SMRT – ISMRM Forum: DTI: Is it ready for the clinic?

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Over the past 20 years diffusion MRI has become an established technique used in both research and clinical settings. In short, diffusion weighted imaging (DWI) is a technique sensitive to the random motion of water molecules in tissue and is to date, the only non-invasive method capable of probing tissue microstructure *in vivo*. Diffusion imaging is commonly used in conventional radiological image interpretation to aid in the diagnosis and management of neurological disorders, such as hyperacute stroke as it has proven to be a highly sensitive indicator of likely irreversible tissue damage due to cytotoxic oedema. Quantitative parameters derived from the diffusion tensor (DTI), principally apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps, have also provided insight into conditions such as multiple sclerosis, schizophrenia, and vascular dementia [1].

Diffusion-based fibre tracking (tractography), the practice of identifying the path of white matter fibre tracts from diffusion weighted MRI signal, requires three essential steps. First the acquisition of appropriate data, second the correct estimation of fibre orientations, and finally the application of an appropriate tracking algorithm. The reliability of tractography results is dependent on all three of these steps. From a radiographers perspective it is also essential to appreciate that these steps are interdependent, i.e. data collection needs to be consistent with the tractography method intended to be used for data analysis and vice versa.

In the clinical context there are two main approaches to the tractography process, namely diffusion tensor based techniques and higher order models. In order to provide the appropriate quality of data for the purpose of tractography, it is imperative that the fundamental differences between these approaches are appreciated.

- *Data acquisition:* Currently the diffusion tensor model is the most widely used approach to extract fibre directions from diffusion data. This in large is part due to its availability to clinicians via 'push-button' tractography software packages supplied by the major manufactures of MRI equipment. Ideally, diffusion weighted data utilised for all tractography studies should be obtained with high signal-to-noise ratio, high spatial resolution and a minimum b-value of 1000 to achieve appropriate diffusion weighting. The theoretical advantage of the tensor mathematical framework is that it only requires a minimum of six directions to characterise the diffusion tensor ellipsoid [2]**,** hence such data can in theory be acquired in relatively short scan times. More recent work suggests that a minimum of twenty directions are necessary for a robust measure of anisotropy [3]**.**

- *Estimation of fibre orientations:* It is well known that such tensor based methods are fundamentally flawed. A single diffusion tensor is unable to characterise multiple fibre orientations within a single voxel [4-5], hence the technique is unable to describe the path of white matter fibres in regions where there are crossing fibres represented within a single voxel. This fundamental limitation of DTI based methods has been addressed by the development of higher order methods capable of describing multiple fibre orientations within a single voxel using 'high angular resolution diffusion weighted imaging' (HARDI) data. From a clinical perspective this requires diffusion weighted signal to be sampled more densely than for routine DTI sequences, typically more than 40 directions, resulting in longer acquisition times.

- *Tracking algorithms:* Finally, once the diffusion data are acquired and the fibre orientations have been characterised, a tractography algorithm is required to generate the white matter tracts. Algorithms most commonly used in conjunction with diffusion tensor data are generally based on the deterministic algorithms [6-7]. The limitations of deterministic algorithms have been addressed by a multitude of approaches, the most common alternatives being probabilistic methods [8-9]**.** From a post processing perspective it is important to note that all tractography algorithms require accurate fibre orientation estimates and that no algorithm can compensate for incorrect estimates.

Although many tractography methods have been proposed, at present validation of fibre tracking techniques is difficult due to the lack of an appropriate 'gold standard'. In this talk, the practical considerations of acquiring diffusion data for the purpose of tractography will be discussed. The implications of using a DTI based vs. higher order tractography methodologies [10] in the clinical setting will be illustrated using *in vivo* data. In particular the tractography results of patients undergoing clinical-research (for example, pre-surgical assessment studies) will be used to illustrate how such methods may be used appropriately and the consequence of utilising inappropriate data in the clinical setting.

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