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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 neuraxis structures, white matter (WM) tracts. There are numerous neurosurgical applications for MR DTI including: (1) Tumor grading and staging: (2) Pre-surgical planning (determination of resectability, determination of surgical approach, identification of WM tracts at risk); (3) Intraoperative navigation (tumor resection that spares WM damage, epilepsy resection that spares WM damage, epilepsy resection that spares WM damage, accurate location of deep brain stimulation structures); (4) 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 neurosurgical 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 diffusion of the pulse rapid in a minimum of six directional axes is sufficient to resolve a diffusion vector in three dimensional space describing the overall diffusion of a sample, 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 predominantly in a single direction. Myelinated fibers are relatively anisotropic with diffusion preferentially along the axis of the fiber. DTI data are depicted in parametric maps that assign colors to different directions (e.g., anterior, posterior, central, 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, subcutaneous stimulation mapping has served as the gold standard for intraoperative neuroanatomical localization, 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 theoretically 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 depicting WM-tumor interactions. Lause et al. evaluated preoperative DTI images of 6 patients with brain lesions and observed various patterns of tumor-induced damage, which were categorized into deviation, 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 function experiencing 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 deviation, deformation, infiltration, 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 prognosis 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 and differentiation between tumor types. Byrnes et al. studied 28 patients with either glioblastoma or brain metastases using FA values. Mean FA was significantly lower in the edema surrounding metastatic tumors than surrounding glioblastomas. Imaging was able to accurately discriminate between tumor type for 87.5% (14 of 16) of glioblastomas and 83.3% (12 of 15) of metastases, as validated by histology. Similarly, Tropme et al. used various DTI metrics to distinguish between fibroblastic 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 meninngioma fibers are nonopically shaped (43%), and fibroblastic meningiomas were determined by volume, from which the authors concluded 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
with subtotal resection occurring in about disrupting the pyramidal tract, a high precise was designed. Without having to worry

ing for treatment of a brainstem cavernous

fMRI and structural MRI into an ultra-

tumors, they noted DTI was essential in one particular case where the lesion compressed the CST and medial lemniscus posteriorly. In this instance, the standard sub-

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tumors, they noted DTI was essential in one particular case where the lesion compressed the CST and medial lemniscus posteriorly. In this instance, the standard sub-

resubmitted from the preoperative phase 6 patients with tumors in the internal capsule (PLIC) must first be

accounts for, a task for which DTI is appro-

since was designed. Without having to worry

Tumor Resection Sparing WM Damage

Mamata et al.20 3 Various Tumors Types

identification of WT at risk

Preoperative Assessment

Identification of WM Damage

Chen et al.9 48 Temporal Lobe Epilepsy

Price et al.26 25 Varying WHO Grade Tumors

Intraoperative navigation

DTI may be utilized for intraoperative neuro-

anatomy may help to avoid injury to critical

Intraoperative views allowed visualizations

if not previously identified. Encour-

avoided during surgery than relying only on

Intraoperative views allowed visualizations

Prevention of damage to WM tracts is criti-

by manipulate the distance, the anatomic content of tumor location and WM tract involvement can be
determined. One group developed individually-

tailed procedures, based on patient anatomy, and found that the usefulness of DTI was most appreciated in the preparation of brainstem resections, where numerous nuc-

tumors may be vulnerable to injury if not accounted for. While treating 9 patients with brainstem lesions, they noted DTI was essential in one particular case where the lesion compressed the CST and medial lemniscus posteriorly. In this instance, the standard sub-
occurrent tract approach would have likely destroyed parts of the WM tracts, so the surgeon instead opted for a retromastoid approach. Indeed, surgical approach should incorporate not just the location of the lesion, but also its relation to various WM tracts.

Rausman et al.37 showed that DTI could be soundly incorporated with functional (f) MRI and structural MRI into an ultra-

sound based neuronavigation system to develop tailor-made preoperative planning as well as navigation based on updated multi-

modal information during surgery. Here, 24 patients with primary gliomas underwent DTI and fMRI to determine the location and

orientation of VM in relation to brain lesions. Patien outcomes were divided into 3 catego-

gories: Gross Total Resection (3 patients), 90% Resection36,40, and Subtotal Resection. No surgically

induced deficits occurred in the first two groups, whereas one Subtotal Resection case resulted in expressive aphasia and hemiplegia.

The authors concluded that the tandem use of DTI and fMRI provides a far superior mode of identifying functional systems to be avoided during surgery than relying only on

An example of a brainstem cavernous angioma that was utilized to treat a patient with a brainstem cavernous angioma. This case was selected because it illustrates the potential of DTI in identifying eloquent tracts near critical structures, such as the pyramidal tract. The tumor was located in the lateral aspect of the brainstem, close to the entry point of the pyramidal tracts, making it a challenging case for surgery. DTI was used to map the surrounding WM tracts, which were then used to guide the surgical approach. The tumor was successfully resected, and the patient experienced no neurological deficits postoperatively.

Table 1. Categorized Clinical Applications of MR DTI

<table>
<thead>
<tr>
<th>Application</th>
<th>Author</th>
<th>No. of Patients</th>
<th>Patient Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Staging</td>
<td>Chen et al.9</td>
<td>10</td>
<td>Brainstem Lesions</td>
</tr>
<tr>
<td>Identification of WM Pathology</td>
<td>Deng et al.20</td>
<td>20</td>
<td>Glioma</td>
</tr>
<tr>
<td>Globostroma/Metastases Differentiation</td>
<td>Byrnes et al.28</td>
<td>28</td>
<td>Globostroma</td>
</tr>
<tr>
<td>Globostroma/Metastases Differentiation</td>
<td>Tiope et al.30</td>
<td>30</td>
<td>Meningioma</td>
</tr>
<tr>
<td>Fibrosarctic/Benign Meningioma</td>
<td>Jolapara et al.21</td>
<td>21</td>
<td>Meningioma</td>
</tr>
<tr>
<td>Abietal Fibrosarctic/Benign Meningioma Differentiation</td>
<td>Xu et al.35</td>
<td>35</td>
<td>Glioma</td>
</tr>
</tbody>
</table>

Table 2. Neural Pathways Already Tracked Using MR DTI

<table>
<thead>
<tr>
<th>Pathways Tracked</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyramidal Tract</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Corpus Callosum</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Optic Radiation</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Geniculocalcarine Tract</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Medial Lemniscus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Internal Capsule</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Superior Longitudinal Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Prefrontal-caudal-thalamic Pathway</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Anterior Thalamic Radiation</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Dentatorubrothalamic Tract</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Meyers’s Lobe</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Uncinate Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Geniculocalcarine Tract</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Inferior Frontocippital Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Inferior Longitudinal Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Pericallosal/Parietal/Frontal</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Sub-cingulate Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Amygalo-striatal Tract</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Anterior Commissure</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Corona Radiata</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Medial Longitudinal Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Frontal Fasciculus</td>
<td>Chen et al.9</td>
</tr>
<tr>
<td>Cuneate Fasciculus</td>
<td>Chen et al.9</td>
</tr>
</tbody>
</table>

Table 3. DTI Applications for Different Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Evaluate WM Damage</td>
</tr>
<tr>
<td>Quantity Tumor Infiltration</td>
<td>Evaluate Tumor Resectability</td>
</tr>
<tr>
<td>Surgical Design</td>
<td>Identify WM Tracts at Risk</td>
</tr>
<tr>
<td>Ensure Maximal Resection</td>
<td>Prevent Over-resection</td>
</tr>
<tr>
<td>Account for Intraoperative Brainshift</td>
<td></td>
</tr>
</tbody>
</table>

Epilepsy

Surgical Design

Optic Duct Tract

Parkinson’s

Locate Deep Brain Stimulation Targets

Myoclonus Cystoma

Locate Deep Brain Stimulation Targets

Pain Management

Visualize Pain Pathway Connections

Informed consent was obtained from all patients and the study protocol was approved by the institutional review board. The data were analyzed using statistical software (SPSS, version 24). The results are presented as mean ± standard deviation. The significance level was set at p < 0.05. The relationship between the duration of surgery and the extent of resection was assessed using Pearson’s correlation coefficient. The difference in the extent of resection between the groups was analyzed using the Mann-Whitney U test.
Diffusion Tensor Imaging (DTI) has become a powerful tool for characterizing fiber tracts. DTI is currently unable to differentiate between WM tracts that cross one another. For example, Meyer’s loop courses through the thalamus in the floor of the lateral ventricles in the distance between Meyer’s loop and the temporal lobe. A major issue identified in the analysis of DTI images is the difficulty to predict the location – and therefore avoid – Meyer’s loop during the resection. This difficulty is related to the lateral placement of Meyer’s loop in respect to where resection would occur. In addition, Meyer’s loop and tractography. Using this information, quantitative statistics could be gathered that allowed patients to be assigned to high-risk or low-risk categories for expected outcomes.

The significance of this valuable information prior to surgery is highlighted by a study by Watanabe et al.10 While treating patients with glioblastoma multiforme, the study found that patients who had a greater understanding of the risks involved and the likelihood of postoperative visual field deficits to occur. This directly impacted clinical decision-making, as two patients declined to have surgery after being informed of the risks, and two other patients decided to first pursue alternative medications before attempting surgery.

There are some inherent limitations to DTI. The tractography generated by DTI will vary according to the slice thickness, vector-step length, and size and location of regions of interest. Further, the interpretation of images is directly related to the user’s anatomical knowledge of WM tracts. In other words, the user must actively interpret the tract data for themselves.

The future of DTI is promising. Researchers are currently many of the existing challenges to ensure greater accuracy and precision. Encouraging results have already been reported in terms of differentiating fiber bundles, and DTI has been able to reliably depict the location, hand, foot, and lip fibers within the CST. Progress is being made also in identifying smaller fiber tracts. Similarly, researchers have recently begun to establish a protocol and determine optimization parameters for interventional intraoperative imaging applications may be taken.9,10

References