Metrics for Distinguishing Axon Disorder from Demyelination in Regions of Decreased Fractional Anisotropy

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Introduction: Decreasing fractional anisotropy (FA) has been observed during the progression of epilepsy [1], as a result of demyelination in multiple sclerosis (MS), and following ischemic events. We present a metric that may be of use in assessing whether decreases in anisotropy are the result of general deterioration (as in MS) or decreasing collinearity (as thought to occur in epilepsy).

Methods: All of the proposed metrics are based on the (tensor assumption independent) "g-value" as defined by Pipe in 2003 [2]. This value is the energy normalized, cross-correlation of the vectorized directional diffusivities and is calculated as Equation 1. The three metrics presented are the auto-g-value (G(A,A)), the cross-g-value (mean(G(A,B)), A≠B), and the ratio of cross-g-value to auto-g-value. The auto-g-value is a relative measure of autocorrelation and thus the most directly related to FA. If FA is lowered as a result of inconsistency in axon arrangement (a general decrease in collinearity), it is expected that the average auto and cross-g-value of a pixel will go down. In contrast, if FA is lowered as a result of demyelination, the average cross-g-value is expected to be impacted less, especially in comparison to the auto-g-value.

Results and Discussions: Average cross- and auto-g-value images are heavily weighted towards white mater and show structural information similar to FA maps. A ratio image of the cross-g-value versus the auto-g-value indicates how much of the internal structure is preserved in the neighborhood. Figure 1 shows examples of these metrics as well as the FA and apparent diffusion coefficient (ADC) image for the same slice. Figure 2 shows an MS lesion as it appears in the ADC image and the resulting ratio image. As anticipated, the lesions appear bright in the ratio image (2B) indicating that the decrease in the auto-g-value is accompanied by a smaller relative decrease in the cross-g-value. While diffusion is occurring in a less restricted environment due to demyelination, the general ordering of the axons is preserved.
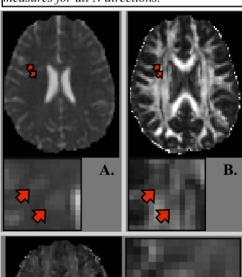
Conclusions: Metrics were presented that provide a scalar assessment of white matter integrity as well as cross-voxel alignment. The metrics are calculated without parametric assumptions or user selection of regions of interest. A ratio of the cross versus auto-g-value was used to highlight preservation of local axon order in observed lesions.

References: [1]A.J. Cadotte, "Temporal Lobe Epilepsy: Anatomical and Effective Conectivity", IEEE Trans. Neural Syst. Rehabil. Eng., vol.17, no.3, pp.214-223, 2009., [2] J.G.Pipe, V.G.Farthing, "A Correlative Measure for Processing Multiangle Diffusion-Weighted Images", Mag. Reson. Med., vol. 49, pp. 536-542, 2003.

Figure 1: *Normal White matter images. A: Apparent Diffusion Coefficient. B: Fractional Anisotropy. C: Auto-g-value. D. Cross-g-value. E. Cross-g-value to Auto-g-value ratio. B-D show similar information regarding white-matter anatomy. E indicates the degree to which the structure is preserved in the neighborhood.*

$$G(A,B) = \frac{\sum_{n=1}^{N}[(a_n - \bar{a})](b_n - \bar{b})}{\sqrt{\sum_{n=1}^{N} a_n^2}\sqrt{\sum_{n=1}^{N} b_n^2}}$$

Equation 1: *The G-value equation for the energy normalized cross-correlation of the directional diffusivities in pixels A and B. N is the number of diffusion directions encoded. a_n and b_n are the measured diffusions for pixels A and B along direction n, and $\bar{a}$ and $\bar{b}$ are the mean diffusion measures for all N directions.*
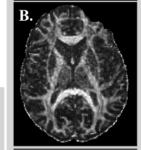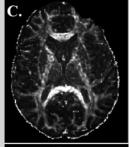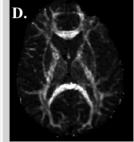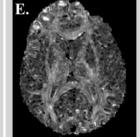

Figure 2: *A multiple sclerosis lesion (region of severe demyelination) is shown both as it appears in the ADC map (A) FA image (B) and in the image of the cross- to auto-g-value ratio (C). The relative brightness in the ratio image indicates that the broader order of the axons is less impacted than diffusion anisotropy.*