Talk Title: Fiber Tracking Techniques and Challenges in the Spinal Cord

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Speciality area: Diffusion Tensor Imaging

Target audience: The course is designed for clinical researchers interested in the use of Diffusion Tensor Imaging tractography for white matter mapping.

Highlights:

- DTI tractography provides non-invasive mapping of white matter fibers
- Validation of DTI tractography findings remains a challenge
- DTI tractography holds promise for clinical diagnosis and treatment of spinal cord disease and injury

Outcomes/Objectives:
This course will enable learners to:

- understand the basic principles of DTI tractography
- identify the challenges of DTI tractography in the spinal cord
- discuss the clinicial applications of DTI tractography in spinal cord disease and injury

Diffusion Tensor Imaging (DTI) tractography has opened up the possibility of studying the complex organization of white matter fibers *in-vivo*. This course presents the basic principles, current challenges and clinical applications of DTI tractography in the spinal cord.

Anatomy of the spinal cord

The spinal cord is a long cylindrical structure that lies in the vertebral canal, and extends from the foramen magnum to the lower border of the first lumbar vertebra. The structure is divided in 31 segments (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal) that correspond to the 32 pairs of spinal nerves associated with localized regions. In transverse section, the spinal cord consists of a butterfly-shaped central gray substance surrounding by a mantle of white matter. The white matter is divided into posterior, lateral, and anterior columns, each of which contain tracts related to specific functions. The posterior columns carry afferent pathways that conduct sensory impulses from the body. The lateral columns include axons that travel from the cerebral cortex to contact spinal motor neurons, also referred to as corticospinal tracts. The anterior columns carry both ascending information about pain and temperature, and descending motor information [Carpenter 1996]. Among the clinically important ascending and descending white matter tracts are the corticospinal tract, the dorsal column-medial lemniscal system, the lateral spinothalamic tract, and the spinocerebellar tracts [Kandel 2012].

Principles of Diffusion Tensor Imaging Tractography

DTI tractography provides a non-invasive window on the architecture of white matter fibers. By mapping the diffusion of water molecules along axonal bundles, the technique offers the possibility to infer non-invasively the three-dimensional trajectory of fibers *in-vivo*. In the past decade, a wide range of DTI tractography algorithms using deterministic-based and probabilitic-based approaches has been developed [Jones 2011]. Tractography techniques have been applied to a number of brain disorders which include stroke, multiple sclerosis and neurodegenerative disease [Johansen-Berg 2013]. In addition, tractography reconstructions can provide clinically relevant information on peritumoral white matter anatomy for guiding tumor resections [Golby 2011]. Still, tractography remains a challenging technology based on complex data acquisition and mathematical models that rely on many assumptions. Tractography reconstructions provide a macroscopic representation of the underlying white matter anatomy, and DTI tracts are not actual axonal fibers due to the difference in scale between the size of a voxel and the diameter of an axon. Therefore, white matter pathways identified through post processing of DTI data can be misused or misinterpreted [Jones 2012]. While the technique makes further inroads into clinical practice, the choice of the appropriate tractography method and tract selection strategy in the absence of ground truth remains a challenge. In the past decade, the scientific community has developed a series of complementary approaches to generate validation datasets to overcome the lack of practical gold standard. These approaches include the generation of synthetic and physical phantoms constructed with a known absolute ground truth, the injection of invasive tracers in animal model experiments, and the use of carbocyanine dyes in post-mortem studies on human subjects [Barbieri 2011] [Fillard 2010] [Dauguet 2006] [Seehaus 2013]. More recently, the DTI Tractography Challenge (http://dti-challenge.org) has been initiated as a working group to evaluate the performances of different tractography techniques on neurosurgical data, and to define standards to ascertain quality features for neurosurgical guidance [Pujol 2013].

Current Challenges

DTI imaging in the spinal cord poses difficulties due to the small size of the structure, physiological motion, and the heterogeneous magnetic properties of surrounding tissues [Stroman 2014]. The spinal cord is a relatively small cylindrical structure, which widens laterally in the cervical and lumbosacral enlargement. The sagittal diameter of the cervical and lumbar enlargement is about 7.5 mm and 7 mm respectively; the transverse diameter of the cervical and lumbar enlargement is 13 mm and 9 mm respectively [Ko 2004]. Therefore, high axial-plane resolution is required to reduce partial volume effects in which the signal arises from both the cord and the cerebral spinal fluid. A second difficulty in spinal cord imaging is due to physiological motion caused by cerebrospinal fluid pulsation. The cerebrospinal fluid flows down the spinal cord canal and back up to the brain with each heart beat, which causes the spinal cord to move within the spinal canal. Cardiac gating can help reducing the imaging artefacts but it increases the acquisition time, and can induce respiratory motion artefacts. A third challenge arises from the heterogeneous magnetic properties of surrounding tissues. The differences in magnetic properties between bone, soft tissues and air create local field inhomogeneities which result in image distorsion and signal loss. Several image acquisition techniques have been developed to help solve these issues. These techniques include multi-shot echo planar imaging, line scan imaging, parallel imaging and reverse gradient method [Voss 2006] [Wheeler 2002] [Robertson 2000] [Tsuchiya2008] [Maier 2005]. In addition, improved post-processing methods can provide a better distinction between grey and white matter structures [Mohammadi 2013]. As new acquisition and post-processing techniques improve the SNR and spatial resolution of the images, DTI tractography holds promise for non-invasive exploration of white matter fibers of the spinal cord.

The possibility to depict fibers displacement, deformation and interruption may provide clinically useful information for treatment planning and follow-up of spinal cord lesion.

Clinical applications

Current clinical applications of DTI tractography in the spinal cord include spinal cord compression, multiple sclerosis and arteriovenous malformations [Wheeler-Kingshott 2014]. Spinal cord compression can be caused by various pathological conditions such as tumors, degenerative changes, traumas and inflamatory processes. In patients presenting with spinal cord tumors, DTI tractography can help visualize the deformation and displacement of spinal cord tracts at the level of the lesion, which may provide useful information for the assesment of tumor resectability during surgical planning [Ducreux 2006] [Vargas 2008] [Setzer 2010]. The use of DTI tractography to assess the extent and severity of spinal tract damages in patients presenting with cervical spondylotic meylopathy has been recently investigated [Wen 2013]. Results show that tractography-based analysis could detect the microstructural difference between healthy and myelopathic spinal cord. In compression caused by traumas such as penetrating stab wounds, DTI tractography can provide visualization of injured fiber tracts at the injury zone [Vedantam 2012]. DTI tractography may also supplement conventional structural MR imaging by depicting changes in tract morphology in focal lesions of the spinal cord in multiple sclerosis patients, and at the level of the nidus in patients presenting with arterio-venous malformations [Vagas 2008][Ozanne 2008].

DTI tractography holds great promise for clinical diagnosis and treament of spinal cord disease and injury. Improvement in data acquisition combined with refinement and standardization of post-processing methods will accelerate the transfer of spinal cord DTI from research to the clinics.

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