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Editorial

The Directional Metrics of Diffusion

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EDITORIAL

Nowadays, the diffusion imaging sequences have become the major component of magnetic resonance imaging armamentarium. Sensitivity of these sequences to motion of water molecules in and around the cells and noninvasiveness are thought to allow them as powerful tools to explore the pathophysiological processes occurring in living organisms. Of several powerful diffusion imaging sequences, Diffusion-Weighted Imaging (DWI), Diffusion Tensor Imaging (DTI), and Diffusion Kurtosis Imaging (DKI) are commonly applied in clinical and clinical research purposes, thought to be at least related to short acquisition time.

Diffusion of water molecules can be presented in three orthogonal axes [1,2]. In highly organized structures such as white matter of the brain, one of these three orthogonal axes possesses larger diffusivity than the other two axes. This direction usually belongs to the principal direction of axons; and diffusivity and kurtosis in this direction are termed as Axial Diffusivity (AD) and Axial Kurtosis (AK). Diffusion in the other two directions is usually evaluated by averaging their magnitude; the average magnitude of diffusivity and kurtosis in these two directions are termed as Radial Diffusivity (RD) and Radial Kurtosis (RK).

Substantial efforts have been/ are being made to explore the clinical values of these directional metrics of diffusion, along with other metrics. Evaluation of the directional metrics is principally based on the expectation that the sensitivity and specificity in probing the changes are higher with these metrics [3]. The results of many works show that these directional metrics are useful for determination of disease severity and prediction of outcome. To give a few examples, persistent AD reduction for 3 months has been found out as predictor of poor visual outcome in patients with acute optic neuritis [4]. A recent work on the patients with amnestic mild cognitive impairment has shown that the extracellular fraction of AD and RD of the callosal body correlate strongly with processing speed which determines cognition [5]. The results of some of these research works also agree with the aforementioned expectation. A recent article has reported that the sensitivity and specificity in distinguishing low and high-grade gliomas by these directional metrics are superior to those by Fractional Anisotropy (FA) [6].

Both elevation and reduction in the magnitude of these directional metrics are reported with physiological changes (i.e., development or aging) and pathological conditions. In developing brain, reduction in directional diffusivities (remarkably the radial component) and elevation in directional kurtoses are observed; which are thought to be related to neural organization [1,7]. On the other hand, elevation in directional diffusivities and reduction in directional kurtoses have been reported with aging; which are suggestive of neural tissue degeneration [8]. As for pathological conditions, reduction in directional diffusivities and elevation in directional kurtoses are observed in acute ischemia and brain tumors [6,9]. Although it is common to observe the changes in both axial and radial components, selective/ preferential involvement of either component of diffusion may also be observed. It has been reported that only the axial component of diffusion is altered in acute optic neuritis [4].

The knowledge about the exact underlying mechanisms which lead to the changes in these directional metrics is desirable. From the observations of selective involvement of only one directional component of diffusion, one might expect that the underlying mechanisms which cause a change in each component can be unveiled. There had been several studies which attempted to explore these mechanisms: Song et al evaluated the changes in directional diffusivities on shiverer mice, which are experimental models of dysmyelination. It was observed that only the radial component of diffusion was altered in these animals [10]. In their extended work on the mouse models of experimental allergic encephalomyelitis, the researchers observed that only the axial component of diffusion was altered in areas of axonal degeneration [11]. Further, in another work on mouse models of axonal damage followed by demyelination, early changes in the axial component of diffusion and subsequent changes in the radial component were observed [12]. All these observations suggest that the changes in AD are reflected by axonal degeneration and those of MD dysmyelination or demyelination. These observations were followed by several clinical research reports which attempted to explore the ongoing pathophysiological processes through AD and RD, citing the results of Song et al. Nevertheless, the universal acceptance upon the fact that the changes in the axial and radial components of diffusion reflect alterations in axon and myelin integrity respectively has still been prevented, possibly by failure to reproduce these observations

by other researchers' works [13-15]. According to the other researchers, the changes in the radial component of diffusion are not specific for dysmyelination/ demyelination. Similarly, the changes in the axial component of diffusion are not limited to axonal degeneration. A recent observation of similarity in the AK values between the normal cerebral white and gray matter also suggests that factors other than axonal integrity may contribute to AK [3].

In conclusion, from the existing evidences, incorporation of the directional metrics of diffusion in evaluation of diffusion imaging findings can be advantageous (i.e., sensitivity and specificity in detection of the microstructural abnormalities can be improved with these metrics). Alteration in the directional metrics of diffusion may reflect alteration in axonal or myelin integrity, but not exclusive of other factors. Further works are still necessary to determine the factors affecting the directional metrics of diffusion and if the changes in the axial and radial components of diffusion represent altered axonal and myelin integrity respectively. This may demand development of experimental models for each possible factor and special fixation techniques. Until controversies about the factors affecting the directional metrics of diffusion are solved, interpreting altered axonal and myelin integrity as the sole contributing factors for the changes in the directional metrics of diffusion should be avoided/ done with extreme caution.

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