Chapter

Pre-Surgical and Surgical Planning in Neurosurgical Oncology - A Case-Based Approach to Maximal Safe Surgical Resection in Neurosurgery

Hanan Algethami, Fred C. Lam, Rafael Rojas and Ekkehard M. Kasper

Abstract

Use of functional neuroimaging capabilities such as fMRI, DTI, MRP, MRS, AS-PET-CT, SPECT, and TMS as noninvasive tools to visualize intrinsic brain and spine morphology in relation to function have developed over the past 30 years. Amongst these imaging modalities, functional magnetic resonance imaging (fMRI) is of particular interest since it follows the physiological coupling between neuronal electrical activity and metabolic structural (cellular) activity as it relates to tissue vascularity and perfusion states. This structure–function *synesis* (from the Greek noun, σύνεσις = being together), leads to three effects that contribute to the fMRI signal: an increase in the blood flow velocity, a change in the mean blood volume, and most importantly, alterations in the blood oxygenation level. The latter effect has lent to the development of blood-oxygenation-level-dependent or *BOLD* fMRI, which has been used in establishing the topographic relationship between eloquent cortex and neurosurgical planning. As an adjunct to this modality, MRI-based diffusion tensor imaging (DTI) allows further detailed radiographic assessment of fiber tracts in the brain in relationship to the surgical lesion of interest. Herein we review the roles of fMRI and DTI for presurgical mapping to allow for maximal safe resection procedures in neurosurgery with case-based illustrations.

Keywords: fMRI, DTI, neurosurgery, eloquent cortex, neuronavigation, neuromonitoring, tumor resection, neurosurgical oncology

1. Introduction

The goals of neurosurgical resection are best described by the statement: "*maximal safe resection with minimal morbidity*". In oncological neurosurgery, this often encompasses achieving a gross total resection (GTR), which can be challenging depending on the location (i.e. eloquent cortex), ease of accessibility (i.e. superficial *vs.* deep), and the presence of vital *en passant* fiber tracks. Pioneering work by Dr. Wilder Penfield at the Montreal Neurologic Institute by performing

craniotomies and resections allowed for safe resection of epileptogenic foci in the brain, resulting in seizure control in his patients (superbly outlined in his recent biography) [1]. This concept was soon applied by Penfield and his team to other pathological entities affecting the cortex and subcortical areas and was subsequently adopted by many academic neurosurgical centers worldwide.

Penfield's pioneering brain mapping techniques have since laid the groundwork for the development of intraoperative cortical stimulation techniques to guide maximal safe extent of resection (EOR). However, we now understand the limitations of this technique, including the progressive decline in the spatial resolution of bipolar stimulation throughout the course of surgical resection; iatrogenic edema caused by tissue retraction and/or resection altering the resistance and conductance of brain tissue requiring adjusted increases in applied stimulus strength at the price of decreased spatial resolution; and finally, adjustment of stimulation parameters which could lead to spurious spread of excitation to areas not immediately next to the point of stimulation, which could introduce further uncertainty in determining the EOR. Another caveat is the fact that awake surgery also requires a larger craniotomy than the actual size of the lesion or area to be removed due to the fact that greater cortical access is often needed to place multiple electrodes over the hemispheric surface to localize both the lesional site as well as the topography of adjacent possibly eloquent brain areas.

Various emerging, invasive monitoring techniques have expanded the scope and utility of this approach such as: Extracellular cortical stimulation via implanted on-lay grids for epilepsy patients; Foramen ovale electrodes inserted via transbuccal access for patients with mesial temporal sclerosis; And/or intraoperative cortical surface stimulation with bipolar Ojemann-type electrodes. The latter is sometimes used in combination with monopolar fiber-track-stimulation via pointy tip electrodes for patients with deep seated intra-axial lesions, amongst other modalities. Another option is the application of transcranial (scalp) stimulation techniques for evoked motor or sensory potentials (MEPs or SEPs) to monitor the integrity of functional pathways. However, not all patients are suitable to undergo awake procedures or these invasive types of monitoring nor are all neurosurgeons trained to perform surgeries using these methods. Another disadvantage of these awake monitoring techniques is that a surgical procedure itself is required before valuable functional information can be obtained. As a result, important patient management decisions must be made upfront without complete knowledge of the anatomic relationships between the lesion borders and functionally eloquent cortex [2]. For these reasons, we consider it beneficial to obtain comprehensive preoperative imaging, in particular, fMRI and DTI, to identify eloquent cortex controlling movement, primary sensory perception, vision, and speech, and to understand the spatial relationships between critical *en passant* fiber tracts and these functionally eloquent cortical regions to allow for surgical planning and determining the EOR.

1.1 A historical perspective on functional magnetic resonance imaging

In 1890, Sir Charles Sherrington and Dr. Charles Roy at Cambridge University were amongst the first neuroscientists to experimentally demonstrate a link of brain function to cerebral blood flow [3]. In 1963, Drs. Linus Pauling and Charles Coryell reported differences in the magnetic properties of blood based on the oxygenation status of hemoglobin. Oxygen-carrying hemoglobin (oxy-Hgb) was weakly repelled by magnetic fields, whereas blood with de-oxygenated hemoglobin (deoxy-Hgb) was attracted by a magnetic field. However, it was not until the 1990's when two American researchers at Bell Laboratories in Murray Hill, New Jersey, recognized the utility of this phenomenon to study the oxygenation state of the brain using

MRI and clearly demonstrated that the metabolic effect of neuronal activation in brain tissue yielded distinct magnetic properties which correlated with deoxy-Hgb and oxy-Hgb concentrations. Ogawa and colleagues then demonstrated that blood oxygen level derived (BOLD) signals could be used to generate intrinsic MRI contrast which could be further augmented by gradient-echo techniques [4]. Kwong and colleagues then followed with the use of gradient-echo and inversion recovery echo planar imaging sequences to map signal changes within the human primary motor and visual cortices [5]. These studies laid the groundwork for the development of distinct protocols that are used in modern day fMRI studies.

1.2 The utilities of diffusion weighted and diffusion tensor imaging

Diffusion weighted imaging (DWI) assesses the restricted diffusion of intracellular water molecules in the brain and is routinely used for stroke assessment in hypoxic and metabolically compromised regions of the brain. Hypoxia-induced breakdown of the energy-dependent transmembrane potential can be demonstrated early on in the ischemic process by applying three gradient-directions to DWI sequences to estimate the "average diffusivity" allowing for very early radiographic detection (within minutes of the ischemic insult).

Diffusion tensor imaging (DTI) takes advantage of the fact that there is directionally restricted diffusion of molecules in certain tissues depending on the observer's viewing angle (i.e. along *vs.* perpendicular to nerve fibers) [6]. In DTI, each voxel has one or more pairs of parameters: a rate of diffusion and a preferred direction of diffusion, described in terms of three-dimensional space, for which that parameter is valid [7]. The properties of each voxel of a single DTI image are usually calculated by vector or tensor math from six or more different diffusion weighted acquisitions, each obtained with a different orientation (or viewing angle) of the diffusion sensitizing gradients [8]. The diffusion tensor model is a rather simple model of the diffusion process, assuming homogeneity and linearity of the diffusion within each image voxel. In order to measure the tissue's complete diffusion profile, one needs to repeat the MR scans and apply different directions (and possibly strengths) of the diffusion gradient for each scan. The high information which is contained by a DTI voxel makes it extremely sensitive to subtle pathologies in the brain. In addition, the directional information can be exploited at a higher level of structure to select and follow neural tracts through the brain — a process called *tractography*. The underlying molecular directional restriction is also called *anisotropic diffusion*. Such directionality can be color coded in three dimensions (anterior/posterior, superior/inferior, and lateral/medial) which is useful to visualize the axonal tract organizations of the brain. Fiber tractography is therefore an added three-dimensional reconstruction technique based on DTI data to assess axonal directions using the collected primary diffusion restriction data. DTI can therefore provide additional structural information about the organization of the white matter in and around primary and secondary brain lesions which is useful to the surgeon in procedural planning.

1.3 Current status of the field

Modern imaging technologies such as BOLD fMRI and DTI, as briefly outlined above, have allowed for significant improvements in the surgical team's ability to minimize perioperative neurosurgical morbidity. The complementary use of other non-invasive imaging modalities such as CT angiography or MR perfusion scans, MR spectroscopy, 3D single-molecule super-resolution microscopy, and more recently transcranial magnetic brain stimulation [9], further permits the

surgical team to gain significant insight into the access and resectability of certain lesions and to reliably predict the maximally safe EOR. Furthermore, the ability to use these imaging modalities to engage patients is crucial in the obtained consent process.

One of the hindrances to such technology-driven and more transparent surgical disease management strategies remains the fact that not all these highly informative technologies are widely available. Hospital funding for subspecialty-trained MRI physicists and MRI technicians may be limited and there is hesitancy to implement these technologies due to several factors, including: 1) The absence of large scale randomized clinical trials to support the routine integration of fMRI and DTI for pre-operative surgical planning; 2) The problems encountered in some earlier fMRI studies with respect to precise spatial location of a lesion; 3) The inability to correlate imaging features to electrical activity surrounding the tumor in some earlier studies; 4) The inability to use fMRI for distinguishing brain regions that are considered not primary eloquent sites, yet appear to be essential areas for circuit functions *vs* those areas that may be sacrificed without causing a lasting major neurological deficit; and 5) High interobserver variability in fMRI threshold determinations and DTI segmentation algorithms, which require specialty training and experience. The situation is further complicated by the fact that many ancillary health care practitioners (including medical-, neuro-, and radiation oncologists) are not familiar enough with the potential that fMRI and DTI can bring to presurgical planning and the roles they can play for improving surgical outcomes.

2. fMRI and DTI methodology and limitations

Depiction of the classic surface anatomy of the brain has proven to be useful in native (non-lesional) cases, where anatomy is undistorted by pathological processes. High-resolution, thin-cut T2-weighted, FLAIR, and MPRAGE sequences provide a detailed morphological map to establish eloquent regions of the brain. Eloquent regions specifically refer to primary areas of the cerebral cortex which carry a distinct function which cannot be simply substituted by other areas or neuronal circuitry, including: a) Primary sensorimotor cortex; b) Primary auditory cortex; c) Primary visual cortex; and d) Primary expressive language area (Broca's Area). Distortion of these regions by space-occupying lesions can pose challenges for even the most skilled surgeon to safely navigate the resection safely based on gross anatomical landmarks alone. In these situations, presurgical fMRI superimposed on MPRAGE sequences can help the surgeon to achieve three goals:

1. To better assess determining the spatial relationship of a given lesion to the proximity of any eloquent area of concern and thus allow the surgeon to gauge the maximally safe EOR.

2. To better select patients who may benefit from intra-operative mapping in the situations where there may be considerable variability between anatomical loci and functional foci.

3. To provide a roadmap for the surgery itself by integrating fMRI with intraoperative neuro-navigation.

Limitations of BOLD fMRI are related to dependence of the technique to neurovascular coupling, hence any delays in hemodynamic response following neuronal activation leads to poor temporal resolution on fMRI with alterations

of BOLD signal in regions of the brain with altered blood flow [10]. BOLD fMRI is task-related imaging and hence is subject to statistical rules and interpretation of data. Another use of BOLD signal application is resting-state fMRI (rs-fMRI), which does not require a stimulus or task and acquires spontaneous BOLD signal alterations [11]. Data acquisition occurs while the patient is at rest or by inferring resting-state data from periods of rest embedded within a series of tasks [12]. The lack of a need for a patient to perform tasks may overcome the limitations of BOLD fMRI in patients with neurologic, neurosurgical, and psychiatric conditions hence the growing popularity of the rs-fMRI for use in the clinical setting.

From early fMRI studies by Yetkin and colleagues, a now historic rule had been established that *the minimal safe distance between a lesion margin and the resection border should measure about 10 mm* [13]. This paradigm was established based on the observation that the rate of neurological deficits significantly increase when the distance between the margin and resection border falls below 10 mm [2]. It needs to be noted though, that this much quoted study result was significantly underpowered, thus not allowing to draw strong conclusions since these observations were obtained in a very small sized single center cohort with only a handful of patients entered in each group. Another criticism of the golden rule of a "must-respect minimal distance" comes from the fact that the observed BOLD signal in any given fMRI study represents the display of a **statistical threshold signal value** that can be arbitrarily set and adjusted by the fMRI analyst/investigator and that the underlying signal to noise ratio is profoundly dependent on a variety of technical factors as well as intraoperative scenarios (i.e., brain relaxation and progressive shift with resection). Vascular re-routing of blood by a lesion (commonly called "venous contamination") can also generate false signals that need to be accounted for. These can be assessed by a matching CTA/CTV scan.

One further aspect that was criticized in the past by fMRI skeptics is the lack of connectivity information in primary fMRI data which points to the fact that BOLD fMRI signal is a surface related signal of oxygen brain metabolism, not taking into account subcortical structures such as fiber tracts. As detailed above, the latter aspect can be remedied by simultaneous integration of modern DTI data. Once uploaded and fused on a single modern intraoperative neuronavigation platform (e.g., BrainLab; Stryker/Synaptiv) this adds the fiber tract component to the surgical planning step. This capability is especially valuable for deep seated intra-axial lesions such as gliomas which may be infiltrative to those tracts or in close topography to these essential structures. Another use of this imaging technology is the scenario, where surgical access to deep seated lesions is required and traversing the white matter is best accomplished via a route that minimizes damage to fibers running towards essential cortical regions.

A recent survey across American neurosurgical departments with a residency program assessing the surgeons' uses and experience with preoperative fMRI in surgical planning for neuro-oncology patients [14]. Indications and surgeons' preferences for using fMRI in pre-surgical planning were dominant hemisphere and functionally eloquent location of lesions, motor symptoms, and aphasia. Most common reasons for fMRI amongst surgeons surveyed included identifying language laterality (which yielded the highest interrater reliability), planning the extent of resection, and discussing surgical planning with patients. The majority of surgeons ordered fMRIs in patients with low- and high-grade gliomas (94% and 82%, respectively). However, 77% of surgeons resected an fMRI-positive functional site if it was "cleared" by cortical stimulation, and 98% of responders reported that if there was a discrepancy between fMRI and intraoperative mapping that they would rely on intraoperative mapping. There have been concerns about the sensitivity and specificity of fMRI, especially for language mapping, with sensitivity ranging from

59–100% and specificity ranging from 0–97% when compared across 9 published studies [15]. Tumors of oligodendroglioma subtype, tumor relative cerebral blood volume (CBV) > 1.5 on MR perfusion imaging, lower cortical CBV, and distance to tumor have also been shown to cause higher false-positive fMRI signals [16]. Southwell and colleagues presented another limitation of using pre-surgical fMRI planning in its inability to offer surgeons the ability to account for compensable areas that can be resected and critical areas that need to be preserved, leading to underselection of patients for surgery and increase the likelihood for achieving subtotal resections due to miscalculation of needing to preserve seeming critical areas [17]. They also achieved an average 90% resection with no new postoperative neurological deficits in a series of 58 glioma patient resections, further pointing out the limitations of fMRI [17].

Similarly, a study incorporating 96 individual surgical planning cases using DTI of ground-truth white matter tracts from 20 research groups found a high false-positive rate with many of the tractograms representing more invalid than valid bundles [18]. This was further corroborated by a study by Mandelli and colleagues demonstrating relatively poor performance in differentiating lateral vs. medial projections [19]. Leclercq and colleagues compared DTI to intraoperative subcortical language mapping and found that while 17 out of 21 positive cortical stimulation sites corresponded to DTI tractograms, negative tractograms did not rule out the presence of white matter tracts [20]. Another study reported intraoperative image distortion in over one-third of cases, negating the use of DTI whilst favoring the use of cortical stimulation as the superior intraoperative mapping modality [21]. Finally, a prospective study randomizing 328 glioma patients to either DTI, 3D MRI, or routine neuronavigation reported a higher rate of GTR in higher-grade glioma patients, however, the increase in GTR was only reported in high-grade tumors whilst the neuronavigation in the control arm did not utilize cortical stimulation and the authors only reported outcomes for motor function [22]. These above studies serve to indicate that functional imaging modalities such as fMRI and DTI are still in their infancy and should be used as an adjunct along with more established tools such as neuronavigation and cortical stimulation.

3. Case illustrations

3.1 Case 1: 36 year-old male with a recurrent atypical parasagittal meningioma

A 36 year-old male who had undergone a prior resection for a parasagittal meningioma 4 years ago at an outside institution was referred to our neurosurgical outpatient tumor clinic by radiation oncology with minimal gait abnormalities and a recurrent tumor in the same location. Pre-surgical post-contrast T1WI and CT demonstrated a large parasagittal contrast-enhancing lesion spanning the anterior to middle sections of the superior sagittal sinus (SSS, **Figure 1A–C**, yellow arrows). CT angiography reconstruction scans demonstrated significant occlusion of the SSS (**Figure 1D and E**, yellow arrows). fMRI scan localized the primary motor area (yellow) and the sensory area (green) just posterior to the lesion (**Figure 1F–I**), predicting likely success of resection as long as we remained anterior to these eloquent areas, only expecting a temporary supplementary motor area (SMA) syndrome. Surrounding venous anatomy was also taken into consideration during pre-surgical planning.

Thorough discussions with the patient regarding the spatial and anatomical relationships of his recurrent tumor to the functional eloquent regions of the brain, as shown on fMRI, were taken with an explanation of the risks of the surgery,

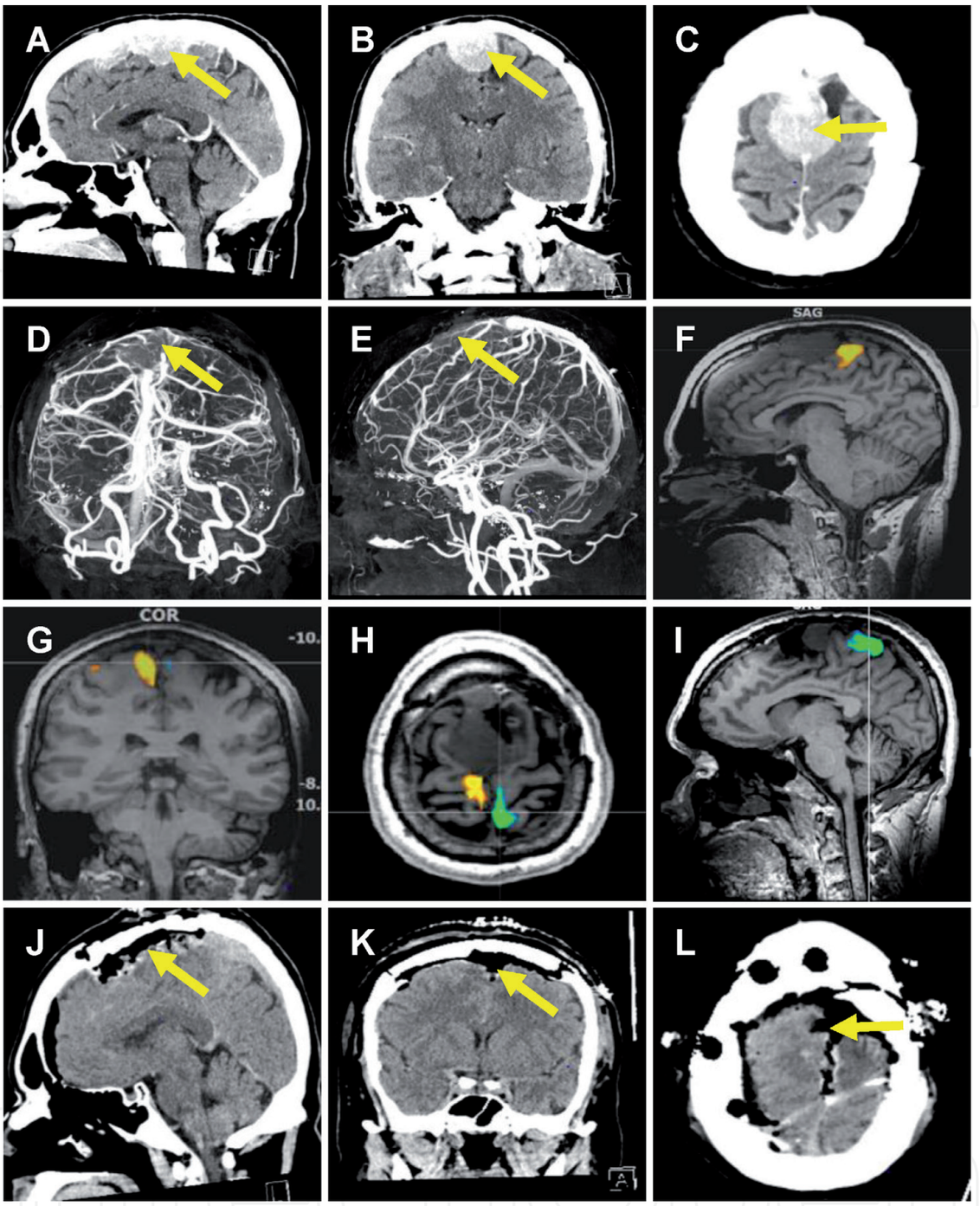

Figure 1.
Recurrent atypical meningioma. Pre-op MRI A) sagittal, B) coronal, and C) axial T1WI post-contrast scans showing a large, en plaque, recurrent parasagittal meningioma. Pre-op CTA D) coronal and E) sagittal views showing occlusion of the anterior third of the superior sagittal sinus. Pre-op fMRI showing F) sagittal, G) coronal views of the primary sensorimotor cortex (yellow) and H) axial, and I) sagittal views of the left primary motor cortex innervating the right leg (green). Post-op MRI J) sagittal, K) coronal, and L) axial TWI post-contrast scans showing resection of the meningioma.

including vascular injury to the sinus, and a post-operative SMA syndrome which would likely recover over the course of weeks. Surgery was recommended and the patient was taken to the operating room. A bilateral craniotomy was performed with intraoperative neuronavigation and the osseous midline bridge was dissected off. The SSS was tied off just anterior and posterior to the lesion, leaving the next surface draining veins intact. Surface mapping was used to confirm the motor strip location. A near gross total resection (GTR) was accomplished (**Figure 1J–L**) with a minimal 5 mm tumor cuff remaining which was encasing a draining vein in the posterior left SSS.

The patient woke up from surgery with a dense bilateral leg plegia, suggestive of a predicted SMA syndrome which recovered after 8 weeks requiring rehabilitation and physical therapy. He has since regained complete lower leg function and mobility at 6-months follow-up. Pathology came back WHO Grade II atypical meningioma. The patient was referred back to radiation oncology for post-operative stereotactic radiosurgery (SRS) to the tumor bed and the remaining cuff of tumor.

3.2 Case 2: 40 year-old male with a brainstem ependymoma

A 40 year-old male presented with cervical myelopathy (bilateral sensory loss in the hands, broad based gait, neck pain, and clonus). Imaging revealed a heterogeneously enhancing, intrinsic, intra-axial lesion at the craniocervical junction, with cystic and solid components (**Figure 2A** and **B**, yellow arrows). The index surgery was performed conventionally with intraoperative neuromonitoring (IOM) of somatosensory and motor evoked potentials (SSEPs and MEPs, respectively)

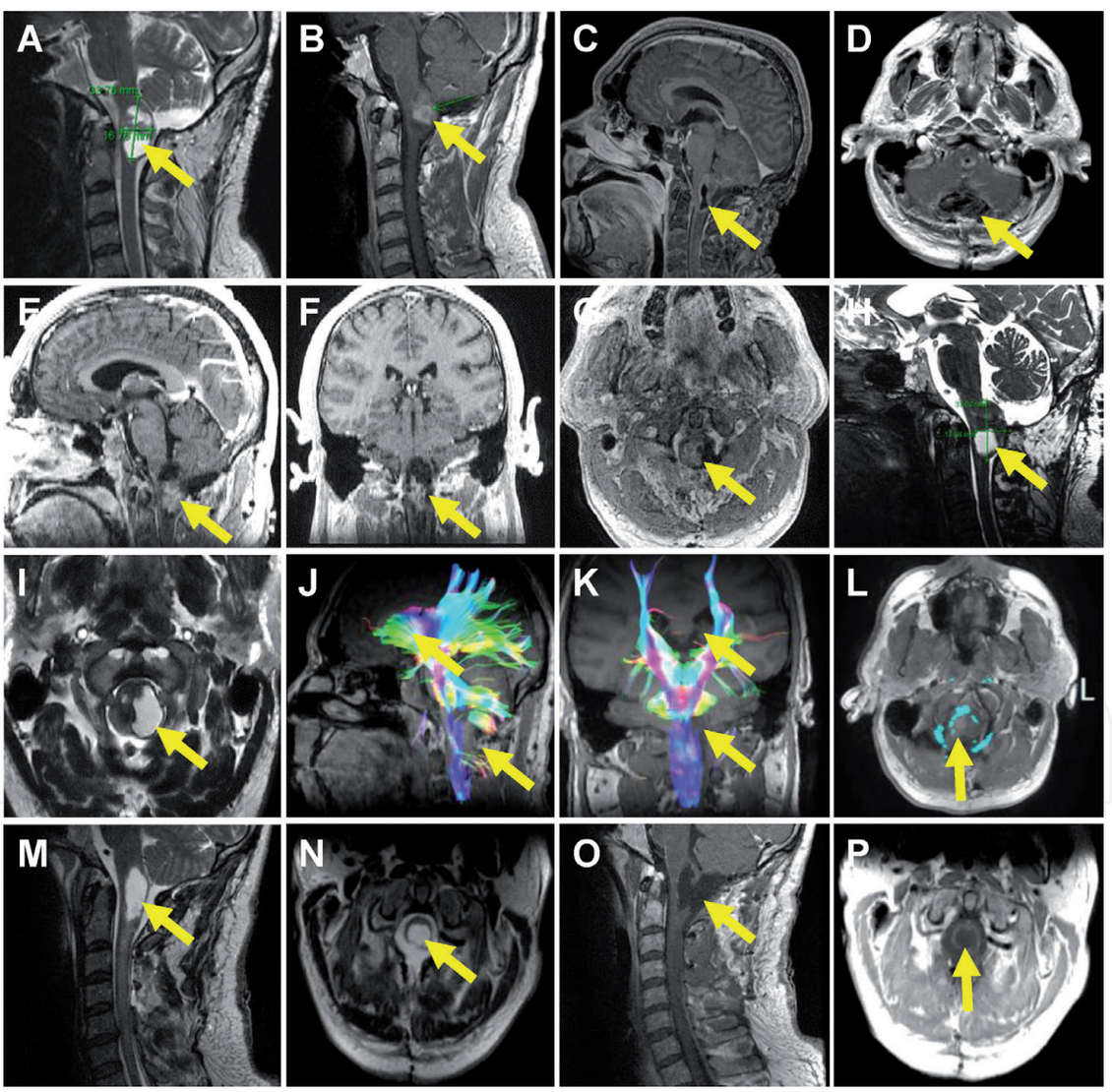

Figure 2.
Intra-axial cervico-medullary recurrent ependymoma. Pre-op MRI A) sagittal T2WI and B) sagittal T1WI post-contrast scan showing cystic partly enhancing lesion. Post-op MRI C) sagittal and D) axial T1WI post-contrast scans showing generous resection. Post-contrast E) sagittal, F) coronal, G) axial T1WI and H) sagittal, and I) axial T2WI showing tumor recurrence in the previous surgical bed. Pre-op fMRI showing J) sagittal, K) coronal, and L) axial views of the recurrent tumor completely displacing the motor fibers. Post-op MRI M) sagittal, N) axial T2WI and O) sagittal, P) axial T1WI post-contrast scans of the repeat resection cavity. Yellow arrows indicate location of the tumor.

via a posterior midline dorsal raphé approach with a myelotomy just inferior to the obex. Further resection was halted when the patient demonstrated prolonged drops in blood pressure and periods of asystole with ongoing dissection. Intra-operative frozen section pathology revealed a low-grade ependymoma. Post-operative imaging demonstrated a generous decompression (**Figure 2C** and **D**, yellow arrows). The patient had complete recovery of his myelopathy and he deferred adjuvant treatment, choosing to have follow-up surveillance with sequential imaging.

After 3 years of surveillance, the patient re-presented with recurrent symptoms and a recurrent tumor in the same location though significantly larger (**Figure 2E–I**). DTI images were acquired, clearly depicting that the pyramidal tract was displayed anterior and lateral to the lesion (**Figure 2J–L**, yellow arrows), allowing for a surgical window from posterior for resection. Resection for recurrent disease was again performed with IOM of SSEP, MEPs, monitoring of cranial nerves 5, 7, 9, and 12, as well as direct nerve stimulation. A suitable plane was established allowing for a gross total resection of what now was diagnosed as a tanycytic ependymoma. Only minimal amplitude drops in SSEPs were encountered during the surgery. Due to the manipulation of the recurrent surgical bed and delicate nature of the surgery, the patient was kept intubated following the surgery on high-dose steroids to prevent peri-operative edema of the surrounding brain stem tissues. He was successfully extubated on post-operative day 3 with no neurological deficits. Post-operative imaging showed no residual disease and a slim rim of cervical medullary parenchyma that carried all functional tracts with a large access window posteriorly positioned exactly between the posterior funiculus (**Figure 2M–P**, yellow arrows).

3.3 Case 3: 68 year-old female with a left subfrontal glioma

A 68 year-old female patient presented to our emergency department with new onset speech arrest episodes interpreted as seizures and secondary manifestation as Grand Mal. She had an unremarkable past medical history and no systemic signs of infection. The patient was started on antiepileptic drugs with an MRI scan revealing multiple ring enhancing lesions in the left frontal lobe (**Figure 3A–C**, yellow arrows). Differential diagnosis included primary CNS malignancies (e.g. malignant glioma), secondary malignancy (e.g. metastasis or lymphoma), or abscess. fMRI scan showed localization just adjacent to Broca's area but without infiltration of the frontal operculum (**Figure 3D–F**). A frontotemporal image-guided craniotomy was performed with intraoperative frozen pathology indicative of malignant glioma. Post-operative imaging demonstrated a generous resection (**Figure 3G–I**, yellow arrows). The patient went on to receive post-operative concurrent chemo-radiation as per the Stupp protocol.

3.4 Case 4: 38 year-old male with a fourth ventricular ganglioglioma

A 38 year-old male presented with episodes of headaches and nausea with no neurological deficit. MRI scan revealed a 1.5 cm ring enhancing lesion in the inferior 4th ventricle that was considered to be a neoplasm or infection (**Figure 4A–C**, yellow arrows). It was difficult to ascertain from the MRI scans whether the lesion was intra-axial or intraventricular. CTA showed low vascularity of the lesion (**Figure 4D–F**, yellow arrows). DTI showed displaced corticospinal fibers with a suitable access corridor from posterior using a planned unilateral telovelar approach (**Figure 4G–I**, yellow arrows). Surgery was performed with IOM, SSEP, MEP and cranial nerves 5, 7, 8, 9, and 10 monitoring. A small remnant of tumor was left laterally in situ since attempts for a complete resection caused cranial nerves 9 and 10 signal changes. Successful

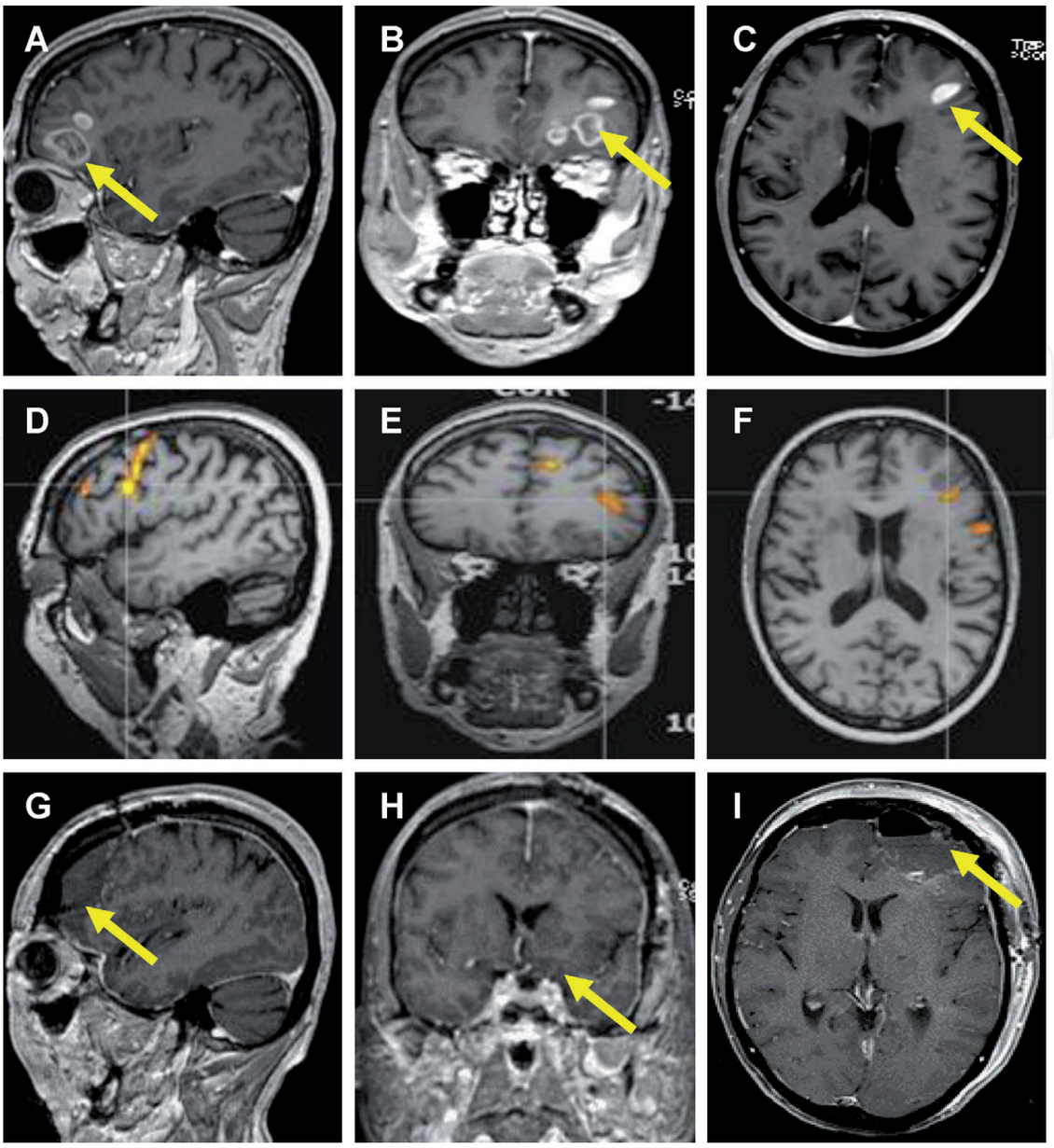

Figure 3.
Left sub-frontal glioma. Pre-op MRI A) sagittal, B) coronal, and C) axial T1WI post-contrast scans showing solid-cystic, multi-focal, enhancing lesions in the left subfrontal cortex. Pre-op fMRI scans showing D) sagittal, E) coronal, and F) axial anterior inferior frontal gyrus, Broca's area, and composite language map. Post-op MRI showing G) sagittal, H) coronal, and I) axial T1WI post-contrast scans of the frontal resection cavity.

subtotal resection was accomplished with pathology revealing a benign WHO Grade I ganglioglioma (**Figure 4J–L**, yellow arrows). The patient did not suffer any surgical morbidity and is being followed with surveillance imaging. Should there be further progression of disease, SRS *vs* a second repeat resection could be contemplated.

3.5 Case 5: 53 year-old female with a recurrent left temporal lobe glioma

A 53 year-old female had a previous subtotal resection of a small left temporal lobe GBM followed by concurrent chemo-radiation as per the Stupp protocol. She presented 2 years later to our institution's multidisciplinary tumor board, neurologically intact, with a left recurrent temporal lobe lesion (**Figure 5A–C**, yellow arrows). The differential diagnosis was recurrent disease *vs* radiation necrosis or pseudo-progression.

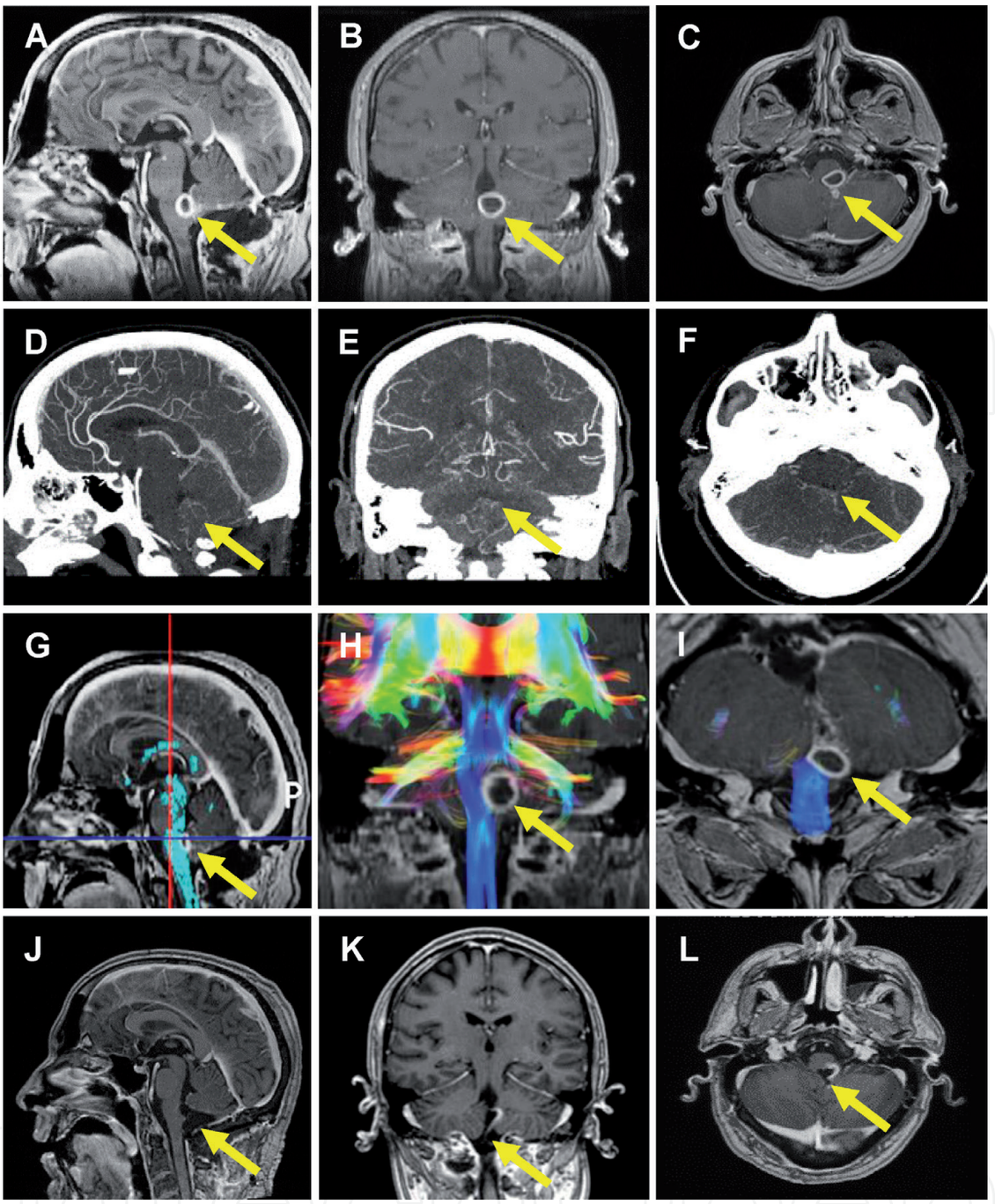

Figure 4.
Fourth ventricular ganglioglioma. Pre-op MRI A) sagittal, B) coronal, and C) axial T1WI post-contrast scans showing ring-enhancing cystic lesion originating from the floor of the 4th ventricle. Pre-op CTA D) sagittal, E) coronal, and F) axial views to assess vascularity of the lesion. Pre-op fMRI G) sagittal, H) coronal, and I) axial images showing clear anteromedial displacement of the pyramidal tracts by the lesion. Post-op MRI J) sagittal, K) coronal, and L) axial T1WI post-contrast scans assessing near total resection of the tumor. Yellow arrows depict location of the lesion.

MR perfusion (MRP) scan confirmed a hyper-perfused area in the left middle temporal fossa corresponding to the area of enhancement on MRI (**Figure 5D**, yellow arrow). Given the location of the recurrence (anterior to the 6 cm line measured from the temporal tip) with predominantly mesial extension with no proximity to the superior temporal gyrus and sparing anatomical language areas, we decided to perform a conventional asleep temporal lobe resection without the need for awake surgery with language mapping. The patient did not have any post-operative neurological deficits with good radiographic evidence of resection of contrast-enhancing disease (**Figure 5E** and **F**, yellow arrows) and a generous anterior mesio-temporal

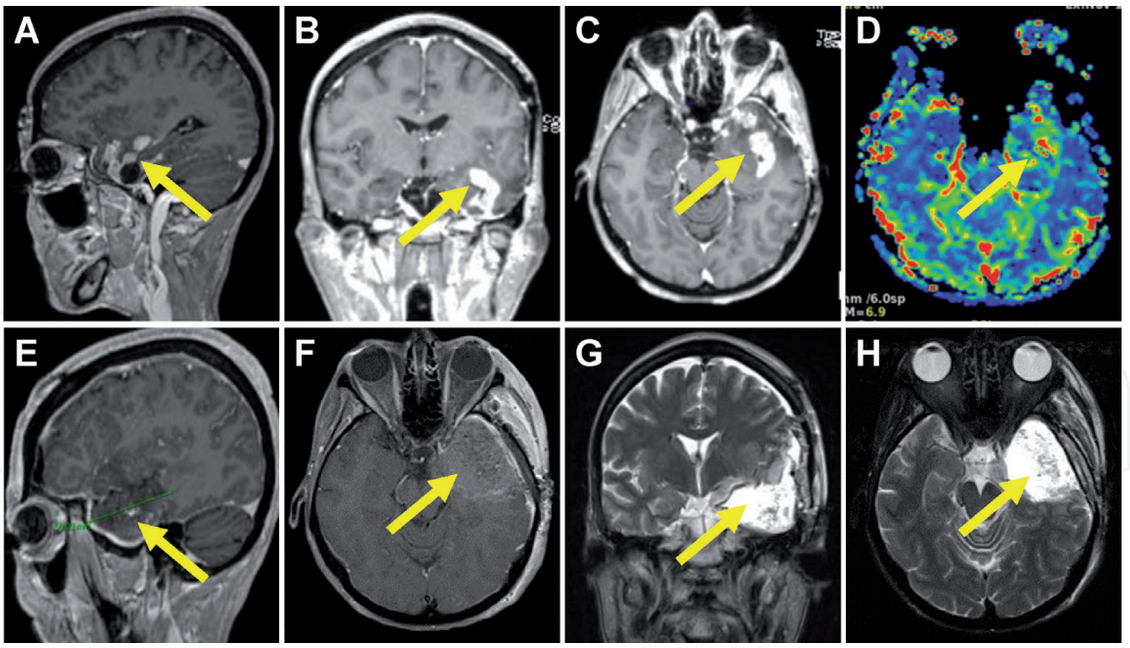

Figure 5.
Left mesiotemporal recurrent glioma. Pre-op MRI A) sagittal, B) coronal, and C) axial T1WI post-contrast scans of a left intra-axial anterior temporal lobe recurrent glioma. D) MR perfusion scan showing relative increased cerebral blood velocity in the left anterior temporal lobe corresponding to the area of increased enhancement on MRI. Post-op MRI E) sagittal, F) axial T1WI post-contrast, and G) coronal, and H) axial T2WI scans of the resection cavity. Yellow arrows define tumor bed.

resection cavity (**Figure 5G** and **H**). This case demonstrates the ability to do a safe maximal surgical resection in the absence of DTI or fMRI as long as there is strong correlation with other imaging modalities such as MRP delineating areas of suspected disease recurrence and an adequate anatomical distance between the resection margins and eloquent areas of the brain.

4. Conclusion

In summary, the combination of non-invasive functional and metabolic neuroimaging modalities such as fMRI and MRP in conjunction with anatomical mapping modalities such as DTI can help inform neurosurgical planning for lesions associated with eloquent cortex or in challenging anatomical locations such as the brainstem. Collaboration with a multidisciplinary team including neurosurgeons, neuro-oncologists, neuroradiologists, radiation oncologists, medical imaging physicists, and neurorehabilitation specialists, will help offer patients a comprehensive treatment plan which will achieve maximal surgical resection, disease control, and improved quality of life and survival.

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References

[1] Leblanc, R., *Radical Treatment*. 2020: McGill-Queen's University Press. 288.

[2] Sunaert, S., *Presurgical planning for tumor resectioning.* J Magn Reson Imaging, 2006. 23(6): p. 887-905.

[3] Raichle, M.E., *A brief history of human brain mapping.* Trends Neurosci, 2009. 32(2): p. 118-126.

[4] Ogawa, S., et al., *Brain magnetic resonance imaging with contrast dependent on blood oxygenation.* Proc Natl Acad Sci U S A, 1990. 87(24): p. 9868-9872.

[5] Kwong, K.K., et al., *Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation.* Proc Natl Acad Sci U S A, 1992. 89(12): p. 5675-5679.

[6] Alexander, A.L., et al., *Diffusion tensor imaging of the brain.* Neurotherapeutics, 2007. 4(3): p. 316-329.

[7] O'Donnell, L.J. and C.F. Westin, *An introduction to diffusion tensor image analysis.* Neurosurg Clin N Am, 2011. 22(2): p. 185-196, viii.

[8] Soares, J.M., et al., *A hitchhiker's guide to diffusion tensor imaging.* Front Neurosci, 2013. 7: p. 31.

[9] Sollmann, N., et al., *Intra- and interobserver variability of language mapping by navigated transcranial magnetic brain stimulation.* BMC Neurosci, 2013. 14: p. 150.

[10] Hermes, D., M. Nguyen, and J. Winawer, *Neuronal synchrony and the relation between the blood-oxygen-level dependent response and the local field potential.* PLoS Biol, 2017. 15(7): p. e2001461.

[11] Lv, H., et al., *Resting-State Functional MRI: Everything That Nonexperts Have Always Wanted to Know.* AJNR Am J Neuroradiol, 2018. 39(8): p. 1390-1399.

[12] Korgaonkar, M.S., et al., *Establishing the resting state default mode network derived from functional magnetic resonance imaging tasks as an endophenotype: A twins study.* Hum Brain Mapp, 2014. 35(8): p. 3893-3902.

[13] Yetkin, F.Z., et al., *Functional magnetic resonance imaging assessment of the risk of postoperative hemiparesis after excision of cerebral tumors.* Int J Neuroradiol, 1998. 4: p. 253-257.

[14] Stopa, B.M., et al., *Preoperative functional MRI use in neurooncology patients: a clinician survey.* Neurosurg Focus, 2020. 48(2): p. E11.

[15] Giussani, C., et al., *Is preoperative functional magnetic resonance imaging reliable for language areas mapping in brain tumor surgery? Review of language functional magnetic resonance imaging and direct cortical stimulation correlation studies.* Neurosurgery, 2010. 66(1): p. 113-120.

[16] Kuchcinski, G., et al., *Three-tesla functional MR language mapping: comparison with direct cortical stimulation in gliomas.* Neurology, 2015. 84(6): p. 560-568.

[17] Southwell, D.G., et al., *Resection of gliomas deemed inoperable by neurosurgeons based on preoperative imaging studies.* J Neurosurg, 2018. 129(3): p. 567-575.

[18] Maier-Hein, K.H., et al., *The challenge of mapping the human connectome based on diffusion tractography.* Nat Commun, 2017. 8(1): p. 1349.

[19] Mandelli, M.L., et al., *Quantifying accuracy and precision of diffusion MR tractography of the corticospinal tract in*

brain tumors. J Neurosurg, 2014. 121(2): p. 349-358.

[20] Leclercq, D., et al., *Comparison of diffusion tensor imaging tractography of language tracts and intraoperative subcortical stimulations.* J Neurosurg, 2010. 112(3): p. 503-511.

[21] Ostry, S., et al., *Is intraoperative diffusion tensor imaging at 3.0T comparable to subcortical corticospinal tract mapping?* Neurosurgery, 2013. 73(5): p. 797-807; discussion 806-7.

[22] Wu, J.S., et al., *Clinical evaluation and follow-up outcome of diffusion tensor imaging-based functional neuronavigation: a prospective, controlled study in patients with gliomas involving pyramidal tracts.* Neurosurgery, 2007. 61(5): p. 935-48; discussion 948-9.