

FIBER-TRACKING THROUGH MULTIPLE SCLEROSIS LESIONS USING PROBABILISTIC TRACKING

A. B. Pine¹, S. Jones², M. Lowe², K. Sakaie³, and M. Philips²

¹Cleveland Clinic Lerner College of Medicine, Cleveland, OH, United States, ²Radiology, Cleveland Clinic Foundation, Cleveland, OH, United States,

³Department of Radiology, Cleveland Clinic Foundation, Cleveland, OH, United States

INTRODUCTION Multiple sclerosis (MS) is a condition characterized by progressive demyelination of axons and loss of white matter (WM) integrity in the CNS. Brain injury in MS patients includes both inflammatory and demyelinating changes that range from lesions that do not cause overt loss of function to those that result in complete transection of axons, long-term axonal degeneration, and thus severe functional deficits. Such deficits are pathway-specific inasmuch that function in connected brain regions and degree of such connectivity is compromised following disruption of individual WM pathways. It is of interest, therefore, to develop highly sensitive pathway-specific markers of MS disease progression, and use them to evaluate axonal integrity of fibers that propagate through MS lesions. Diffusion tensor imaging (DTI) is widely used for localization of individual WM pathways. Even though DTI methods are sensitive to detection of acute and chronic MS lesions and the lesion burden in normal appearing white matter (NAWM), the quantification of pathway-specific axonal damage depends on the ability of such methods to track the entire length of fibers as they propagate through the lesions. Traditional deterministic methods use the MR signal that encodes the directionality of water diffusion to construct a diffusion tensor, which in turn describes the vector of the preferentially oriented diffusion of water in each location throughout the brain. Once obtained, the direction of such a vector is deterministically integrated along these directions to produce a line. Although this line often mimics the actual directions of axonal fibers, it only maps the direction of maximal diffusion. While this technique is conceptually straightforward and may work well for large fiber bundles in normal brain tissue, it is unstable and often breaks down when it experiences crossing fibers or a region of low anisotropy, leading to inaccurate estimation of tracking, or failure to identify tracks at all. The effect of MS lesions is likely to be similar, since the effect of a lesion is inflammatory in nature increasing isotropy of water diffusion. **Deterministic methods are thus poorly suited to track through lesions.** In contrast, **probabilistic tracking, when combined with non-tensor fiber orientation distribution estimation methods**, can avoid such pitfalls. It is hypothesized that methods utilizing probabilistic tracking are capable of propagating tracks through such isotropic anomalies as MS lesions. **This study specifically aimed to validate probabilistic tracking as a reliable tool that allows fiber tracing to propagate through MS lesions.** Additionally, driven by the overall goal to characterize WM integrity in MS patients, this work has begun applying this method to quantitatively evaluate diffusion parameters of fiber tracks that traverse MS lesions.

MATERIALS AND METHODS Patients were selected from a cohort of MS patients followed at the Cleveland Clinic's Mellen Center, whose T_2 and FLAIR images showed a well-defined MS lesions along one corticospinal track (CST) but no lesion along the contralateral CST. Whole brain DWI data was acquired with high angular resolution (71 directions) on a Siemens TIM Trio 3T MRI scanner equipped with a 12-channel receive-only head array. Fiber orientation at each voxel was estimated using spherical deconvolution combined with regularization optimized by generalized cross validation [Sakaie]. Seed and target regions were designated for probabilistic tracking, with each step determined by rejection sampling [Tournier]. The number of tracks intersecting a given voxel reflected the connectivity between that voxel and the seed/target regions. The following **three-phase methodology** was applied: The seed region was initially placed on the lesion with the entire pial surface selected as a target. Subsequent tracking generally revealed two predominant tracks, connecting the lesion to the pial surface and to the cerebral peduncle. These locations formed the seed and target for the second step, and subsequent tracking was observed to approximate the lesion. The seed and target was then adjusted to ensure the track propagates through the lesion. In the last step, contralateral CST tracks were computed using homologous targets and seeds on the contralateral side. These contralateral CST tracks served as the control tracks. Finally, whole brain diffusion tensor maps of fractional anisotropy, mean diffusivity, longitudinal diffusivity, and transverse diffusivity were calculated by first least-squares fitting the 71 acquired diffusion profiles to each of the six independent tensor elements, and then calculating the corresponding tensor based values. Convolution of these maps with tracks provided track-specific characteristics such as diffusivity and FA in order to evaluate track-specific damage.

RESULTS AND DISCUSSION The propagation of fiber tracks through the MS lesion is qualitatively shown in the Figure 1. An overlay of voxels that represent fibers crossing the MS lesion is superimposed on the lesion itself, indicating a good match. As an example of a quantitative measure of the through-lesion tracking, the number of voxels that represent fibers propagating through the lesion (Figure 2, red diamonds) is compared to the number of voxels that represent fibers traversing through the homologous lesion-free region in the contralateral hemisphere (blue squares). As shown, the two curves are similar throughout the tracks including the region of the lesion (slices 33-38), thus suggesting that the lesion does not significantly alter the tracking trajectory as might be expected in case of termination or deflection of the fibers near the lesion. Figure 3 is an example of the behavior of transverse diffusivities for the tracks that propagate through the lesion (red squares, slices 33-38) and those that propagate through the homologous region in the contralateral hemisphere (blue diamonds). It shows that transverse diffusivity is elevated in the vicinity of the lesion possibly indicating demyelination. The smaller peak (slices 10-13) shows elevation of the transverse diffusivity due to passing through crossing fibers.



FIGURE 1

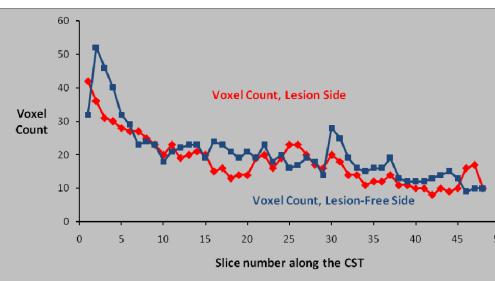


FIGURE 2

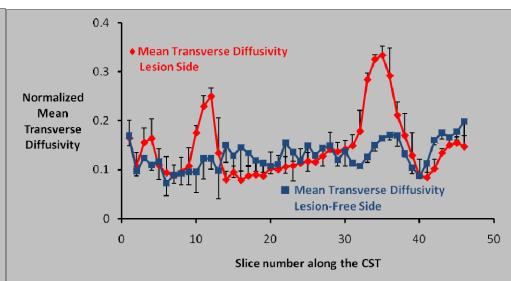


FIGURE 3

CONCLUSIONS This study demonstrated robustness of probabilistic tracking in propagating fiber through such regions of reduced anisotropy as MS lesions. Therefore, using probabilistic methods, the integrity of white matter fibers along their entire length can be interrogated even if they traverse such anomalous regions. This study also demonstrates that with the trajectory of through-lesion fibers identified, clinically relevant parameters of white matter integrity can be easily evaluated quantitatively.

REFERENCES

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