

# Jacobs Journal of Medical Diagnosis and Medical Imaging

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Editorial

## The Feasibility of Quantifying White Matter Connectivity Using Diffusion MRI

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Received: 04-29-2015

Accepted: 05-02-2015

Published: 05-07-2015

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### Abstract

Diffusion MRI is a unique technique for non-invasively probing structural connectivity of human brains. However, quantitative estimate of white matter fibre connectivity based on diffusion MRI is not feasible due to the bias produced systematically in the process of streamlines tractogram reconstruction. SIFT (Spherical-deconvolution informed filtering of tractograms) is a newly developed methodology to tackle this issue and to provide robust and accurate quantification of structural connectivity. This should be particularly beneficial for brain research that aims to characterise and compare structural connectome of human brains.

**Keywords:** Diffusion MRI; Connectome; Structural Connectivity; Fibre Density

Diffusion-weighted (DW) magnetic resonance imaging (MRI) came into existence in the mid-80s [1] and had been extraordinarily successful during the past 30 years, particularly in MRI of the central nervous system. The driving force of diffusion imaging is to monitor natural microscopic displacements of water molecules that occur in brain tissues as part of the physical diffusion process. In other words, water molecules are used as a probe that can reveal microscopic details about tissue architecture. Its major clinical domain of application has been neurological disorders, especially for the management of patients with acute ischemic stroke. It is also rapidly becoming a standard for white matter disorders, as diffusion tensor imaging (i.e. DTI) [2] can reveal abnormalities in white matter fibre structure and provide quantitative maps of brain integrity based on diffusion anisotropy. More recently, it has been demonstrated that diffusion MRI has potential in providing direct features of tissue microstructures [3,4], or even in detecting changes in brain

regions associated with neuronal activation [5].

The utmost important feature of diffusion MRI is that it is currently the only in vivo technique capable of providing directional feature of white matter fibre and creating three-dimensional fibre connectivity map (or so-called streamlines tractogram) using fibre-tracking techniques. A number of advanced diffusion modelling methods have been proposed for accurately extracting local fibre orientation information from diffusion imaging data [6]. It has triggered tremendous expectations on exploring structural brain network in the rapidly evolving field of human connectomics [7]. This is typically achieved by construction of the connectivity matrix using streamlines tractogram in conjunction with brain parcellation scheme to provide quantitative measures of white matter connections between pairwise grey matter regions, and then followed by graph theoretical analysis of brain network characteristics [8]. This emerging methodology pro-

vides opportunities for understanding topology and physical properties of structural brain network in either healthy or disordered status.

Despite promising applications of this analysing scheme, issues regarding to quantification of structural connectome based on streamlines tractogram have been well-documented [9]. Thus, the validity of any conclusion regarding to brain network properties drawn from this approach remains ambiguous. One of the most critical issues is the fact that the number of streamlines connecting brain grey matter regions is known to be an unreliable quantitative marker of structural connectivity due to multiple confounding factors in the process of tractogram reconstruction. Therefore, it is actually inadvisable to infer structural brain network based on streamline density [9]. Since the streamlines tractogram is untrustworthy, there is considerably diversity in the way of analysing structural connectomes: Some studies omitted the biological nature of fibre connection density and adopted 'unweighted' structural networks where connections were represented in a binary fashion; and some others maintained structural connectomes weighted by streamline count whereas applying a threshold value of fibre connection number or probability to filter out some weakest connections. Although this may help to simplify structural network analysis, modifying the sparsity of structural connectome may also alter network properties and introduce additional uncertainties.

The issues relating to quantification of streamline density described above can potentially be addressed through application of an emerging technique entitled SIFT: Spherical-deconvolution informed filtering of tractograms [10]. The mechanism of SIFT imposes a model that maps a streamlines reconstruction back to the acquired diffusion imaging data, and modifies a reconstruction to improve its correspondence with the image data given this model. The number of streamlines connecting two brain regions then becomes a proportional estimate of the cross-sectional area of the white matter fibre pathway connecting those regions. The mechanism itself can also effectively reduce known bias in streamline density [10].

These novel methods (such as SIFT [11]) aim to produce globally-optimal white matter reconstructions for the construction and interrogation of the structural connectivity, and has been demonstrated to have the capability of providing robust streamline tractogram reconstruction with accurate quantitative properties, which helps to improve overall biological plausibility and accuracy of structural connectome. The combination of those advanced diffusion MRI methodologies and the well-developed graph theoretical analysis will be able to facilitate quantification of structural connectivity and relevant

application in the emerging field of brain science.

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