Diffusion MR Tractography As a Tool for Surgical Planning

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KEYWORDS

• MR imaging • Diffusion tensor imaging
• Tractography • Surgical planning • Brain
• Motor tract

Diffusion MR tractography has rapidly become an important clinical tool that can delineate functionally important white matter tracts for surgical planning. One of the goals of brain surgery is to avoid damage to eloquent cortex and subcortical white matter. Diffusion tractography remains the only noninvasive method capable of segmenting the subcortical course of a white matter tract. This article reviews the technical and clinical issues surrounding presurgical diffusion tractography, including traditional diffusion tensor imaging (DTI) methods and more advanced high angular resolution diffusion imaging (HARDI) approaches, such as q-ball imaging. An overview of the presurgical DTI and q-ball tractography protocols used at our institution is also provided.

Tractography based on diffusion MR exploits the correlation between water diffusion and brain structure to delineate the course of white matter pathways.[1–5] The brain's white matter is highly organized into fasciculi comprised of densely packed axons. Axonal membranes, myelin, and other structures affect the pattern of Brownian motion of water within white matter.[6] Tractography follows a white matter tract from voxel to voxel in three dimensions by assuming that the direction of least restricted diffusion corresponds with the orientation of axons.

The quantitative assessments of tissue microstructure central to the scientific applications of diffusion MR are not directly used for presurgical tractography. Instead, the goal of presurgical tractography is simply to identify the position of eloquent pathways, such as the motor, sensory, and language tracts. The shortcomings of DTI fiber tracking have driven the development of advanced HARDI techniques to provide more accurate presurgical tractography. This article includes a description of the most recent applications of q-ball tractography, one of these HARDI methods, to surgical planning. As DTI and HARDI tractography become more widely used for patient diagnosis and treatment, it is critical for users to understand the capabilities and limitations of these techniques.

SPECTRUM OF BRAIN MAPPING TECHNIQUES

Tractography complements the information available from an array of brain mapping techniques available for surgical planning. Brain mapping techniques are differentiated by invasiveness, accuracy, and their physiologic basis. Diffusion MR is inherently noninvasive and does not, in most applications, directly detect brain function. Instead, tractography uses the diffusion of water to observe the microstructure of brain tissue, construct the gross anatomy of major white matter pathways, and then infer the trajectory of the delineated tract. Other noninvasive functional mapping techniques, such as functional MR imaging,[7–10] magnetoencephalography,[11–13] and electrocorticography,[14] observe physiologic changes associated with brain function. However, these techniques are restricted to localizing activity in the gray matter.

Cortical and subcortical electrical stimulation directly determines the function of neurons and remains the gold standard for functional mapping during neurosurgery.[15,16] Stimulation is highly invasive, however, and subcortical stimulation

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Magn Reson Imaging Clin N Am 17 (2009) 205–214
doi:10.1016/j.mric.2009.02.002
1064-9689/09/$ – see front matter

cannot be performed until the resection cavity is close to the target pathway.[17] Localization with stimulation also is subject to inaccuracies from the penetration of electrical current into surrounding tissues and variations in excitation thresholds.[18,19] In the clinical setting, it is advantageous to use more than one brain mapping technique. Independent aspects of physiology are observed with each mapping technique, and their combined results can be used to validate each other and improve the confidence of surgical planning decisions.

ROUTINE PRESURGICAL DIFFUSION TENSOR IMAGING TRACTOGRAPHY PROTOCOL

Translating DTI tractography into a useful clinical tool requires efficient integration of the technique into presurgical protocols. This section describes the presurgical DTI fiber-tracking protocol developed and routinely performed at University of California San Francisco. DTI tractography of the motor tract is prescribed for any brain tumor case with a lesion near the motor tract that involves awake or asleep intraoperative cortical stimulation mapping. The protocol involves image acquisition, post processing, quality assurance, and integration with a surgical navigation system.

DTI acquisition sequences are readily available on all commercial MR scanner platforms. The following discussion provides several general guidelines for acquiring diffusion MR data suitable for tractography; more detailed specifications can be found in a recent review.[20,21] A minimum of six diffusion gradient directions is required to calculate the diffusion tensor; however, significant improvements in data quality can be obtained by increasing the number of directions.[22] For tractography, the slices must be contiguous and should not be thicker than 3 mm. At our institution, a typical acquisition at 1.5 T on a GE scanner has TR/TE = 11 s/78 ms, 3-mm thick slices, matrix = 128 $\times$ 128, field of view = 260 $\times$ 260 mm, ASSET factor = 2, and 15 diffusion directions with two averaged acquisitions at b = 1000 s/mm^2. Total diffusion imaging time is less than 8 minutes. In addition to diffusion MR, high-resolution three-dimensional T1- and T2-weighted anatomic images are acquired for use with the surgical navigation system. The postcontrast three-dimensional T1-weighted spoiled gradient recalled and the three-dimensional T2-weighted fast spin echo volumes have voxel resolution of 1 $\times$ 1 $\times$ 1.5 mm.

DTI tractography is performed with multiple regions of interest using an algorithm based on the deterministic fiber assignment by continuous tracking method.[4] Fiber tracks are first generated from a region drawn in the cerebral peduncle with the aid of the b = 0 s/mm^2 echo planar images from the DTI sequence (**Fig. 1**A) and the postprocessed DTI anisotropy map. The starting region encompasses the entire cerebral peduncle, although the motor tract only occupies a fraction of this region. An overly large starting region reduces the potential for user-introduced error. Tractography algorithms such as the fiber assignment by continuous tracking method require a minimum anisotropy threshold to be specified for propagation of the ''streamline'' outlining the fiber trajectory. If the fiber track encounters a voxel with anisotropy below the threshold, which is usually caused by the presence of gray matter or cerebrospinal fluid, the streamline is terminated at that location. A relatively low fractional anisotropy threshold of 0.1 is used for presurgical tractography to assist in following white matter tracts through regions of edema or tumor infiltration, which exhibit low diffusion anisotropy.[23] Each voxel in the starting region is densely seeded with 27 starting points evenly arranged in a 3 $\times$ 3 $\times$ 3 grid to improve fiber tracking performance.[2]

Extraneous fiber tracks are removed through the use of multiple target regions of interest (**Fig. 1**). The fiber tracks are first targeted to a region drawn in the posterior limb of the internal capsule. Then a second target region is drawn around fiber track bundles anterior to the central sulcus within the precentral gyrus. Fiber tracks passing through all three regions are retained as the delineated pyramidal tract (See **Fig. 1**).

The echo planar images are unsuitable for surgical navigation because of poor image contrast and geometric warping artifacts that compromise anatomic fidelity, so the DTI tractography must be co-registered to the high-resolution anatomic images. The b = 0 s/mm^2 echo planar images are first aligned to the anatomic images using automated image registration.[24,25] A three-dimensional affine 12-parameter model with a maximum of 50 iterations is used for registration. The registration's performance is checked by comparing the position of sulci, ventricles, and cortex. The transformation matrix is applied to the DTI fiber track mask, and the registered mask is fused to the high-resolution anatomic images. Voxels that contain fiber tracks are given intensities 1.5 times higher than the brightest anatomic feature in the image (**Fig. 1**C, D). This ''hot white'' intensity ensures that fiber tracks can be distinguished easily from T2-hyperintense lesions and cerebrospinal fluid.