Neurosurgical Applications of Magnetic Resonance Diffusion Tensor Imaging

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Abstract
Magnetic Resonance (MR) Diffusion Tensor Imaging (DTI) is a rapidly evolving technology that enables the visualization of neuroanatomical structures within the brain. This technique has been applied to various clinical applications, including tumor grading and staging as the gold standard for intraoperative neuronavigation, yet this technique does not visually delineate myelinated neurons, crudely outlining WM tracts. Post-operative assessment and monitoring (identification of WM damage, identification of tumor recurrence). Limitations of MR DTI include difficulty tracking small and crossing WM tracts, lack of standardized data acquisition and post-processing techniques, and practical equipment, software, and timing considerations. Overall, MR DTI is a useful tool for planning, performing, and following neurological procedures, and has the potential to significantly improve patient care. Technological improvements and increased familiarity with DTI among clinicians are next steps.

Introduction
Magnetic Resonance (MR) imaging uses magnetic fields to temporarily alter proton (hydrogen atom) orientation and then measures the energy emitted upon proton relaxation, enabling discrimination of tissues with different proton (water) compositions. Water molecules naturally diffuse in accordance with Brownian motion (imagine a drop of dye spreading out in a glass of water). A series of magnetic pulses can be applied to measure the inter-pulse magnitude and direction of proton diffusion. On a pixel-by-pixel basis, this diffusion is described by the Apparent Diffusion Coefficient (ADC), which can be determined in multiple axes. Mori et al found that the application of diffusion pulse in a minimum of six directional axes is sufficient to resolve a diffusion vector in three dimensional space describing the overall diffusion characteristics, or a tensor (thus the name diffusion tensor imaging (DTI)). This approach has been particularly useful in identifying myelinated axons. The term anisotropy refers to the degree by which protons diffuse predominately in a single direction. Myelinated fibers are relatively anisotropic with diffusion predominantly along the axis of the fiber. DTI data are depicted in parametric maps that assign colors to different directions (e.g., anterior, posterior, ventral, dorsal, right, left). Thus, MR DTI visually depicts the water molecules within myelinated sources, crudely outlining WM tracts.

DTI has been validated by comparison with experimental histological specimens. Further proof of concept includes experiments where DTI-identified WM tracts were electrically stimulated and produced predicted physiologic responses. Traditionally, subcortical stimulation mapping has served as the gold standard for intraoperative neuronavigation, yet this technique does not visually delineate the intraparenchymal path of WM tracts. In contrast, DTI depicts WM tracts as they course through the central nervous system. Numerous innovative clinical applications of DTI have been described in the literature. Herein we thematically describe them and discuss limitations and future directions.

Tumor grading & staging
Tumor evaluation with DTI enables discrimination between different types of CNS lesions and visualization of WM tracts depicts WM-tumor interactions. Lauer et al evaluated preoperative DTI images of 6 patients with brain lesions and observed various patterns of tumor-induced damage, which were categorized into invasion, deformation, infiltration, or apparent tract interruption. Preoperative knowledge of the WM-tumor interaction contributed to good clinical outcomes, as 4 patients with preoperative impaired motor functioning experienced complete symptom resolution postoperatively. Chen et al applied this knowledge in a study of 10 patients with brainstem lesions. Prior to resection, some form of deformation, demyelination, or apparent tract interruption was diagnosed in each patient. Visualization of the tracts again after surgery ensured the tracts returned to their proper location. The authors concluded that WM tract imaging provided abundant risk stratification and prognostic information. DTI can be used to evaluate specific tumor characteristics including extent of infiltration. One parameter called fractional anisotropy (FA) is a scalar value (ranging from 0-1) and is used to describe the degree of anisotropy of a diffusion process. Deng et al found a negative correlation between the FA value and degree of tumor infiltration in twenty patients with gliomas, as lower FA values were observed in the areas of higher glioma infiltration. FA is a promising quantifiable marker of tumor infiltration (that cannot be otherwise determined from conventional MR images).

FA values aid differentiation between tumor types. Byrnes et al studied 28 patients with either glioblastoma or brain metastasis using FA values. Mean FA was significantly lower in the edema surrounding malignant tumors than surrounding glioblastomas. Imaging was able to accurately discriminate between tumor type for 87.5% (14 of 16) of glioblastomas and 83.3% (10 of 12) of metastases, as validated by histology. Similarly, Tropine et al used various DTI metrics to distinguish between fibrillar and benign meningiomas, concluding that FA values are the valuable predictors. After evaluating 30 patients with WHO grade 1 meningiomas, the authors reported that in comparison to benign subtypes, fibroblastic meningiomas present with higher FA values. Interestingly, the two categories demonstrate different tumor shapes; while tumors formed by benign meningiomas are predominantly spherically shaped (80%), a large amount of fibroblastic meningioma tensors are non浙ically shaped (43%). Jolapara et al studied 21 tumor patients using DTI and found that atypical and fibroblastic meningiomas had higher mean FA value than benign meningiomas. The authors also evaluated Spherical Anisotropy, another measure of FA looking at the degree to which molecules are traveling in equal directions, and found higher Spherical Anisotropy values in benign meningiomas when compared to atypical and fibroblastic meningiomas. No reliable method of differentiating between atypical and fibroblastic meningiomas was found. Finally, Xu et al determined that FA values are useful in differentiating between recurrent tumors and radiation-induced injury. Here, thirty-five glioma patients who had previously undergone radiotherapy underwent DTI. The average FA values were significantly higher in the group of recurrent tumors than that of the radiation-injured injury group. These studies demonstrate the diagnostic power of DTI.

Presurgical planning
Before a patient’s operation begins, DTI information can assist surgical planning in several ways. It may be used to evaluate tumor resectability and determine surgical feasibility. Setzer et al studied 14 patients with gliomas and found that other spinal cord tumors and categorized them according to the interaction between the lesion and the surrounding WM tracts. Lesions were considered resectable (Type 1) when no fibers entered the lesion. Type 2 consisted of lesions that contained only the minority of fibers from a given tract, and was considered resectable only if less than 30% of the tumor, by volume, contained fibers. Lesions were deemed non-resectable (Type 3) when the majority of the lesion contained fibers or the tumor had already demonstrated destruction of fibers. These classifications were clinically translatable: all 5 Type 1 lesions were fully resected, the Type 2 case deemed resectable was fully resected, while 1 of 2 unresectable Type 2 tumors was unresectable, and 5 of 6 Type 3 lesions were unresectable, as evidenced at time of biopsy. Surgical planning is enhanced by preoperative visualization of fibers, which allows for preoperative decisions. Yu et al studied 16 brain tumor patients using DTI to reconstruct lesion location and relationship to the surrounding WM, which informed surgical planning that preserved vital tracts and maximized tumor resection. The study group demonstrated a significantly higher extent of tumor removal and postoperative improvement in locomotor function when compared to a control group whose presurgical planning included only conventional MRI methodology. Qin et al studied 45 patients with suspected gliomas and used DTI to acquire a better understanding of the anatomical relationship between the tumor and pyramidal tract, including the direction of the pyramidal tract to the tumor, how the lesion invaded the pyramidal tract, and the distance between them. The authors noted that because this information was available to them in the planning stage, a surgical approach that was unambiguous and...
precise was designed. Without having to worry about disrupting the pyramidal tract, a high degree of gross total resection was possible (73.3%), with subtotal resection occurring in 13.3%. Postoperative clinical outcomes were encouraging, as 85% of the 40 patients who participated in a follow-up visit 6 months later had high Barthel Performance Status scores (80-100).

Chen et al. navigated the corticospinal tract and medial lemniscus using DTI in preparation for treatment of a brainstem cavernous angioma. Based on the orientation of the lesion to these critical WM structures, they concluded that a subtemporal presigmoid approach would provide a “safe corridor” where the lesion could be accessed. The lesion was subsequently removed while the CST and medial lemniscus remained fully intact. Likewise, Mushel et al. reported their experience utilizing DTI in the pre-operative treatment planning of 6 juvenile pilocytic astrocytoma cases. In order to select the appropriate surgical approach, the fibers of the posterior limb of the internal capsule (PLIC) must first be accounted for, a task for which DTI is appropriately suited. This method was especially useful in one case where DTI identified that PLIC fibers deviated abnormally, and a more lateral approach was therefore utilized. In all 6 cases, however, gross total resection of all cystic and solid tumor was possible.

Table 1. Categorized Clinical Applications of MR DTI Application | Author | No. of Patients | Patient Type
--- | --- | --- | ---
Tumor Staging | Chen et al. | 10 | Brainstem Lesions
Glioblastoma/Metastases Differentiation | Deng et al. | 20 | Glioma
Glioblastoma/Metastases Differentiation | Byrnes et al. | 28 | Glioblastoma
Fibroblastic/Benign Meningioma | Tropico et al. | 30 | Meningioma
Atypical or Fibroblastic/Benign Meningioma Differentiation | Jolpata et al. | 21 | Meningioma
Recurrent Tumor/Radiation-Induced Injury Differentiation | Xu et al. | 35 | Glioma

Presurgical Planning | Setzer et al. | 14 | Intramedullary Spinal Cord Tumor
Yu et al. | 16 | Various Tumors Types
Qiu et al. | 45 | Suspicious Gliomas
Chen et al. | 9 | Brainstem Lesions
Identification of WM Traacts at Risk | Clark et al. | 4 | Various Tumors Types

Intraoperative Navigation | Mamata et al. | 3 | Various Tumors Types
Wu et al. | 118 | Pyramidal Tract Lesion
Nimsky et al. | 38 | Pyramidal Tract or Optic Radiation Lesion
Nimsky et al. | 19 | Metastatic Melanoma
Nimsky et al. | 16 | Temporal Lobe Epilepsy
Hity et al. | 1 | Metastatic Melanoma

Postoperative Assessment | Chen et al. | 48 | Temporal Lobe Epilepsy
Yapogurth et al. | 21 | Temporal Lobe Epilepsy
Winston et al. | 10 | Medial Refractory Epilepsy
Price et al. | 25 | Varying WHO Grade Tumors

Table 2. Neural Pathways Already Tracked Using MR DTI Pathways Tracked | Application
--- | ---
Pyramidal Tract | Corpus Callosum
Optic Radiation | Cerebellar Tract
Medial Lemaniscus | Internal Capsule
Superior Longitudinal Fasciculus | Papeo-ENDO-thalamic Pathway
Anterior Thalamic Radiation | Dentato-rubro-thalamic Tract
Meyers’ Loop | Uncinate Fasciculus
Geniculocalcarine Tract | Inferior Frontocorticall Fasciculus
Frontal Occipital Fasciculus | Inferior Longitudinal Fasciculus
Parieto-occipital PBS/ventricular 
Pain Pathways | Sub-cortical Fasciculus
Anterior Commisures | Coera Radiata
Inferior Longitudinal Fasciculus | Medial Longitudinal Fasciculus
Cingulum | Uncinate Fasciculus
Cuneate Fasciculus | Radiographic Tract

table 3. DTI Applications for Different Diseases Disease | Use
--- | ---
Cancer | Evaluate Tumor Infiltration
| Evaluate Tumor Resectability
| Surgical Design
| Identify WM Traacts at Risk
| Ensure Maximal Resection
| Prevent Over-resection
| Account for Intraoperative Brainshift

Intraoperative navigation DTI may be utilized for intraoperative neuro-navigation that facilitates tumor resection while minimizing WM tract damage. Mamata et al. have been attributed with first reporting on the feasibility of incorporating DTI into surgical procedures. They describe the protocol with which DT images were taken during the neuroradiological procedures of three patients, creating additional benefits to the preoperative DTI advantages previously discussed. Specifically, intraoperative changes in fiber orientation due to surgically induced brain deformation were detected, and intraoperative mapping of WM anatomy may help to avoid injury to critical WM tracts. A study by Wu et al. reflects the enormous impact that intraoperative DTI may have on patient outcome. Here, 238 patients with gliomas in the vicinity of the pyramidal tract were randomized into two groups. 118 patients had DTI of the pyramidal tract incorporated into their neuro-navigation for their procedures while the 120 patients in the control group used only anatomic MRI in conjunction with neuronavigation. The study group presented with a significantly better postoperative outcome based on a number of different elements, including higher occurrence of gross total resection (72.0% to 51.7%), greater incidence of improvement of motor function (18.6% to 3.9%), lower incidence of deterioration of motor function (33.5% to 32.4%), higher KPS scores at 6 months follow up (86 ± 20 to 74 ± 28), and a longer survival (40 ± 20 months to 30 ± 14.0). Further, a hazard ratio reported 43.6% reduction in the risk of death when using DTI. Hickey et al. were the first to report the use of DTI-guided intraoperative neuro-navigation to resect a deeply situated metastasis. Tractography of a patient with malignant melanoma to the paraventricular WM of the CST. Postoperatively, the patient showed no intratumoral recurrence and intact neurological function, suggesting that both the CST and pyramidal tracts remained preserved. Nimsky et al. applied intraoperative DTI during resections of 38 patients with various brain abnormalities and found intraoperative imaging to be a useful marker that surgical objectives were achieved. Intraoperative views allowed visualizations when showing an acceptable amount of resection had occurred and that MW tracts had returned to their natural positions. A second study by Nimsky et al. implemented intraoperative imaging during resections of 19 patients.
Benefits have also been seen in the area of Deep Brain Stimulation (DBS), where DTI has been used to navigate to target sites of therapy. The first instance of DTI-based fiber tract targeting in DBS surgery was done by Coenen et al.11 They created a patient with longstanding parkinson disease from miosyctosis. DTI was used to visualize the dentatorubrothalamic tract which had been previously identified as a target for movement disorders. Electrodes were successfully implanted and the tremor was alleviated. The authors note that this technique depends on a high degree of mapping accuracy, which is achieved through DTI. In a similar report by Coenen et al.11 DTI targeted the dentatorubrothalamic tract as it passed through the thalamus in the treatment of an individual suffering from tremor-dominant Parkinson’s disease. Similar to the previous case, the tremor symptoms were alleviated postoperatively. The authors found this form of scanning provides a superior atlas for stereotactic surgical strategies. Owen et al. showed that DTI can help further our understanding of specific pathways using a patient who underwent a lamina 25 years prior and had since experienced extreme hypersensitivity and excruciating back pain. By mapping out the fiber tracts that were connected to DBS electrodes implanted in the patient’s periaqueductal/periventricular grey areas, the authors developed an enhanced understanding of pain pathways and were subsequently able to alleviate the patient’s pain.

Postoperative assessment

DTI has shown the ability to accurately assess both the tract damage and predict postoperative outcomes. Chen et al.12 used DTI-based fiber tracking in 48 patients undergoing anterior and posterior fossa decompression to determine the space between Meyer’s loop and the temporal tip. This distance was found to be highly significant in determining the challenges patients may face during surgery. In another report, two different fiber tracts cross one another – for example, patients coming in contact with the Superior Longitudinal Fasciculus – postpro- cedure visualization for neurosurgical planning. Neurosurgery 68, 1239-1251 (2010).


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