A Simplified Method of Accurate Postprocessing of Diffusion Tensor Imaging for Use in Brain Tumor Resection

BACKGROUND: Use of diffusion tensor imaging (DTI) in brain tumor resection has been limited in part by a perceived difficulty in implementing the techniques into neurosurgical practice.

OBJECTIVE: To demonstrate a simple DTI postprocessing method performed without a neuroscientist and to share results in preserving patient function while aggressively resecting tumors.

METHODS: DTI data are obtained in all patients with tumors located within presumed eloquent cortices. Relevant white matter tracts are mapped and integrated with neuron-avigation by a nonexpert in < 20 minutes. We report operative results in 43 consecutive awake craniotomy patients from January 2014 to December 2014 undergoing resection of intracranial lesions. We compare DTI-expected findings with stimulation mapping results for the corticospinal tract, superior longitudinal fasciculus, and inferior fronto-occipital fasciculus.

RESULTS: Twenty-eight patients (65%) underwent surgery for high-grade gliomas and 11 patients (26%) for low-grade gliomas. Seventeen patients had posterior temporal lesions; 10 had posterior frontal lesions; 8 had parietal-temporal-occipital junction lesions; and 8 had insular lesions. With DTI-defined tracts used as a guide, a combined 65 positive maps and 60 negative maps were found via stimulation mapping. Overall sensitivity and specificity of DTI were 98% and 95%, respectively. Permanent speech worsening occurred in 1 patient (2%), and permanent weakness occurred in 3 patients (7%). Greater than 90% resection was achieved in 32 cases (74%).

CONCLUSION: Accurate DTI is easily obtained, postprocessed, and implemented into neuronavigation within routine neurosurgical workflow. This information aids in resecting tumors while preserving eloquent cortices and subcortical networks.

KEY WORDS: Diffusion tensor imaging, Glioma, Resection, Surgery, Tractography

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reserving subcortical connectivity is crucial in optimizing functional outcomes of patients undergoing surgery for

ABBREVIATIONS: DEC, directionally encoded color; DTI, diffusion tensor imaging; FA, fractional anisotropy; IFOF, inferior fronto-occipital fasciculus; SLF, superior longitudinal fasciculus

Supplemental digital content: is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.operativeneurosurgery-online.com). intra-axial brain tumors. Diffusion tensor imaging (DTI) attempts to aid in the preservation of these subcortical networks by providing a framework for localizing these tracts in relation to the surgical target. DTI takes advantage of the anisotropic diffusion of water along white matter fiber bundles, which can be assessed with magnetic resonance imaging (MRI). Postprocessing platforms are used to map the tracts, which can then be integrated into neuronavigation. This permits the neurosurgeon to ascertain the location and orientation of major white matter tracts for preoperative and intraoperative decision making.

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The exact utility and practical application of DTI in brain tumor resection continue to be refined. On the one hand, the historical difficulty in obtaining DTI (especially with respect to postprocessing) has made its implementation in neurosurgical practices somewhat limited. Adding to this barrier, the majority of studies describing DTI are placed within a methodological framework that emphasizes the physics and computational analysis of the modality itself, a perspective that is less directly applicable to neurosurgeons wanting to apply DTI to clinical practice. On the other hand, fundamental questions about the utility of the tool have been raised by leaders in the field, ¹⁻⁸ highlighting the limitations of this potentially valuable tool in practice. In short, the role of DTI in neurosurgery has not been clearly defined.

This article presents a simple DTI postprocessing method and a framework for the application of DTI to intra-axial brain tumor resection. We demonstrate that DTI is easily postprocessed without the use of neuroscientists. We quantify the accuracy of this tractography via comparison with ground truth data, intraoperative stimulation mapping. We discuss the current state of DTI and address its drawbacks while emphasizing its overall value as an adjunctive tool.



FIGURE 1. Corticospinal tract. A, the start region of interest box is placed on the axial image in the midbrain. B, the thickness is adjusted in the sagittal plane. C, the tract is shown in blue.

METHODS

This study was performed with approval from our institutional review board (approval 3199). From February 2012 to March 2015, we obtained DTI for all patients undergoing resection of intra-axial brain tumors by the senior author located near presumed eloquent cortices. From January 2014 to December 2014, this consisted of 82 patients. Forty-three of these patients underwent intraoperative speech and motor mapping, and these patients form the study population.

Image Acquisition

MRIs are obtained with a GE Signa high-definition 1.5-T MRI system 1 to 2 days before surgery. High-resolution T1-weighted data are acquired (repetition time < 50 milliseconds; echo time = 5.2 milliseconds; 1.5-mm thickness; 120 slices; field of view = 26; matrix = 256×256 ; flip angle = 20°) for coregistration with diffusion tensor data. T1-weighted contrast-enhanced, T2, and T2/fluid-attenuated inversion-recovery sequences are also obtained. DTI data are obtained with a single-shot echo-planar imaging sequence (repetition



FIGURE 2. The superior longitudinal fasciculus. **A**, the start region of interest box is placed on the axial image encompassing the green fibers. **B**, the thickness of the box is increased in the sagittal plane. **C**, the tract is shown in red.

time = 8300 milliseconds; echo time = 94.6 milliseconds; 27 slices; field of view = 26; matrix = 128×128 ; B value = 1000 s/mm^2). Diffusion gradients are applied along 25 directions, and the isotropic voxel size measures 2.0 mm³. We do not acquire functional MRI data.

Postprocessing

The video (see Video, Supplemental Digital Content 1, https:// academic.oup.com/ons/article/2608024/A-Simplified-Method-of-Accur ate-Postprocessing-of#supplementary-data), demonstrates the steps of postprocessing and tractography, outlined as follows. Diffusionweighted MRI data sets are imported into the StealthViz S7 software with StealthDTI application (Medtronic, Dublin, Ireland). The *StealthViz with StealthDTI Application Reference Guide* is used to assist with postprocessing, which is performed by the company representative. After the data sets are imported, background masking is performed by manually changing the threshold for each data set as needed. This is done by adjusting the threshold slider left or right until blue is no longer seen in the brain parenchyma. Each diffusion-weighted data set is then automatically registered to the B0 dataset. No change is made unless misalignment occurs in the registration. The B0 data set is then



FIGURE 3. The inferior fronto-occipital fasciculus. **A**, start and end region of interest boxes are placed on the axial image in the occipital and frontal lobes, respectively. **B**, the region of interest boxes are adjusted to the appropriate thickness in the sagittal plane to include the thickness of the lobes. **C**, the tract is shown in pink.

TABLE 1. Demographics of Patients With Diffusion Tensor Imaging and Awake Craniotomies

Patients, n (%)	43
Men	24 (56)
Women	19 (44)
Age (mean \pm SD), y	53 ± 15
Tumor side, n (%)	
Left hemisphere	31 (72)
Right hemisphere	12 (28)
Eloquent location, n (%)	
Left posterior temporal	12 (28)
Left posterior frontal	8 (19)
Left insula	6 (14)
Left parietal-temporal-occipital junction	5 (12)
Right posterior temporal	5 (12)
Right posterior frontal	2 (5)
Right insula	2 (5)
Right parietal-temporal-occipital junction	3 (7)
Pathology, n (%)	
High-grade glioma	28 (65)
Low-grade glioma	11 (26)
Other	4 (9)

coregistered to the MRI. The tensor data are computed automatically, forming the directionally encoded color (DEC) and fractional anisotropy (FA) maps.

Tractography

The following tracts form our routine DTI program: the corticospinal tract, superior longitudinal fasciculus (SLF), inferior fronto-occipital fasciculus (IFOF), and optic radiations. We consider the arcuate fasciculus to be a part of the SLF. The optic radiations were not studied in this report because we do not test visual fields during stimulation mapping. We do not map the inferior longitudinal fasciculus because we have not found a consistent correlation between this tract and a speech modality.

The fiber tracking tool card is used to compute the tracts. Default parameters are used for seed density (1.00) and minimum fiber length (0.00). Maximum directional change is increased from a default value of 45° if a large deflection of fiber orientation is anticipated because of the location of the tumor. Regions of interest are selected on the MRI

TABLE 2. Corticospinal Tract: Diffusion Tensor ative Results ^a	Imaging Intraoper-
Positive map	
Expected (with DTI), n	24
Observed (with stimulation), n/N	24/24
Negative map	
Expected (with DTI), n	19
Observed (with stimulation), n/N	19/19
Sensitivity, %	100
Specificity, %	100
IDTL diffusion tonsor imaging	

TABLE 3. Superior Longitudinal Fasciculus: Diffusion Tensor Imaging Intraoperative Results^a

Positive map	
Expected (with DTI), n	32
Observed (with stimulation), n/N	31/32
Negative map	
Expected (with DTI), n	11
Observed (with stimulation), n/N	10/11
Sensitivity (95% confidence interval), %	97 (91-100)
Specificity (95% confidence interval), %	91 (74-100)
^a DTL diffusion tensor imaging	

by the company representative using established points.9 To identify and depict the corticospinal tract, the start region is placed within the ipsilateral midbrain (Figure 1). For the SLF, the start region is placed within the anterior-posterior fibers (in green on the DEC map) of the frontoparietal region, just lateral to the fibers of the corona radiata (blue on the DEC map). This is demonstrated in Figure 2. For the IFOF, the start region is placed in the occipital lobe, and an end region is placed in the frontal lobe (Figure 3). Default values of FA start value (0.20) and apparent diffusion coefficient (ADC) stop value (0.10) are used. We use the following colors for tracts: blue for corticospinal, orange or red for SLF, and pink for IFOF. It should be noted that these colors do not relate to the DEC map; they were chosen arbitrarily at the time we implemented the DTI program. Start and stop fiber-tracking parameters may be adjusted by changing the threshold value of FA. Fiber tracking may be further refined in selected areas by adjusting the midregion and end-region values when deemed necessary. Tumors are occasionally segmented and 3-dimensionally reconstructed at the discretion of the neurosurgeon.

The imaging data are then exported and loaded onto the Stealth-Station for preoperative and intraoperative planning and navigation. The steps from importing the data sets to constructing the tracts are routinely performed in <20 minutes.

Preoperative Use of DTI

The first consideration in using DTI to resect tumors is the goal of the surgery. In all cases, there must be a tradeoff between preserving function

TABLE 4. Inferior Fronto-Occipital Fasciculus: Differing Imaging Intraoperative Results ^a Imaging Intraoperative Results ^a Imaging	fusion Tensor
Positive map	
Expected (with DTI), n	11
Observed (with stimulation), n/N	9/11
Negative map	
Expected (with DTI), n	28
Observed (with stimulation), n/N	28/28
Sensitivity, %	100
Specificity (95% confidence interval), %	82 (59-100)

^aDTI, diffusion tensor imaging. In 4 cases, the inferior fronto-occipital fasciculus was obliterated by tumor.

and maximizing the extent of resection. This is done on a personalized level with the input of the patient, his or her family, and a multidisciplinary team of providers.

To plan the stimulation mapping, the tumor is assessed in relation to the DTI tracts. Both the cortical terminations and the subcortical networks must be evaluated. These relationships will dictate the cortical and subcortical disconnections needed to separate the tumor from eloquent neural structures. If tracts are not expected to be in the field, a negative map is planned. If the tract is near the planned surgical trajectory, a positive map is planned.

For SLF, we assessed 3 regions: the frontal cortical ramus (during a naming task), the temporal rami (during naming and occasionally reading), and the parietal ramus (during a spatial line bisection task). We have found a considerable amount of variability in the SLF from person to person, and traditional cortical landmarks often do not always represent the cortical terminations of these tracts. For example, the Broca area is often not the site of the termination of the frontal ramus of SLF. Therefore, DTI is useful in providing a framework for locating and avoiding the tract. Function is expected where the ramus terminates cortically. The IFOF was assessed via subcortical mapping with a naming task, primarily during insular and temporal gliomas. For motor function, cortical sites are based on typical gyral landmarks. Subcortical connectivity was assessed particularly with regard to where the fibers of the corticospinal tract coalesce within the corona radiata to form the internal capsule.

Intraoperative Use of DTI

Intraoperatively, DTI is used to guide stimulation mapping, which is performed in a negative mapping paradigm, as described by Sanai and colleagues.¹⁰ Mapping is initiated with an Ojemann electric stimulator at 2 mA. The patient performs relevant continuous double tasking as instructed by a speech pathologist. The spatial task we use is the line bisection task in which the patient bisects a line on a touch screen during continuous stimulation, as described elsewhere.¹¹ Intraoperative electrocorticography is used to monitor for afterdischarge potentials. Stimulation proceeds until positive sites or afterdischarge potentials are identified. If no positive site is found, the current is increased in a stepwise fashion up to 6 mA. Numbered labels are placed on the cortex at the site of arrest. All sites are tested 3 times.



Once cortical mapping is complete, the operating microscope is brought into the field. Cortisectomy is performed. The disconnection proceeds downward in subcortical white matter with the goal of separating eloquence from noneloquence. Subcortical white matter is stimulated every several millimeters at the highest tolerated current used during cortical stimulation. After the tumor has been disconnected from eloquent tract, tumor resection proceeds.

For the purposes of this study, the accuracy of DTI tracts was defined as a positive stimulation site found within approximately 5 mm of the appearance of the tract on neuronavigation.

Patient Outcomes

Extent of resection was determined by the neuroradiologist and operating neurosurgeon. Permanent motor deficits were evaluated over the course of clinical follow-up by the operating neurosurgeon. Speech deficits were assessed by a speech pathologist both preoperatively and postoperatively. The evaluation consists of reading, naming (using a modified version of the Boston naming test), and other language testing.

Statistical Analysis

Patient demographics, results, and patient outcomes were summarized with descriptive statistics. The sensitivity of DTI was calculated as the percentage of positive maps via stimulation mapping that were predicted by DTI. Specificity of DTI was calculated as the percentage of patients with negative maps via stimulation mapping that were predicted by DTI.

RESULTS

Patient Demographics

In 2014, we used DTI on 82 patients. Of these, 43 patients received awake craniotomies for speech and motor mapping. Patient demographics are listed in Table 1. There were 24 men and 19 women. The mean patient age was 53 years. The most common pathology was high-grade glioma, occurring in 29 patients (65%). Seventy-two percent of tumors were left-sided.

Seventeen patients had posterior temporal lesions (12 leftsided, 5 right-sided). Ten patients had posterior frontal lesions



FIGURE 5. Expected negative map for corticospinal tract. T1-weighted magnetic resonance imaging in the coronal **A**, sagittal **B**, axial **C**, and 3-dimensional **D** views. The tract runs superior and medial to the tumor within the internal capsule.

(8 left-sided, 2 right-sided). Eight patients had insular lesions (6 left-sided, 2 right-sided). Eight patients had parietal-temporal-occipital junction lesions (5 left-sided, 3 right-sided).

Intraoperative Results

DTI-expected findings were compared with direct electric cortical and subcortical stimulation mapping (Tables 2-4). A positive map was expected for the corticospinal tract in 24 cases. That is, in 24 cases, we expected to encounter the tract during stimulation mapping, manifested as a decrease in motor function during stimulation within 5 mm of the DTI tract. An example of an expected positive map for the corticospinal tract is displayed in Figure 4. In each of these 24 cases, motor was identified with stimulation. A negative map was expected for the corticospinal tract in 19 cases. That is, in 19 cases, the tract was not expected to be identified in the field via stimulation mapping. An example of an expected negative map was found

in all 19 of these cases. Thus, the sensitivity and specificity were each 100%.

For the SLF, a positive map was expected in 32 cases. An example of an expected positive map for the SLF is shown in Figure 6. A positive map was found in all but 1 of these 32 cases (1 false positive). A negative map was expected in 11 cases. An example of an expected negative map for the SLF is shown in Figure 7. A negative map was observed in 10 of these 11 cases (1 false negative). The sensitivity and specificity for SLF were 97% and 91%, respectively.

For the IFOF, a positive map was expected in 11 cases. An example of an expected positive map for the IFOF is shown in Figure 8. A positive map was observed in 9 of these 11 cases (2 false positives). A negative map was expected in 28 cases. An example of an expected negative map for the IFOF is shown in Figure 9. A negative map was observed in all 28 of these cases. The sensitivity and specificity of IFOF were 100% and 82%, respectively.



FIGURE 6. Expected positive map for the superior longitudinal fasciculus (SLF). T1-weighted magnetic resonance imaging in the coronal **A**, sagittal **B**, axial **C**, and 3-dimensional **D** views. The tumor is deep to the frontal operculum containing the frontal ramus of the SLF. The disconnection is made inferior and anterior to the frontal ramus of SLF via stimulation mapping for speech arrest during double tasking.



FIGURE 7. Expected negative map for the superior longitudinal fasciculus (SLF). T1-weighted magnetic resonance imaging in the coronal **A**, sagittal **B**, axial **C**, and 3-dimensional **D** views. Given the displacement of the frontal and temporal rami of the SLF, a clear cortical path into the tumor is evident.

Outcomes

The primary objective of this data set was not to study patient outcomes, and clearly, this cannot be assessed rigorously, given patient heterogeneity. However, we include these data, displayed in Table 5, for the purposes of validating our method. Gross total resection was achieved in 24 cases (55.8%), and > 90% of the tumor was resected in another 8 patients (18.6%). Eighty percent to 89% of the tumor was resected in 5 patients (11.6%), 70% to 79% in 2 patients (4.7%), and 60% to 69% in 2 patients (4.7%). Two biopsies were performed, both cases in which the relatively small tumor was located almost entirely within eloquent brain on stimulation mapping and DTI.

No patients were lost to follow up. Thirty-eight patients had normal speech preoperatively, and 37 of these retained normal speech postoperatively. Five patients had speech deficits preoperatively, and none of these permanently worsened postoperatively. The overall speech preservation rate was 97.7%.

Thirty-seven patients had no motor deficits preoperatively, and 35 of these retained full motor function, although some were

transiently weak postoperatively. Six patients had motor deficits preoperatively, and 1 of these had permanent increased weakness postoperatively. The overall motor preservation rate was 93.0%.

DISCUSSION

One of the major limiting factors preventing widespread use of DTI is an incomplete understanding of the current state of the technology. To that end, the purpose of this study is to demonstrate the ease of postprocessing DTI data. We show that the tracts can be mapped by nonexperts simply and accurately. With this methodology, we found that the DTI-modeled tracts were accurate compared with ground truth, stimulation mapping. Positive maps were found via cortical or subcortical stimulation mapping in a total of 65 cases (24 corticospinal, 32 SLF, 9 IFOF). Positive sites were within 5 mm of the DTI tract in 64 of these cases (overall sensitivity, 98%). Thus, in only 1 case was function identified where it was not expected, an outcome that suggests incomplete tract representation. Negative maps were found via



FIGURE 8. Expected positive map for the inferior fronto-occipital fasciculus (IFOF). 12-weighted magnetic resonance imaging in the coronal **A**, sagittal **B**, axial **C**, and 3-dimensional **D** views. The IFOF wraps over this tumor superiorly and medially. Subcortical stimulation mapping is expected to be positive along the superior margin of the tumor.

stimulation mapping in a total of 60 cases (19 corticospinal, 11 SLF, 30 IFOF). Negative maps were expected preoperatively in 57 of these cases (overall specificity, 95%). Thus, in 3 cases, no function was found in the vicinity of the tract on DTI (1 SLF, 2 IFOF), an outcome that suggests either an erroneous map or nonessential fibers.

Our method uses a company representative without a postgraduate education to postprocess DTI data. This may be contrasted with the methodology at many institutions in which the postprocessing is done only by neuroscientists or neuroradiologists. This may be logistically challenging from the standpoint of both personnel and time and clearly is a viable option only at large academic centers. Similarly, the highly technical nature of DTI literature¹²⁻¹⁷ has made daily practical application difficult for many neurosurgeons. However, with the use of newer software programs, tracts can be produced quickly and consistently by a trained person without an extensive neuroscience or physics background. In most cases, we use the default settings for the software package. When we change a variable, it is predictable.

For example, we increase the maximum directional change angle when the tumor interrupts the expected path of the fiber tract to account for the deflection that may have taken place.

Several challenges have been raised with regard to the utility of DTI. The key points are the following: (1) In general, DTI is imperfect in resolving fiber bundle anatomy; (2) results depend on both user-defined and equipment-specific variables; (3) it is sometimes difficult to determine cortical terminations of tracts; and (4) the peritumoral area may distort or destroy the fiber bundles in a way that may not depict reality.¹⁻⁸ Each of these is an important consideration that limits the role of DTI tractography; it does not follow, however, that DTI has no adjunctive role in brain tumor operations.

There are several key elements to using DTI safely and effectively, centered on knowing the limitations of the tool. Others have stated that inaccurate representation of the tracts raises the possibility of injuring the tracts. We agree that injury to tracts is possible if caution is not exercised. Resection in regions of potential eloquence should proceed along a functional subcortical



FIGURE 9. Expected negative map for the inferior fronto-occipital fasciculus (IFOF). T1-weighted magnetic resonance imaging in the coronal **A**, sagittal **B**, axial **C**, and 3-dimensional **D** views. The IFOF runs sufficiently medial to this large frontoparietal tumor.

boundary with direct electric stimulation. That is, DTI directs the search for function subcortically with electric stimulation; it should never supplant cortical and subcortical stimulation, which remains the gold standard for defining tracts intraoperatively.¹⁸ Similarly, the potential for fiber distortion by infiltrating tumor must be considered. Although this is likely an inherent limitation of DTI, the parameters used to reconstruct the tracts can be optimized to limit this to some degree. For example, using an FA threshold value of 0.15 to 0.2 best reconstructs partly infiltrated tracts.¹⁹ Our methodology uses an FA value of 0.2. We increase the maximum directional change to a value $> 45^{\circ}$ if we expect the tumor to have deflected the path of fibers. As is well known, brain shift must be taken into account when neuronavigation is used, which also applies to tractography. Another argument against the use of DTI is that it may preclude an operation by suggesting that the tumor is unresectable without compromising important white matter tracts.⁶ However, we never use DTI to decide whether a resection is possible. As in other cases, our

intraoperative actions in these cases are dictated by stimulation mapping.

Our negative stimulation mapping paradigm uses currents of 2 to 6 mA. Other centers may use higher currents, which may increase the chances of identifying positive sites. However, currents >6 mA increase the risk of seizures, and in our experience, it is quite challenging to map after a seizure, particularly in the setting of a pre-existing dysphasia. This is a tradeoff between seizure risk and identifying all cortical sites.

The limitations of DTI likely preclude its use as a standalone guide for knowing the exact location of white matter tracts. The information should be validated with subcortical mapping or should be used only as a general guide. Our results demonstrate that function, as determined by intraoperative speech and motor mapping, was located within 5 mm of the DTI in most cases. Thus, DTI informs the surgeon where to look for function during subcortical mapping. As with other tools in our field, it should be used with an awareness of its shortcomings.

TABLE 5. Patient Outcomes	
	n (%)
Extent of resection, %	
100	24 (55.8)
90-99	8 (18.6)
80-89	5 (11.6)
70-79	2 (4.7)
60-69	2 (4.7)
Biopsy	2 (4.7)
Language	
No preoperative deficit	38
No postoperative deficit	37 (97.4)
Permanent deficit	1 (2.6)
Preoperative deficit	5
Stable or improved postoperatively	5 (100)
Permanent worsened deficit	0 (0)
Overall speech preservation	42/43 (97.7)
Motor	
No preoperative deficit	37
No postoperative deficit	35 (94.6)
Permanent weakness	2 (5.4)
Preoperative deficit	6
Stable or improved postoperatively	5 (83.3)
Permanent worsened deficit	1 (16.7)
Overall motor preservation	40/43 (93.0)

Limitations

Our study has several limitations that warrant acknowledgment. First, we assessed only a single platform for DTI. Although in principle we would expect this method to be translatable to other platforms, we did not validate any other system. Relating to our outcomes, we do not have a control group who underwent surgery without DTI. Therefore, we have no direct comparison for our results. However, the primary purpose of this report is to demonstrate the relative ease of DTI postprocessing rather than evaluating efficacy. The outcomes reported are used to show that we saw little morbidity after our resections, which were typically aggressive. Another limitation of our study is its retrospective nature. We believe this study has important and valuable conclusions for neurosurgeons, although a prospective study would perhaps have been more informative.

CONCLUSION

We provide a simple guide for the processing and use of DTIs that can be achieved without a neuroscientist. We have found that the fiber tract anatomy is quite accurate as a framework for mapping, serving as a mental construct of the subcortical networks. We await with anticipation the clinical availability of new technologies that address the inherent weaknesses of DTI. However, at the present, DTI remains a worthwhile tool. We hope this will be a valuable guide to others.

Disclosures

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REFERENCES

- Nimsky C. Fiber tracking: we should move beyond diffusion tensor imaging. World Neurosurg. 2014;82(1-2):35-36.
- 2. Farquharson S, Tournier JD, Calamante F, et al. White matter fiber tractography: why we need to move beyond DTI. *J Neurosurg.* 2013;118(6):1367-1377.
- Fernandez-Miranda JC. Editorial: beyond diffusion tensor imaging. J Neurosurg. 2013;118(6):1363-1365; discussion 1365-1366.
- Lerner A, Mogensen MA, Kim PE, Shiroishi MS, Hwang DH, Law M. Clinical applications of diffusion tensor imaging. *World Neurosurg.* 2014;82(1-2):96-109.
- Feigl GC, Hiergeist W, Fellner C, et al. Magnetic resonance imaging diffusion tensor tractography: evaluation of anatomic accuracy of different fiber tracking software packages. *World Neurosurg.* 2014;81(1):144-150.
- Duffau H. The dangers of magnetic resonance imaging diffusion tensor tractography in brain surgery. *World Neurosurg.* 2014;81(1):56-58.
- Duffau H. Diffusion tensor imaging is a research and educational tool, but not yet a clinical tool. World Neurosurg. 2014;82(1-2):e43-e45.
- Potgieser AR, Wagemakers M, van Hulzen AL, de Jong BM, Hoving EW, Groen RJ. The role of diffusion tensor imaging in brain tumor surgery: a review of the literature. *Clin Neurol Neurosurg.* 2014;124C:51-58.
- 9. Catani M, Thiebaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex.* 2008;44(8):1105-1132.
- Sanai N, Mirzadeh Z, Berger MS. Functional outcome after language mapping for glioma resection. N Engl J Med. 2008;358(1):18-27.
- Fernandez Coello A, Moritz-Gasser S, Martino J, Martinoni M, Matsuda R, Duffau H. Selection of intraoperative tasks for awake mapping based on relationships between tumor location and functional networks. *J Neurosurg.* 2013;119(6):1380-1394.
- Behrens TE, Woolrich MW, Jenkinson M, et al. Characterization and propagation of uncertainty in diffusion-weighted MR imaging. *Magn Reson Med.* 2003;50(5): 1077-1088.
- Seo Y, Wang ZJ, Morriss MC, Rollins NK. Minimum SNR and acquisition for bias-free estimation of fractional anisotropy in diffusion tensor imaging: a comparison of two analytical techniques and field strengths. *Magn Reson Imaging*. 2012;30(8):1123-1133.
- Lori NF, Akbudak E, Shimony JS, et al. Diffusion tensor fiber tracking of human brain connectivity: acquisition methods, reliability analysis and biological results. *NMR Biomed.* 2002;15(7-8):494-515.
- Mori S, van Zijl PC. Fiber tracking: principles and strategies: a technical review. NMR Biomed. 2002;15(7-8):468-480.
- Lazar M, Alexander AL. An error analysis of white matter tractography methods: synthetic diffusion tensor field simulations. *Neuroimage*. 2003;20(2): 1140-1153.
- Jeurissen B, Leemans A, Tournier JD, Jones DK, Sijbers J. Investigating the prevalence of complex fiber configurations in white matter tissue with diffusion magnetic resonance imaging. *Hum Brain Mapping*. 2013;34(11): 2747-2766.
- Ille S, Sollmann N, Hauck T, et al. Combined noninvasive language mapping by navigated transcranial magnetic stimulation and functional MRI and its comparison with direct cortical stimulation. J Neurosurg. 2015;123(1):1-14.
- Stadlbauer A, Nimsky C, Buslei R, et al. Diffusion tensor imaging and optimized fiber tracking in glioma patients: histopathologic evaluation of tumor-invaded white matter structures. *Neuroimage*. 2007;34(3):949-956.

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COMMENTS

• he past decade has seen DTI increasingly integrated into surgical neuro-oncology,^{1,2} to guide: a) preoperative stratification of risk; b) planning of surgical approach; and c) determine the surgical boundaries in eloquent areas of the brain, and minimize postoperative deficit. For tumors in or near eloquent areas of the brain, there has been a paradigm shift from emphasizing cortical, functional centers to a "connectomic" or "hodological' organization,3 to preserve subcortical, white matter integrity. Currently, DTI is utilized in many academic centers as it requires sophisticated post-processing and may not be readily available in the community. The current paper focuses on this obstacle to widespread integration of DTI into universal neurosurgical practice. The anatomically depicted tracts are validated intraoperatively with direct cortical and subcortical stimulation, which is still the gold standard for mapping, but the DTI can guide the surgeon to the specific fiber tract. In order to facilitate post-processing, instead of using a radiologist, a neurosurgeon, or a neuroscience "expert" (often a PhD), the supplier of the software (e.g., Medtronic [StealthVizTM]) would identify the clinically relevant fiber tracks for hospitals lacking such an expert.

What is needed is a simple, practical, universal method that can produce reproducible maps of the key fiber tracts: arcuate fasciculus/ SLF (language); corticospinal tract (motor) and optic radiations (vision). The current manual, deterministic, operator-dependent method can be time-consuming, and depends on the operators knowledge of anatomy, experience, robustness of the software, and the specific settings for FA and fiber length among a wide range of variation. One method to greatly reduce the planning time is to use a constant FA threshold and fiber length constant to eliminate "noise" and identify the key fiber tracts.⁴ Advancements in software (Brainlab; DynaSuite; Medtronic; DTI Studio) have made the current iterations of software more userfriendly. Using a commercially available software package, the neurosurgeon can obtain a DTI "on the fly" in a few minutes. Such an approach is individualized, yet prone to artifacts, and lacks standardization.

Potential confounding variables that affect DTI include anatomic variations, overlap and with other tracts, vasogenic edema, and tumor infiltration.⁵ Ideally, the next iteration of software for neuronavigation would include a standardized map of key white matter tracts, and would adapt the individual patient's altered tracts based on a common platform, much like a GPS device in a car navigation uses a Google or a MapQuest background map. Advanced imaging with HARDI (high angular resolution diffusion-weighted imaging) tractography also

provides a more accurate portrayal of the white matter tracts; such a fiber bundle atlas with a clustering, probabilistic approach, termed Adaptive Clustering is being developed.⁶ Currently, there is a variation in accuracy among the different manufacturers of DTI software.⁷

The current work, using the Medtronic (StealthVizTM) system provides a nice, instructional movie on the steps necessary to manually display key fiber tracts. The authors propose that for non-academic centers, the processing can be performed by a company representative without the need for the surgeon to invest time in learning the steps, or to hire a technical person in the hospital budget. Such "outsourcing" might make economic sense, but it would be better in my view, if the modern surgeon was familiar with white matter anatomy,^{8,9} and adapt the use of DTI much as he/she would any surgical tool. The extra time for preparing a DTI map should be recognized by a CMS-CPT code, which would also facilitate the widespread adaptation of DTI.

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- Abdullah KG, Lubelski D, Nucifora PG, Brem S. Use of diffusion tensor imaging in glioma resection. *Neurosurg Focus*. 2013;34:E1, doi: 10.317/2013.
- Brem S, Meyers CA, Palmer G, Booth-Jones M, Jain S, Ewend MG. Preservation of neurocognitive function and local control of one to three brain metastases treated with surgery and carmustine wafers, Cancer. 2013;119:3830-3838
- De Benedictis A, Duffau H. Brain hodotopy: from esoteric concept to practical surgical applications. *Neurosurgery*. 2011;68:1709-1723.
- Jain S, Brem S. Method to rapidly visualize essential neural pathways using fractional anisotropy (FA) threshold and fiber length (FL) constants for surgical planning and intraoperative, computer-assisted, 3-dimensional tracking (US Patent # 8788015), issued 7/22/2014).
- Stadlbauer A, Nimsky C, Buslei R, et al. Diffusion tensor imaging and optimized fiber tracking in glioma patients: Histopathological evaluation of tumor-invaded white matter structures. *NeuroImage*. 2007;34:949-956.
- Tunç B, Parker WA, Ingalhalikar M, Verma R. automated tract extraction via atlas based Adaptive Clustering. *Neuroimage*. 2014;102:596-607.
- Feigl GC, Hiergeist W, Fellner C, et al. Magnetic resonance imaging diffusion tensor tractography: evaluation of anatomic accuracy of different fiber tracking software packages. *World Neurosurg.* 2014;81:144-150.
- Catani M, Thiebaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex*. 2008;44:1105-1132.
- Yagmurlu K, Vlasak AL, Rhoton AL Jr. Three-dimensional topographic fiber tract anatomy of the cerebrum. *Operative Neurosurg*, 2015;11:274-305.