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Comparison of Compressed Sensing Diffusion Spectrum Imaging and Diffusion Tensor Imaging in Patients with Intracranial Masses

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Abstract

Purpose—To compare compressed diffusion spectrum imaging (CS-DSI) with diffusion tensor imaging (DTI) in patients with intracranial masses. We hypothesized that CS-DSI would provide superior visualization of the motor and language tracts.

Materials and Methods—We retrospectively analyzed 25 consecutive patients with intracranial masses who underwent DTI and CS-DSI for preoperative planning. Directionally-encoded anisotropy maps, and streamline hand corticospinal motor tracts and arcuate fasciculus language tracts were graded according to a 3-point scale. Tract counts, anisotropy, and lengths were also calculated. Comparisons were made using exact marginal homogeneity, McNemar's and Wilcoxon signed-rank tests.

Results—Readers preferred the CS-DSI over DTI anisotropy maps in 92% of the cases, and the CS-DSI over DTI tracts in 84%. The motor tracts were graded as excellent in 80% of cases for CS-DSI versus 52% for DTI; 58% of the motor tracts graded as acceptable in DTI were graded as excellent in CS-DSI ($p=0.02$). The language tracts were graded as excellent in 68% for CS-DSI versus none for DTI; 78% of the language tracts graded as acceptable by DTI were graded as excellent by CS-DSI ($p<0.001$). CS-DSI demonstrated smaller normalized mean differences than DTI for motor tract counts, anisotropy and language tract counts ($p=0.01$).

Conclusion—CS-DSI was preferred over DTI for the evaluation of motor and language white matter tracts in patients with intracranial masses. Results suggest that CS-DSI may be more useful than DTI for preoperative planning purposes.

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Keywords

diffusion tensor imaging; compressed-sensing; diffusion spectrum imaging

Introduction

Diffusion tensor imaging (DTI) is an MRI technique that non-invasively provides *in vivo* information about white matter diffusion and microstructure. DTI based tractography has been shown to be useful in localizing white matter tracts in 3D space to guide brain tumor surgery.(1-3) The technique is limited when encountering crossing fibers and complex fiber tract courses,(4) however, because the simplified single-direction model may inaccurately model anisotropy in the presence of multiple tract directionalities. In addition, tumor-related mass effect and/or edema may reduce anisotropy and limit characterization of complex neuroanatomy. There is a need to resolve multiple fiber directionalities per voxel to generate more accurate tractography maps of white matter tracts, especially in patients with brain tumors.

Diffusion spectrum imaging (DSI) is a higher-order diffusion technique capable of resolving crossing fibers.(5-7) These higher-order techniques have demonstrated improved tract density and white matter mapping in the presence of brain tumors.(8-10) Implementation of such techniques into routine clinical care, however, has been hampered by: (1) long scan times required and (2) reduced signal-to-noise (SNR) resulting from longer echo times (TE) as larger diffusion-encoding gradients waveforms are needed than for conventional DTI (diffusion-encoding b-values typically 2,000-10,000 sec/mm² as compared to the DTI at 1,000 sec/mm²). DSI is capable of relating fiber distribution to the diffusion signal but requires the longest scan time and the longest TE among these advanced diffusion techniques. And although the advent of parallel-imaging using simultaneous multi-slice methods can provide scan time reductions with small SNR penalty,(10,11) such methods require high-channel-count (>16) receiver-coils that may not be widely available. Therefore, an accelerated DSI acquisition may provide a model-free way for accurate white matter mapping within clinically-feasible scan times.

Compressed-sensing (CS) is a recently proposed technique relying on sparse data acquisition and reconstruction.(12,13) CS-DSI provides four-fold or higher accelerations to reduce scan times. Despite its purported advantages, however, there have been no comparisons of CS-DSI versus DTI in mapping the white matter. The purpose of this study was to directly compare CS-DSI against DTI and to quantify the differences in the derived data. Furthermore, these comparisons were performed in patients with brain masses to evaluate the visualization of white matter tracts and its potential clinical utility for surgical planning. We hypothesized that the CS-DSI would provide superior visualization of the primary motor and language tracts.

Materials and Methods

This study was performed in complete compliance with all Health Insurance Portability and Accountability Act regulations. A waiver of informed consent was obtained from the local Institutional Review and Privacy Boards.

Patients

We retrospectively analyzed 25 consecutive patients (cases) with intracranial masses who underwent DTI and CS-DSI for preoperative planning between September 2013 and November 2014. The median age was 49.7 years (range=25.9-86.5), with more males (n=16, 64%) than females (n=9). Cases underwent maximal safe resection as per the treating neurosurgeon (subtotal resection [n=13, 52%], gross total resection [n=11, 44%], or biopsy [n=1, 4%]). There were more left-sided masses (n=17, 77.3%) than right-sided masses (n=8). Pathology revealed 14 high-grade gliomas (glioblastoma, n=7; anaplastic astrocytoma, n=4; anaplastic oligodendroglioma, n=3), 7 low-grade gliomas (low-grade astrocytoma, n=3; low-grade oligodendroglioma, n=2; low-grade oligoastrocytoma, n=2), and 4 other (metastasis, n=2; meningioma, n=1; radiation necrosis, n=1).

MRI Including DTI Acquisition

Using a 3T MR750 (n=19) or MR750w (n=6) scanner (GE Healthcare, Milwaukee, WI, USA) and a Geometry Embracing Method Head and Neck Unit (GEM HNU) 24-channel neurovascular head coil, whole-brain MRI was performed 48 hours before surgery. DTI was acquired with number of T₂ images=1, non-collinear directions=25, TE=82.3-87.7ms (mean, 86.7ms), repetition time (TR)=6.5-13.0s (mean, 9.1s), b=1,000s/mm², matrix=128×128, field-of-view=19.8-21.6cm, slice thickness=3mm, number of excitations=1, number of slices=36-44 (mean, 42), and scan time=2.8-5.6min (mean, 4.0min). In-plane parallel imaging (ASSET=2) was applied to reduce distortion in the phase-encoding direction. Standard clinical sequences included sagittal and axial T1-weighted images; axial FLAIR, T2-weighted, diffusion-weighted, and susceptibility-weighted images; and contrast-enhanced coronal, sagittal, and axial T1-weighted images.

CS-DSI Acquisition and Theory

CS-DSI was acquired with the same spatial resolution using 127 (n=10, R acceleration=4, 1+127=128 q-space points) or 102 (n=15, R acceleration=5, 1+102=103 q-space points) directions, b=6,000-9,375s/mm², TE=102.6-117.3ms (mean, 109.6ms), TR=4.0-9.0s (mean, 6.6s), number of slices=27-52 (mean, 41), scan time=8.5-15min (mean, 12.0min). As compared to CS approaches in MRI that undersample k-space,(14) CS in DSI works by acquiring a randomly undersampled diffusion signal (also known as q-space) and reconstructing the missing data based on the sparsity assumption in a transform space.(15) This CS processing occurs after image reconstruction in image space (via parallel imaging and coil combination default on the MRI scanner). The q-space is an 11-cube Cartesian grid, which has 515 q-space points circumscribed on a unit sphere, for which only 127 (acceleration=4) or 102 (acceleration=5) points had been randomly sampled and the remaining points are missing. CS reconstructs the missing points to fill up the 11-cube Cartesian grid. Similar to k-space sampling, q-space sampling with DSI relies on the Fourier

transform properties to relate q-space to the diffusion propagator, which is used in turn to determine the orientation distribution function (ODF). As described in more detail by Menzel et al.,(15) we applied iterative soft-thresholding with a fast converging Nesterov-type updating scheme to minimize the sum of data consistency term, total variation, and wavelet terms (Symlets) to impose data sparsity constraints. Supplemental Figure 1 illustrates how CS-DSI works, whereby the acceleration factor is inversely proportional to the number of random q-space points sampled.

DTI and CS-DSI Analysis

Head motion and eddy current corrections were performed by means of rigid and linear image registration of each diffusion volume to the non-diffusion-encoded image (also known as the T₂ image) using Elastix (Stefan Klein and Marius Staring, Elastix, <http://elastix.isi.uu.nl/>).(16) DTI and CS-DSI analysis were performed using custom software written in Matlab (Mathworks, Natick, MA, USA).(15,17) The output included the DTI fractional anisotropy (FA) and directionally-encoded color FA (color FA) maps, and the corresponding CS-DSI multidirectional anisotropy (MDA) and directionally-encoded color MDA (color MDA) maps.(18) MDA is analytically equivalent to FA in single-direction Gaussian diffusion but can provide values that better reflect the underlying anisotropy of constituent fibers in voxels containing multi-directional fiber bundles. Streamline tractography was performed for both DTI and CS-DSI according to the fiber assignment by continuous tracking (FACT) method.(19) In order to provide consistency in evaluating the fiber tracts for both DTI and CS-DSI, the angle threshold was set to <38° and the mask was set to an anisotropy threshold of <0.15. The total post-processing time for CS-DSI analysis was about 2 hours (compared to 35 minutes for DTI) on a 12-node Pentium computer with 24 GB RAM, with CS reconstruction taking most of the time.

Tract seeding

DTI and CS-DSI maps and tracts were saved in Nifti format before loading onto a Windows 7 (Microsoft Corp, Redmond, WA) workstation running TrackVis 0.6 (Ruopeng Wang and Van Wedeen, Massachusetts General Hospital, Boston, MA). The tracts were calculated for the whole brain, and TrackVis used as a visualization tool to display on the tracts coursing through the seed spheres. A single experienced operator (a board certified radiologist with a Certificate of Added Qualification in Neuroradiology and >15 years experience in functional imaging) manually placed all seeds in a standard manner (20,21) according to anatomic landmarks on the color FA/MDA maps and the anatomical images including fluid attenuation inversion recovery (FLAIR) and contrast T1-weighted images. For the motor corticospinal tract, spherical seed regions-of-interest (ROIs) were placed in blue (superior-inferior orientated) color FA/MDA voxels in the hand portion of the primary motor cortex identified by the reverse omega sign in the precentral gyrus and in the mid pons.(22) For the language arcuate fasciculus tract, two seeds were placed in the green (anterior posterior oriented) color FA/MDA voxels in the main body of the superior longitudinal fasciculus (SLF) containing all 4 portions of the SLF in the corona radiata located lateral to the descending corticospinal tracts, and a third seed was placed in the blue descending portion of SLF-IV (representing the arcuate fasciculus) along the posterior margin of the sylvian fissure. To minimize potential bias, seeds were fixed at 8 mm diameter spheres and placed in

a random order for each case and only 2-3 seeds were applied per tract using the “and” function (as the “not” function is more susceptible to operator manipulation).

For quantitative and qualitative analyses, the motor and language tracts were reconstructed and labeled as abnormal (ipsilateral to mass) and normal (contralateral to mass). When available (n=14), functional MRI (fMRI) was also used to guide the seeding and confirm reconstructed tracts (*Supplemental Methods*); although helpful, fMRI driven seeding has not demonstrated consistent superiority to anatomic driven seeding.(22,23)

Qualitative Analyses

Two expert readers (radiologists holding Certificates of Added Qualification in Neuroradiology with >18 and >20 years of experience in functional imaging) visually examined the DTI and CS-DSI results over a 2-week period. The results were displayed in TrackVis with the readers being given full interactive control and ability to scroll through the results on 2D images displayed in all 3 orthogonal planes and on 3D images.

The color FA/MDA maps were presented side-by-side and graded as follows: 0=no difference, 1=DTI (FA) superior and 2=CS-DSI (MDA) superior. The readers were blinded to the origin of each imaging data set, and the DTI and CS-DSI maps were presented in a random order to discourage any bias. Disagreements were resolved by consensus.

The motor and language tracts were then overlaid on the 2D and 3D anatomical images and graded using a 3-point scale as: 0=poor, 1=acceptable, and 2=excellent. The readers were asked to assign grades by evaluating the expected anatomy, course of the streamlines, number of streamlines, and number of erroneous streamlines. For language tracts, grades also incorporated the anterior-most extension of the arcuate fasciculus towards Broca's area. (24,25) Readers also graded overall preference for the DTI and CS-DSI tracts as 0=no difference, 1=DTI superior and 2=CS-DSI superior.

Quantitative Analyses

The tract counts (total streamlines per tract) were counted for the motor and language tracts. Language tract lengths were also calculated, because the arcuate fasciculus has a C-shaped, predominantly anterior-posterior course, and because the anterior-most fibers to Broca's area may be truncated by crossing motor fibers.(24) Motor tract lengths were not recorded, as after a slightly inferior medial course into the corona radiata, these have a predominantly superior-inferior course where measurement of length may be skewed by the z-axis coverage of the brain. (DTI had a greater number of slices due to time constraints for the CS-DSI). We also quantified anisotropy by measuring whole tract FA and MDA, and stratified findings by proximity to the enhancing and/or nonenhancing lesions as ≤ 1 cm or >1 cm. For all quantitative metrics, the normalized difference ΔM for each metric M was calculated as

$$\Delta M = \frac{M_{\text{normal}} - M_{\text{tumor}}}{M_{\text{normal}}}.$$

Statistical Analysis

Comparisons between expert reader grades were made using exact marginal homogeneity and McNemar's tests (Cytel Studio StatXact version 10.0, Cytel Software Corporation, Cambridge, MA). Comparisons between DTI and CS-DSI metrics were made using Wilcoxon signed-rank tests (using R version 3.1.2, <http://CRAN.R-project.org>). Significance level was set to 0.05. To adjust for multiple comparisons when examining the 5 quantitative metrics in each group, we applied the Bonferroni method ($p=0.05/5$) to declare $p<0.01$ as statistically significant.

Results

Qualitative Analyses

When comparing the color FA and the color MDA maps, the readers preferred the color MDA maps in 92% of the cases with a mean grade of 1.9. The readers preferred the FA maps in one case (4%) and had no preference in one other case (4%). An illustrative case is shown in Figure 1.

The motor and language tractography results are summarized in Table 1 and illustrative cases are shown in Figures 2-4. The readers preferred CS-DSI in 84% of the cases. The readers preferred tracts generated by DTI in two cases (8%) and had no preference in two cases (8%). Fewer erroneous or false positive tracts (tracts that did not conform to the tract of interest based on the reader's experience and anatomic landmarks) were specifically cited by both readers as an advantage of CS-DSI.

The motor tracts were graded as excellent in 80% of cases for CS-DSI versus 52% for DTI; 58% (7/12) of the motor tracts graded as acceptable in DTI were graded as excellent in CS-DSI ($p=0.02$). The language tracts were graded as excellent in 68% for CS-DSI versus none for DTI; 78% (11/14) of the language tracts graded as acceptable by DTI were graded as excellent by CS-DSI ($p<0.001$). The language tracts were graded as excellent in 68% (17/25) cases or acceptable in 32% (8/25) cases for CS-DSI, as compared to acceptable in 56% (14/25) cases or poor in 44% (11/25) cases for DTI ($p<0.01$). Eighty-eight percent (22/25) of the language tracts were rated as superior in CS-DSI as compared to DTI.

Quantitative Results

The results are summarized in Tables 2-4. CS-DSI demonstrated smaller normalized mean differences than DTI for motor tract counts (0.18 versus 0.42, $p=0.008$), anisotropy (0.02 versus 0.03, $p=0.01$), and language tract counts (0.12 versus 0.43, $p<0.001$). When stratified by proximity to the enhancing tumor and/or nonenhancing peritumoral abnormality, the normalized mean difference remained smaller for the CS-DSI than the DTI motor tract counts (0.28 versus 0.54, $p=0.003$) and language tract counts (0.18 versus 0.55, $p=0.01$) 1cm away, but it was not significant for tracts >1 cm away ($p>0.03$).

Discussion

In this study, qualitative and quantitative results show preference for CS-DSI rather than DTI for the evaluation of white matter tracts in patients with intracranial masses. These results

suggest that CS-DSI may be more useful for preoperative planning purposes than standard DTI.

DSI is an advanced diffusion technique with Cartesian sampling of q-space. Previous applications have required much longer scan times (typically 1-2 hours) that render it impractical for clinical applications. Compressed sensing acceleration allows DSI acquisition within 15 minutes as demonstrated in this study, using data sparsity in the transform domain to reconstruct the sub-Nyquist sampled q-space, and in turn to compute white matter pathways to resolve fiber-crossing regions. Although CS-DSI still requires three-fold longer scan times than DTI, further scan time reductions may be provided by future application of simultaneous multi-slice acquisition (26) not utilized in this study. Moreover, the multiple b-values utilized in CS-DSI may also provide additional quantitative metrics to enable tumor segmentation and heterogeneity evaluation such as neurite density and kurtosis (27,28) unavailable with single b-value DTI.

Intracranial masses and/or adjacent edema are known to adversely affect adjacent tractography results,(29-31) usually resulting in premature termination of tracts due to loss of anisotropy. Because CS-DSI derived MDA maps provide superior discrimination of the underlying anisotropy values,(18) CS-DSI tractography should allow for superior propagation of the streamlines in areas where the calculated anisotropy is decreased due to complex brain anatomy and/or tumor-related compromise. Our results support this hypothesis, as we found smaller normalized differences using CS-DSI as compared to DTI - indicating that tumor-side tract counts were more equivalent to (or less decreased from) the normal-side tract counts.

Qualitative results revealed that 58% (7/12) of the motor tracts rated as acceptable in DTI were upgraded to excellent in CS-DSI; and that 68% (17/25) of the language tracts rated as poor or acceptable by DTI were upgraded to excellent in CS-DSI. These grades reflect reader preference for CS-DSI in areas near the tumor, where DTI was more likely to display false negative results with prematurely terminated results due to tumor-related loss of anisotropy and/or underlying complex fiber anatomy. In addition, both readers commented that more erroneous tracts were consistently present in DTI than in CS-DSI. False positive tractography results are problematic as they may lead to errors in interpretation and in turn to potential surgical avoidance of spurious tracts and suboptimal extent of tumor resection. Our methodology used a simple 2-3 “and” seed tractography technique, where erroneous tracts could be edited indirectly only by adjusting the “and” seed locations, rather than placing additional “and” or “not” seeds to exclude the stray tracts. We advocate this approach because there are fewer opportunities for excessive operator manipulation of the tractography results. We also did not attempt to manipulate the tractography results altering the default minimum anisotropy, turning angle or fiber lengths.

A major constraint in the development of tractography has been the lack of validation. Several studies have described good correlations between DTI results and intraoperative electrical stimulation.(20,21,32-34) The largest of these, by Bello et al.,(20) described DTI as concordant with stimulation in 87.2% (157/180) corticospinal tract cases and in 100% (141/141) arcuate fasciculus cases. When measuring the distance between the subcortical

white matter stimulation site and edges of four different tractography algorithms, Bucci et al. (29) described median offset distances of <1cm (range, 0.5-0.9cm). While white matter stimulation remains the gold standard for tractography in terms of localization and evaluation of tracts, it will be of interest to supplant invasive stimulation with non-invasive white matter mapping with diffusion tractography. White matter stimulation can only be performed in the surgically accessible, usually subcortical, white matter, and it requires high amounts of current (higher than necessary for cortical stimulation) that may induce seizures. Furthermore, negative stimulation results are difficult to interpret because they may represent a true negative where the tract is properly stimulated but not functional, or a false negative where stimulation is performed in the wrong location or excessive sedation is present. Therefore, non-invasive white matter imaging will likely remain a critically important step for treatment planning in patients with intracranial tumors near eloquent brain regions.

Several potential limitations were encountered. First, tractography results are highly variable depending on the software application and operator experience. We attempted to control for both of these variables by using a single software package for streamline tractography and having a single expert operator uninvolved in grading place all the seeds; visual assessment by expert readers is an accepted albeit imperfect non-invasive evaluation technique.(35,36) Second, CS-DSI has an inherent signal-to-noise (SNR) advantage over DTI due to the longer acquisition and greater number of diffusion directions (5-6-fold greater). Our intention was to compare the clinically feasible state-of-the-art CS-DSI sequence against our routine DTI sequence, however, rather than against a non-standard DTI sequence with much longer scan time to match the CS-DSI scan time. Comparing SNR equivalent DTI scans using longer acquisition times is an area of potential future study. Third, because our study was retrospective, we did not have the opportunity to evaluate potential changes in neurosurgical decisions or validate our results through white matter stimulations. Instead, we chose to directly compare the output maps and tracts and examine the accuracy of the data as determined by expert readers and confirmed by quantitative data.

In conclusion, these results suggest that DSI acquisition in clinically feasible times using compressed sensing is superior to DTI for motor and language tract visualization in patients with intracranial masses. Future projects will aim to further reduce CS-DSI scan times and improve processing times through semi-automated tractography seeding efforts. A prospective trial is underway to examine the effect of CS-DSI on neurosurgeon decision making when planning and performing brain surgeries.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Axial (A, C) and coronal (B, D) directionally-encoded color multidirectional anisotropy (color MDA) (A, B) and color fractional anisotropy (color FA) (C, D) maps in a patient with a large left glioblastoma. The color MDA maps demonstrate superior illustration of anisotropy (encoded as brightness) and orientation (encoded in RGB colors) in the tumor affected areas, including the blue corticospinal tract and green superior longitudinal fasciculus voxels.

Figure 2.

CS-DSI (A, B) and DTI (C, D) generated corticospinal tracts (green, CS-DSI; red, DTI) and in a patient with a right frontal lobe anaplastic oligodendroglioma overlaid on coronal (A, C, E) and sagittal (B, D) contrast 3D T1-weighted images. While both CS-DSI and DTI right corticospinal tracts are displaced posteriorly by the large tumor, CS-DSI reconstructed fibers are closer to the posterior margin of the mass than does DTI. Both travel superiorly into the precentral gyrus. The CS-DSI (green) and DTI (red) generated tracts overlaid together (E) demonstrate that while the results are similar, the DTI tracts have straighter and more medial courses below the tumor in the corona radiata.

Figure 3.

CS-DSI tractography overlaid on color MDA maps (A-D) shows truncation of the arcuate fasciculus (B) as it reaches the posterior margin of the enhancing radiation necrosis from treated malignant melanoma. Mid (C) and posterior (D) coronal images show the arcuate fasciculus tract posterior to the necrosis but absent at the plane of the necrosis. Corresponding DTI tractography overlaid on color FA maps (E-H) images demonstrate a thin arcuate fasciculus that stops short of the posterior margin of the radiation necrosis (F).

Figure 4. Tractography of the arcuate fasciculus overlaid on sagittal color MDA (A) and FA (B) maps in a patient with an anaplastic oligodendroglioma in the posterior frontal lobe (not shown).

While both tracts have similar courses and lengths, DTI (B) demonstrates more extraneous fibers extending into the frontal, parietal and temporal lobes.

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Table 1

Distribution of grades assigned for the motor and language tracts.

		DTI		p-value
Hand corticospinal		Poor	Acceptable	Excellent
CS-DSI	Poor	0	0	0
	Acceptable	0	5	0
	Excellent	0	7	13
Arcuate fasciculus		Poor	Acceptable	Excellent
CS-DSI	Poor	0	0	0
	Acceptable	5	3	0
	Excellent	6	11	0

* Statistically significant

Table 2

Comparison of CS-DSI versus DTI for all patients.

Measurement	Normalized Difference	Median (Range)		p-value
		CS-DSI	DTI	
Motor hand				
	Mean tract count	0.18 (-0.18, 0.89)	0.42 (-0.04, 0.97)	0.008 *
	Mean MDA or mean FA	0.02 (-0.08, 0.34)	0.03 (-0.09, 0.42)	0.01 *
Arcuate fasciculus				
	Mean tract count	0.12 (-0.92, 0.76)	0.43 (-0.25, 0.92)	<0.001 *
	Mean MDA or mean FA	-0.00 (-0.08, 0.39)	0.02 (-0.12, 0.45)	0.22
	Mean length	0.06 (-0.26, 0.75)	0.11 (-0.13, 0.90)	0.11

MDA=multidirectional anisotropy (from CS-DSI); FA=fractional anisotropy (from DTI)

* Significant after correcting for multiple comparisons

Table 3

Comparison stratified by patients with tumor and/or edema 1 cm versus >1 cm from the corticospinal tract.

Mean Normalized Difference	Median (range)		p-value
	CS-DSI	DTI	
1 cm separation (n= 11)			
Tract count	0.28 (-0.18, 0.89)	0.54 (0.25, 0.97)	0.003 *
MDA vs FA	0.06 (-0.08, 0.34)	0.08 (-0.05, 0.42)	0.054
>1 cm separation (n=14)			
Tract count	0.16 (-0.09, 0.79)	0.35 (-0.04, 0.88)	0.63
MDA vs FA	-0.01 (-0.07, 0.10)	0.02 (-0.09, 0.17)	0.15

* Significant after correcting for multiple comparisons

Table 4

Comparison stratified by patients with tumor and/or edema 1 cm versus >1 cm from the arcuate fasciculus.

Mean Normalized Difference	Median (range)		p-value
	CS-DSI	DTI	
1 cm separation (n=10)			
Tract count	0.18 (-0.92, 0.76)	0.55 (0.27, 0.92)	0.01 *
MDA vs FA	0.05 (-0.00, 0.39)	0.07 (-0.10, 0.45)	0.70
Tract length	-0.01 (-0.18, 0.75)	0.14 (-0.06, 0.90)	0.03
>1 cm separation (n=15)			
Tract count	-0.02 (-0.18, 0.53)	0.32 (-0.25, 0.72)	0.04
MDA vs FA	-0.03 (-0.08, 0.05)	0.00 (-0.12, 0.14)	0.25
Tract length	0.11 (-0.26, 0.35)	0.09 (-0.13, 0.42)	0.98

* Significant after correcting for multiple comparisons