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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 neural tissue anatomy. In this article, we describe and discuss the role of DTI in the management of various neurological conditions, including gliomas, meningiomas, and gliomedullary tumors. DTI can be used to evaluate specific tumor characteristics including extent of infiltration, which are valuable predictors.

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. Most studies have found that diffusion of the pulse duration in a minimum of six directions is sufficient to resolve a diffusion vector in three dimensional space describing the overall diffusion of water, a tensor (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, ventral, dorsal, right, left). Thus, MR DTI visually depicts the water molecules within myelinated neural structures, 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, subclinical stimulation mapping has served as the gold standard for intraoperative neuromonitoring, 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 schematically describe 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. Lu 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 tumor-WM 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 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 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 to 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 20 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. Brynes et al. studied 28 patients with both 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% (10 of 12) of metastases, as validated by histology. Similarly, Trope 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 I 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-spherically shaped (43%). Jolapara et al. studied 21 tumor types using DTI and found that atypical and fibroblastic meningiomas had higher mean FA 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 radiation therapy underwent DTI. The average FA values were significantly higher in the group of recurrent tumors than that of the radiation-induced 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. noted increased and decreased cranial and 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 transferrable; all 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. Before the operation begins, DTI in the operating room can assist in surgical planning, and may guide an appropriate surgical approach. The authors noted that because this information is based only on the intraoperative DTI images, it must be used in conjunction with other imaging modalities. In the future, real-time DTI may be used to guide surgical navigation and improve patient outcomes.

The study group demonstrated a significantly higher extent of tumor removal and postoperative improvement in locomotor function when compared to a control group whose preoperative planning included only conventional MRI methods. Qin et al. enrolled 60 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 unambiguously
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 Karnofsky Performance Status scores (80-100).

Chen et al.22 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, Moshel et al.14 reported a case where the CST was preserved using similar DTI-assisted surgical techniques. In another case, utilizing DTI in the pre-operative treatment planning of 6 juvenile pilocytic astrocytomas, the lesion was subsequently removed while the CST and medial lemniscus remained intact.

Identification of WM Pathology
Chen et al.21 10 Brainstem Lesions
Deng et al.19 20 Glioma
Byrnes et al.17 28 Glioblastoma
Tenopir et al.11 30 Meningiomas
Sjoltara et al.9 21 Meningiomas
Jia et al.13 35 Glioma

Intraoperative Navigation
Identification of WM Damage
Chen et al.20 4 Various Tumors Types
Mamata et al.16 3 Various Tumors Types
Wu et al.18 118 Pyramidal Tract Lesion
Nimsky et al.19 38 Pyramidal Tract or Optic Radiation Lesion
Nimsky et al.20 19 Metastatic Melanoma
Nimsky et al.21 16 Temporal Lobe Epilepsy
Histy et al.22 1 Metastatic Melanoma

Identification of Tumor Recurrence
Price et al.23 25 Varying WHO Grade Tumors

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.21</td>
<td>10</td>
<td>Brainstem Lesions</td>
</tr>
<tr>
<td>Identification of WM Pathology</td>
<td>Deng et al.19</td>
<td>20</td>
<td>Glioma</td>
</tr>
<tr>
<td>Glioblastoma/Metastases Differentiation</td>
<td>Byrnes et al.17</td>
<td>28</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>Fibroblastic/Benign Meningioma</td>
<td>Tenopir et al.11</td>
<td>30</td>
<td>Meningiomas</td>
</tr>
<tr>
<td>Acoustic Focal/Benign Meningioma Differentiation</td>
<td>Sjoltara et al.9</td>
<td>21</td>
<td>Meningiomas</td>
</tr>
<tr>
<td>Recurrent Tumor/Radiation-Induced Injury Differentiation</td>
<td>Jia et al.13</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>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyramidal Tract</td>
<td>Chen et al.21</td>
</tr>
<tr>
<td>Corpus Callosum</td>
<td>Deng et al.19</td>
</tr>
<tr>
<td>Optic Radiation</td>
<td>Byrnes et al.17</td>
</tr>
<tr>
<td>Cuneate Fasciculus</td>
<td>Tenopir et al.11</td>
</tr>
<tr>
<td>Carotid Artery</td>
<td>Sjoltara et al.9</td>
</tr>
<tr>
<td>Meyer’s Loop</td>
<td>Jia et al.13</td>
</tr>
<tr>
<td>Uncinate Fasciculus</td>
<td>Nimsky et al.16</td>
</tr>
<tr>
<td>Geniculocalcarine Tract</td>
<td>Wu et al.18</td>
</tr>
<tr>
<td>Inferior Frontocortical Fasciculus</td>
<td>Nimsky et al.19</td>
</tr>
<tr>
<td>Inferior Longitudinal Fasciculus</td>
<td>Nimsky et al.20</td>
</tr>
<tr>
<td>Periaqueductal/Ponventricular Pathways</td>
<td>Nimsky et al.21</td>
</tr>
<tr>
<td>Sub-callosal Fasciculus</td>
<td>Histy et al.22</td>
</tr>
<tr>
<td>Anterior Commissure</td>
<td>Price et al.23</td>
</tr>
<tr>
<td>Corona Radiata</td>
<td>Chen et al.20</td>
</tr>
<tr>
<td>Medial Longitudinal Fasciculus</td>
<td>Moshel et al.14</td>
</tr>
<tr>
<td>Occipital Fasciculus</td>
<td>Deng et al.19</td>
</tr>
<tr>
<td>Cuneate Fasciculus</td>
<td>Byrnes et al.17</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>Tumor Infiltration</td>
<td>Quantity Tumor Infiltration</td>
</tr>
<tr>
<td>Tumor Resectability</td>
<td>Evaluate Tumor Resectability</td>
</tr>
<tr>
<td>Surgical Design</td>
<td>Identify WM Tracts at Risk</td>
</tr>
<tr>
<td></td>
<td>Ensure Maximal Resection</td>
</tr>
<tr>
<td></td>
<td>Prevent Over-resection</td>
</tr>
<tr>
<td></td>
<td>Account for Intraoperative Brainshift</td>
</tr>
</tbody>
</table>

DTI software applications enable operators to closely interrogate structures of interest. WM tract location and relationship to brain regions can be visualized. Golby et al.14 demonstrated that operators may choose to depict WM tracts within given distances from structures of interest, such as tumors. By manipulating this distance, the anatomical context of tumor location and WM tract involvement can be discerned. One group developed individually-tailored procedures, based on patient anatomy, and found that the usefulness of DTI was most appreciated in the preoperative diagnosis of brain lesions, where multiple structures are present and WM tracts are 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 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 fMRI. In a similar study by Bertelsen et al.20, DTI and fMRI were both utilized in the treatment of 51 patients with lesions close to eloquent WM structures. The protocol proved to be critical, and led to the alteration of the clinical course in 4 patients (8%).

Intraoperative navigation

DTI may be utilized for intraoperative neuro-navigation that facilitates tumor resection while minimizing WM tract damage. Mamata et al.20 have been attributed with first reporting on the feasibility of incorporating DTI into surgical procedures. They described the protocol with which DTI images were taken during the neuro-surgical 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.21 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. 119 patients had DTI of the pyramidal tract incorporated into their neuroavigation 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 time for 3 months to 14.0). Further, a hazard ratio reported a 43.0% reduction in the risk of death when using DTI. Haky et al.22 were the first to report the use of DTI-guided intraoperative neuro-navigation to select a deep situated metastasis. Tractography of a patient with malignant melanoma on the paraventricular WM of the CST. Postoperatively, the patient showed no intracranial surgical procedures of three patients, creating additional benefits to the preoperative DTI advantages previously discussed. Nimsky et al.23 applied intraoperative DTI during resections of 38 patients with various brain abnormalities and found that intraoperative imaging was a useful marker that surgical objectives were achieved. Intravoxel views allowed visualizations of the tumor margins and the CST and associated WM tracts were undamaged. Nimsky et al.23 applied DTI in the treatment of 51 patients with lesions close to eloquent WM structures. The protocol proved to be critical, and led to the alteration of the clinical course in 4 patients (8%).

Prevention of damage to WM tracts is critical. By imaging 4 tumor patients, Clark et al.24 were able to identify the relative danger to the corpus callosum, CST, and superior longitudinal fasciculus as the space occupying lesions were causing significant displacement of the WM tracts. No longer couring through these expected locations, these tracts would have otherwise been vulnerable to injury during surgery if not previously identified. Encouraging results have been reported by Kamali et al.25, showing that DTI is useful in even determining the placement of smaller tracts. Despite the fiber bundles being considerably thin, the prefronto-caudo-thalamic pathway and anterior thalamic radiation were reliably delineated in 5 healthy controls.

Pre-surgical Planning
Determination of Resectability
Setzer et al.14 14 Intramedullary Spinal Cord Tumor
Yu et al.15 16 Various Tumors Types
Kuo et al.16 45 Suspicious Gliomas
Deng et al.17 9 Brainstem Lesions

Determination of Surgical Approach
Chen et al.18 1 Brainstem Cavernous Angioma
Moshel et al.19 6 Juvenile Placoid Astrocytoma
Golby et al.20 5 Various Tumors Types
Caio et al.21 9 Brainstem Lesions

Identification of WM Tracts at Risk
Clark et al.22 4 Various Tumors Types

Intraoperative Navigation
Tumor Resection Sparring WM Damage
Mamata et al.20 3 Various Tumors Types
Wu et al.21 118 Pyramidal Tract Lesion
Nimsky et al.22 38 Pyramidal Tract or Optic Radiation Lesion
Nimsky et al.23 19 Metastatic Melanoma
Nimsky et al.24 16 Temporal Lobe Epilepsy
Histy et al.25 1 Metastatic Melanoma

Postoperative Assessment
Identification of WM Damage
Chen et al.26 48 Temporal Lobe Epilepsy
Yapich et al.27 21 Temporal Lobe Epilepsy
Winslow et al.28 10 Medial Refractory Epilepsy

Identification of Tumor Recurrence
Price et al.29 25 Varying WHO Grade Tumors


