Reproducible Objective Quantification Scheme (ROQS) for MRI assessment of white matter tract integrity: applications to mild Traumatic Brain Injury (TBI)

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Introduction:
Magnetic Resonance Imaging (MRI) offers the ability to study the aspects of the brain that would not normally be accessible in vivo. Moreover, the use of advanced imaging techniques allows us to study brain tissue microstructure otherwise overlooked by clinical scans. Two such imaging techniques, magnetization transfer imaging (MTI) and diffusion tensor imaging (DTI) give the special ability to quantify changes in myelin.

Annually in the United States over 1.5 million cases of TBI are reported, yet reliable tools for prognosis of persistent symptoms following mild TBI are elusive. Diffuse Axonal Injury (DAI) is the most common form of damage, yet current MRI techniques cannot quantify the integrity of white matter tracts reproducibly. The Reproductive Objective Quantification Scheme (ROQS) presents a tool and guidelines for the selection of 15 reproducible Regions of Interest (ROI) based on anatomically identifiable structures. ROQS is applied to normal volunteers (n=26) imaged with DTI and MTI to establish population parameters for each ROI. This method is then extended to investigate mild TBI patients with the first 10 days of initial head injury.

Magnetization Transfer Imaging
MTI operates under the principle that two spin systems in close proximity have the ability to exchange contrast. Thus given two spin systems with different spin-spin relaxation times (T2) such as protein and water, it is possible for the protein to transfer its magnetization onto the free water pool. Applying an off-resonance pulse does this (Figure 1). The ultimate effect is the protein will exhibit a short relaxation time (TR), while the free water shows a long TR. This causes a decrease in the signal of macromolecules affected by MT (Figure 2). Thus areas of demyelination on T2 weighted images are more visible with MT.

The power of MTI, however, lies in the magnetization transfer ratio (MTR). MTR can be used as a normalized, quantitative measure of the effects of a disease, given by:

\[ \text{MTR} = \frac{M_0 - M_{\text{sat}}}{M_0} \times 100\% \]

where \( M_0 \) refers to the average signal intensity of a region of interest (ROI) and \( M_{\text{sat}} \) refers to the average intensity of the identical ROI when no MT saturation pulse is used. Typically, a disorder appears as a decrease in the MTR. The MTR map is an image where the contrast of the pixel is proportional to the difference in T2 between the spin systems. This pulse creates the MTR effect.

Diffusion Tensor Imaging
DTI is based on the sensitivity MTI has towards the water molecules. Diffusion imaging measures the Brownian motion of water molecules. It is important to note that diffusion is a scalar quantity with no preference for direction. Anisotropy, however, measures the direction of water and the degree of that flow. Anisotropy results from the reduced permeability of water through myelin sheaths. In white matter tracks, myelin sheaths surround axons limiting the motion of water. Thus DTI moves more freely along those fibers than across them (Figure 3).

A 3 x 3 tensor model describing the motion along each direction of 3-dimensional space characterizes the diffusion tensor. DTI then yields useful data such as the apparent diffusion constant \( D_{\text{app}} \) and fractional anisotropy (FA). The anisotropy map offers high contrast images with the ability to locate fiber tracks and the direction they run (Figure 5).

Figure 1. A Radio Frequency (RF) pulse is applied approximately 1200 Hz of the resonance peak of water prior to a standard T2 weighted pulse sequence. This RF pulse saturates water molecules bound to the protein and causes them to transfer its magnetization onto the free water pool due to the difference in T2 between the spin systems. This pulse creates the MTR effect.

Figure 2a. An image of a brainstem without the saturation pulse (no MT). Figure 2b. An image of the same brainstem with the saturation pulse (with MT). The increase in contrast is due to suppression of signal of lipids because of the transfer of magnetization and change in TR.

Figure 3 (top) and Figure 4 (below). Figure 3 is a plot of the diffusion ellipsoid of the corpus callosum. Notice the ellipsoids are elongated along the white matter track while CSF and gray matter is mostly spherical. Figure 4 is an Anisotropy map. The brightness corresponds to the magnitude of FA and the hue to the direction of greatest diffusion anisotropy: red = anterior-posterior, blue = superior-inferior.

References:

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