptoms, seven patients developed postoperative complications. We also included one patient who was deferred surgery in our final results as he might have developed symptoms otherwise. Totally 72% of patients were benefited by preoperative BOLD-fMRI alone. Similarly, in combined BOLD fMRI & DTI (Table 4) technique 18/21 patients improved postoperatively without any new neurological deficits, two patients were deferred surgery and one patient developed postoperative complication. So beneficial outcome here in combined BOLD –fMRI & DTI was 95%.

Table 1- Brain Lesions Evaluated With BOLD FMRI Imaging Alone

S. No	Diagnosis	Location	Distance between eloquent cortex and lesion	Plasticity/opposite dominance	Postoperative morbidity new symptom/ Worsening of existing symptom
1	Glioma	Premotor cortex	<1cm from motor cortex	Plasticity	Weakness, speech disturbances
2	Ependymoma	Precentral gyrus	>1cm motor	Mild plasticity	-
3	Glioma	Anterior temporal lobe	>1cm Wernicke's area	-	-
4	FCD	Left superior frontal gyrus adjacent parasagittal medial frontal region	<1cm motor	-	-
5	AVM	Posterosuperior aspect of middle inferior temporal gyrus	Within Wernicke's area	Plasticity	-
6	Glioma	Superior aspect of Middle frontal gyrus	<1cm motor, Broca's area	Plasticity	-
7	Gliosis	Middle inferior temporal gyrus	>1cm Wernicke's area	Opposite side dominance	-
8	Gliosis	Supramarginal, Heschl'sgyrus	<1cm Wernicke's area	-	-
9	Meningioma	Parasagittal parietal region	<1cm motor	-	-
10	Glioma	Prefrontal, premotor cortex	Within Expected motor/Broca's area	Plasticity	-
11	Glioma	Postcentral gyrus	Within sensory	-	-
12	Glioma	Pars opercularis of parietal cortex	Within Wernicke's area	-	Speech disturbances
13	Cavernoma	Superior ,middle temporal gyrus	Within Wernicke's area		Surgery deferred
14	Glioma	Premotor cortex	>1cm hand motor		-
15	Gliosis	Parietal opercula	>1cm motor cortex		-
16	FCD	Posterior most frontal opercula	>1CM Broca's area		-
17	Glioma	Posterior aspect of orbital frontal gyrus	Within motor		Weakness
18	AVM	Perisylvian	Within Broca's area	Plasticity	-
19	Glioma	Parasagittal high frontal extending into cingulate gyrus	>1cm motor		Altered behaviour
20	Glioma	Anterior aspect of frontal gyrus	Within motor		-
21	glioma	Posterior Superior temporal gyrus	Within Wernicke area	-	Speech deficit
22	Metastasis	Superior frontal gyrus	Within motor	Mild plasticity	Mild weakness
23	gliosis	Superior temporal gyrus	<1cm from Wernicke area	-	-
24	glioma	Parasagittal parietal region	<1cm from motor	-	weakness
25	Meningioma	Near inferior frontal lobe	>1cm from broca's	-	-

Table 2- Brain Lesions Evaluated With BOLD FMRI imaging alone

Location	Surgery deferred	Postoperative morbidity	Good outcome	Total
Within eloquent cortex	1	4	5	10
<1cm from eloquent cortex	-	2	5	7
>1cm from eloquent cortex	-	1	7	8
Total	1	7	17	25

Table 3-Brain Lesions Evaluated With FMRI & DTI tractography

S. No	Diagnosis	Location	Eloquent cortex	Plasticity/ Dominance	Eloquent white matter	Approach	Post-surgical morbidity/ Neurological deficits
1	High grade glioma with mass effect	Parietal occipital	within Wernicke's area	-	SLF destruction		Yes
2	Gliosis	Sup.temporal gyrus	within Wernicke	-	-	-	-
3	Gliosis	Precentral gyrus	<1cm motor	Plasticity	-	-	-
4	ODG	Superior aspect of superior, middle frontal gyrus	>1cm motor cortex	-	CS, CC oedematous	Superior	-
5	Metastasis	Anteroinferior temporal lobe extending inferior frontal gyrus	Within Broca	-	SLF edematous	Anterior approach ,limited resection	-
6	Glioma	Parieto-occipital lobe	Within Wernicke	-	-	Surgery deferred	-
7	Low grade glioma	Superior temporal gyrus	Expected Wernicke area	As opposite side Broca's area and Wernicke dominant	Arcuate fasciculus displacement superiorly	Inferolateral	-
8	Cavernoma	Occipital lobe lingual gyrus , just postero inferior to the calcarine cortex	>1cm from visual cortex	--	Optic radiations medial to lesion	Lateral approach	-
9	Metastasis	Pars opercularis of left inferior frontal Extending anterior temporal pole	Within Broca's area	-	edematous CS tract	Surgery deferred	-
10	Glioma	Inferior , middle temporal gyrus	>1cm from Wernicke	-	Normal tracts	Antero inferior	-
11	FCD	Insular gyrus	<1cm from Broca's area	-	No displacement /destruction	Selective epileptic foci removed	--
12	Glioma	High frontal cortex	<1cm motor	-	SLF fasciculus displacement	Superior	-
13	Glioma	Sup frontal gyrus	>1cm motor	-	CS tract Posterior	Anterior	-
14	Cavernoma	Middle temporal gyrus	<1cm Wernicke		No displcement	Anterior	-
15	Glioma	Superior frontal gyrus, left premotor gyrus	Motor, language	Motor, language on opposite side	Destruction SLF, CS	-	-
16	DNET	Middle frontal	>1cm from motor	-	No displacement /destruction	Superior	-
17	AVM	Middle and inferior temporal gyrus	>1cm Wernicke's area	-	No displacement /destruction	Anterolateral	-
18	Glioma	High frontal cortex	>1cm motor	-	SLF fasciculus displacement anteriorly	Posterior	-
19	Low grade glioma	Inferior , middle temporal gyrus temporal gyrus	>1cm Wernicke area	-	Arcuate fasciculus displacement inferiorly	Anterior	-
20	Glioma	left inferior frontal lobe	<1 cm Broca's area	-	CS tract medial to lesion	lateral	-

21	Gliosis	Posterior aspect of Parietal opercula	< 1cm motor cortex	-	SLF inferior to lesion	lateral	-

Table 4- Brain Lesions Evaluated With Functional MRI &DTI

Location	Surgery deferred	post surgical morbidity/ neurological deficits	Good outcome	Total cases
Within eloquent cortex/WMT	2	1	1	4
<1cm from eloquent cortex/WMT	-	-	7	7
> 1cm Away from lesion eloquent cortex/WMT	-	-	10	10
Total	2	1	18	21

Statistical test was performed by using chi-square test and we got a *P* value of 0.03 (Table 5) which is statistically significant. We concluded that this good outcome is due to added advantage of DTI which provides information for correct surgical approach. 3D tractography has also added additional information like displacement /destruction of eloquent white matter fibres.

TABLE 5: Statistical Difference BetweenPatients Evaluated With Bold FMRI Alone And Combined FMRI-DTI Technique

Study	Total cases	Post surgical morbidity/ Neurological deficits	Good clinical outcome	Surgery deffered as dictated by FMRI	Total satisfactory outcome
FMRI alone	25	7	17	1	18/25(72%)
FMRI-DTI	21	1	18	2	20/21(95%)
P value 0.03(chi –square test)					

2.7 Results

In patients evaluated with BOLD fMRI, satisfactory clinical outcome was72%.But postoperative morbidity (seven patients) was significantly higher comparing to only one case in combined fMRI-DTI study. Significantly increased outcome (95%) in combined BOLD & DTI technique is because of predetermined surgical approach by neurosurgeon with the help of both BOLD & DTI technique. So with the help of BOLD & DTI technique neurosurgeon avoided not only eloquent cortex but also eloquent white matter.

III. Discussion

Functional magnetic resonance imaging measures brain activity by detecting associated changes in blood flow. It relies on the fact that cerebral blood flow and neuronal activations are coupled. Diffusion tensor imaging is the technique that enables the measurement of restricted water diffusion in tissue, fractional anisotropy in order to produce the white matter tract. In the present study, we analysed that combined fMRI-DTI technique is a more useful preoperative technique over fMRI alone. Satisfactory outcome was 95% for patients evaluated with BOLD fMRI & DTI patients compared to 72% for the patients evaluated with FMRI alone with statistical difference of 0.03 .This increased outcome is due to alternate surgical approach provided by DTI technique and language dominance, plasticity development revealed by BOLD technique.

Studies in the literature explains the lack of postoperative neurologic deficits in patients who have undergone preoperative functional MR imaging .The influence of functional MR imaging on treatment has also been suggested in the literature[5,6,7]. In a study by Hossam M. Sakr et al (2011) FMRI provided information regarding pre-operative planning thereby decreased the postoperative neurological deficits and complications[5] . In our study 8 /46 lesions infiltrated eloquent cortex in a particular hemisphere that led the transfer of the functional area to the contralateral side as shown in **Fig 1(**plasticity). All those eight patients were reported by BOLD -fMRI, later confirmed by direct cortical stimulation also. fMRI has the potential to reveal plasticity that could affect the neurosurgeon's decision to offer surgery.

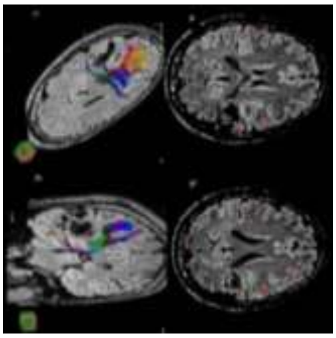

Figure 1(a-e).AVM in left perisylvian region. (a,b)Functional MR images showing, activation in bilateral Broca's area on language comprehension task, suggestive of plasticity. (c-e) 3D DTI tractography showed displacement of arcuate fibers of SLF. As there was plasticity on the contralateral Broca's area, there was minimal postoperative speech deficit.

In the study by Jeffrey R. Petrellaet al[8], Thirty-nine consecutive patients (19 male, 20 female; mean age, 42.2 years) underwent functional MR imaging for possible tumour resection. Treatment plans before and after functional MR imaging differed with significant P value ($P< 0.05$). So in their study, Functional MR imaging enables the selection of a more aggressive therapeutic approach.

Another important issue answered by fMRI is language dominance. Assumptions regarding language dominance that are based solely on handedness may be misleading in some patients. This may result in an unnecessarily conservative treatment approach for certain patients with brain lesions in whom surgery is, in fact, safe and clinically desirable. In our study fMRI was helpful for 2 /46 patients by revealing hemispheric dominance on opposite side of the lesion in which otherwise surgery may be deferred (**Fig2)**. These occurrences reveal that fMRI should routinely be done preoperatively in patients with lesions in the language cortex, particularly when brain lesions are deemed inoperable because of their proximity to essential language cortex[9,10].

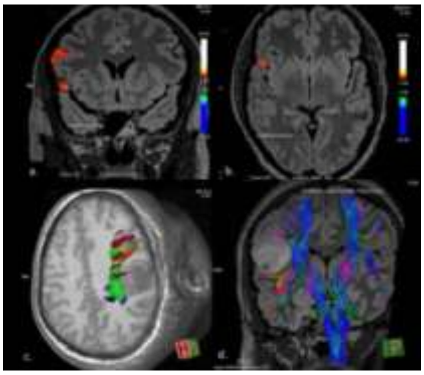

Figure 2((a-d) Oligodendrogliomain the left parietal opercula, Left supra marginal gyrus indenting the posterosuperior aspect of left superior temporal gyrus. a,b - FMRI Images with comprehension paradigm, showing activation in the right Wernicke's area. c,d - 3D-DTI tractography shows medial displacement of the superior longitudinal fasciculus without any destruction. Surgery was performed, there was no postoperative complication.

Eloquent white matter tract identification (**Fig 3**)is difficult intra operatively both by visual inspection and by intra operative cortical stimulation unlike eloquent cortex identification, DTIwas the problem solving tool in these situations. In our study DTI answered most of the queries of neurosurgeon like displacement, destruction of tracts (**Fig 4**)and feasible surgical approach. An advance in the treatment of patients with brain lesions was the ability to co-register functional images onto the anatomical images in the neurosurgical navigational system. In practice, many neurosurgeons still revert to the traditional method of identifying the location of eloquent cortices by direct cortical stimulation. Our neurosurgeons utilised this neuronavigation technique in all 21 patients during surgery. The neurosurgeon can visualize the relationship of the tumour to the adjacent eloquent areas, which aids both in the planning and in the actual resection of the tumour [11,12,13].

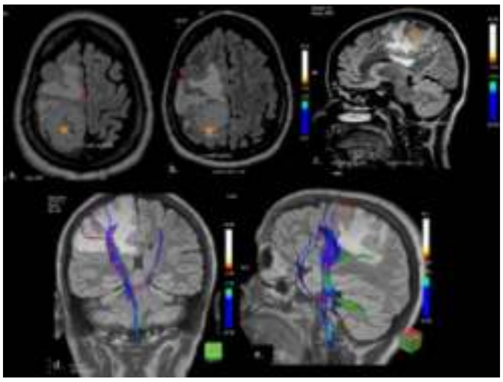

Figure 3.(A-E) a case of right parietal meningioma. Motor cortex functional MRI- structural axial images fused with functional image showing activation in hand motor area .(Figure 3- a,b,c) shows sensory cortex(star) which is away from the lesion(arrow), Figure (d,e)3D DTI tractography image with displacement of CS tract anterolaterally , so surgical approach was posterior and superior, there was no postoperative weakness.

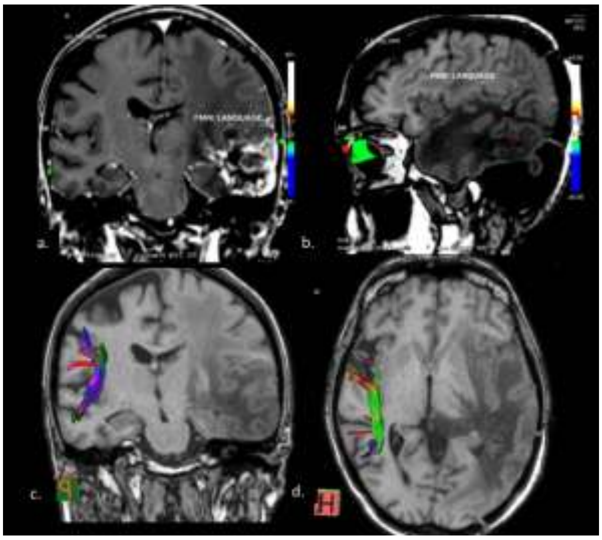

Figure 4(a-d) glioma in left parietotemporal lobe. (a,b) FMRI with language task- show activation within the lesion without any plasticity in opposite side .Figure(c, d) complete destruction of left arcuate portion of superior longitudinal fasciculus, surgeons proceeded with decompression to reduce the mass effect.

In the study conducted by Luciano Mastronardi et al [4], preoperative and intraoperative DTI fiber tracking was used to plan the excision of intracranial tumours in the vicinity of functionally important areas of the brain. In approximately half of cases, the neurosurgeons involved in surgical procedures judged tractography was useful in selecting the safer surgical approach, helpful in defining the borders of tumour resection in relation to WMMT and relevant in enhancing the "surgical confidence" of the neurosurgeon with the procedure. Regarding combined fMRI-DTI approach, only few studies are available. M. Smits M et al imaged 14 subjects with DTI-fMRI. In all patients, they could track the hand fibers of the corticospinal tract bilaterally and the displacement of hand and foot fibers by tumour. Incorporating fMRI into DTI tractography (neuronavigation) in the preoperative assessment of patients with brain tumours may provide additional information on the course of important white matter tracts and their relationship to the tumour[14,15].

IV. Conclusion

Eloquent cortex localisation by fMRI and eloquent white matter localisation by DTI in relation to intracranial lesions definitely help to optimize surgical resection with feasible surgical approach and to prevent new neurological deficits for patients. In addition, this non invasive fMRI and DTI will replace theinvasive intraoperative cortical stimulation technique in a near future.

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