8-1-2012

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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 neuroanatomic structures within the central nervous system. Numerous innovative clinical applications of DTI have been described 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 application of the diffusion pulse in a minimum of six directional axes is sufficient to resolve a diffusion vector in three dimensional space describing the overall diffusion process of water in a pixel (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 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 neuroanatomy, 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 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 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 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 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, Tropin et al described the use of DTI to reconstruct lesion location and orientation was available to them in the planning stage, resulting in a surgical approach that was unambiguous and evidenced at time of biopsy. Surgical planning is enhanced by preoperative visualization of WM tracts and their proper location. 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 preoperative imaging did not include DTI. Qiu et al enrolled 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

Figure 1
(A) T1 gadolinium-enhanced axial view of right-sided cranial tumor; (B) Axial color-encoded DTI image of with tumor circumscribed in red; (C) 3D rendering of tumor fiber relationship with tumor and fiber as opaque objects; (D) Translucent tumor with cutaway view.

benign 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 gene 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 reported a case of a 14-year-old patient with 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 50% 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.

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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 Karnovsky Performance Status scores (0-100).

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, Moshe et al. applied 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.

DTI software applications enable operators to closely interrogate structures of interest. WM tract location and relationship to brain regions can be visualized. Gobbi et al. 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 content 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 preparation of brainstem resections, where numerous nuclei 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 standard suboccipital approach would have likely destroyed parts of the WM tracts, so the surgeons instead opted for a retrosigmoidal approach. Indeed, surgical approach should incorporate not just the location of the lesion, but also its relation to various WM tracts. Rasmussen et al.3 showed that DTI could be seamlessly incorporated with functional (fMRI) and structural MRI into an ultrasound-based neuronavigation system to develop tailor-made presurgical planning as well as navigation based on updated multimodal information during surgery. Here, 24 patients with primary gliomas underwent DTI and fMRI to determine the location and orientation of WM in relation to brain lesions. Patient outcomes were divided into 3 categories: Gross Total Resection (3 patients), >90% Resection4, and Subtotal Resection5. 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 intraoperative fMRI. In a study by Rasmussen et al., fMRI and DTI 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% of patients. Prevention of damage to WM tracts is critical. By imaging 4 tumor patients, Clark et al.8 were able to identify the relative danger to the corona radiata, CST, and superior longitudinal fasciculus as the space occupying lesions were causing significant displacement of these WM tracts. No longer coursing through their 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.,7 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.

Intraoperative navigation DTI may be utilized for intraoperative neuro-navigation that facilitates tumor resection while minimizing WM tract damage. Mamata et al.30 have been attributed with first reporting on the feasibility of incorporating DTI into surgical procedures. They describe the protocol with which DTI images were taken during the neuroradiological procedures of three patients, creating additional benefits to the prospective 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.10 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 neuronavigation 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 5.9%), lower incidence of deterioration of motor function (35.3% to 32.4%), higher KPS scores at 6 month follow ups (86.20 to 74.28), and a longer survival time (13.6 months to 14.0 months). Further, a hazard ratio reported a 43.0% reduction in the risk of death when using DTI. Halky et al. implemented intraoperative navigation to resect a deep situated metastasis. Tractography of a patient with malignant melanoma aided the surgery for a single metastasis within the paraventricular WM of the CST. Postoperatively, this patient showed no intracranial recurrence and intact neurological function, suggesting that both the CST and pyramidal tract were preserved. Nimsky et al. applied intrathecal 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 showing when an acceptable amount of resection had occurred and that MW tracts had returned to their natural positions. A second study by Nimsky et al.8 implemented intrathecal imaging during resections of 19 patients.
Despite reports of 37% and 53% of the optic tracts prior to epilepsy resections to lie between 30.0 – 43.2 mm, made it difficult temporal tip. This range, which was found to resected temporal area. Through the use of DTI, field deficits are common in this treatment, resections and possibly damage the WM, which tract or optic radiation, intraoperative DTI was a precise layout of the fiber tracts throughout to the resection cavity or any remaining tumor. Image data was used for an immediate visual- with lesions located near the pyramidal tract. However, further, the interpretation of images is directly the resection of a brainstem. Thus, when differentiate between WM tracts that cross one another capacity of DTI. Price et al evaluated the images of 25 patients of varying WH grade tumors and reported various WM tract abnormalities. Based on patterns of tumor infiltration or occult tumor not readily seen on conventional MRI, they were able to predict the event of tumor recurrence and design an individualized treat- ment regimens accordingly.

**Discussion**

Diffusion Tensor Imaging (DTI) has become a powerful neurosurgical tool. DTI is currently unable to differ- entiate between WM tracts that cross one another. However, this becomes of clinical relevance when combining different fiber tracts to form one large, averaged tensor that simplifies the pro- cess of classifying tracts. Furthermore, DTI is not able to distinguish between two different fiber tracts across one another – for example, motor tracts coming in contact with sensory tracts. Therefore, DTI provides a useful objective to assess the integrity of that tract. Nonetheless, further, while DTI readily depicts the non-fibrous tracts as these tracts may not be inherently intraoperative neuronavigation for the resection of a brainstem tumor. Neurosurgery 68, 1069-75; discussion 1075-6 (2011).
