Diffusional Restrictivity: Looking at the Slow Water

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Introduction: Diffusivity measurements have provided an important means for characterizing tissue microstructure. The mean diffusivity index ($\overline{D}(t)$) has been found to be a sensitive marker to pathological changes in tissues. $\overline{D}(t)$ is defined as an average of a quadratic function in the diffusion paths lengths of the water protons within a region of interest ($\overline{D}(t) = \langle \delta\mathbf{r}(t) \cdot \delta\mathbf{r}(t) \rangle / 6t$), thus being heavily weighted toward longer diffusion paths. In this abstract, we introduce an alternative metric, the diffusional restrictivity, which primarily depicts contributions from shorter diffusion paths therefore being more sensitive to restricted water compartments and smaller scale structures (slow water). Consequently, the diffusional restrictivity should be less prone to partial volume averaging effects such as cerebrospinal fluid (CSF) contamination and provides a more robust marker of the tissue microstructure.

Theory: *We define the diffusional restrictivity as the regional average of the inverse of a quadratic function of the water protons' displacement:*

$$R_D(t) = 2t\left\langle \frac{1}{\delta\mathbf{r}(t) \cdot \delta\mathbf{r}(t)} \right\rangle \tag{1}$$

It can be shown that the diffusional restrictivity can be approximated by an integral over the unit sphere of a function of the diffusivity and diffusional kurtosis, $D(\mathbf{u})$ and $K(\mathbf{u})$:

$$R_D \approx \frac{1}{12\pi}\int d^3u \frac{3+K(\mathbf{u})}{D(\mathbf{u})}\delta(\mathbf{u}-1) = \frac{1}{4\pi}\int d^3u \frac{1}{D(\mathbf{u})}\delta(\mathbf{u}-1) + \frac{1}{12\pi}\int d^3u \frac{K(\mathbf{u})}{D(\mathbf{u})}\delta(\mathbf{u}-1) = R_{D,G} + R_{D,NG} \tag{2}$$

where we have taken advantage of the sum under the integral to decompose the restrictivity into two terms: one solely dependent on the diffusivity (the Gaussian restrictivity, $R_{D,G}$) and the other dependent on the diffusional kurtosis and reflecting the non-gaussian diffusion contributions to the diffusion signal (the non-Gaussian restrictivity, $R_{D,NG}$). Note that the diffusivity and diffusional kurtosis for a spatial direction, **u**, are easily obtained from the diffusion and kurtosis tensors (1).

Methods: Imaging experiments were conducted on a 3T Trio MR system (Siemens) for four healthy volunteers. Diffusion weighted (DW) images were acquired for 30 gradient directions and six *b* values (from 0 to 2500 s/mm^2) using a refocused-spin-echo EPI sequence. The in-plane resolution was 2 mm × 2 mm and the slice thickness was 4 mm. *Image data processing:* The DW images were first corrected for motion and spatially smoothed using SPM. The diffusion and kurtosis tensors were subsequently calculated similar to (2). The restrictivity values were calculated at each voxel using Eq. [2].

Results: Figure 1 shows the $R_{D,G}$, $R_{D,NG}$, R_D and comparative mean diffusivity maps for several axial slices. The de-emphasis of the high-diffusivity CSF regions is apparent on the restrictivity maps. In contrast to the mean diffusivity, the restrictivity maps show white-gray matter contrast with substantial higher restrictivity in white matter. The best white-gray matter contrast is observed in the $R_{D,NG}$ maps. Restrictivity values (in s/mm^2) across all subjects are listed below for gray matter, several white matter regions, and CSF.

	Gray matter	Centrum semiovale	Cerebral peduncles	Cerebrospinal fluid
$R_{D,G}$	696.30±256.23	1144.80±52.90	1246.84±20.23	267.04±26.77
$R_{D,NG}$	161.35±74.14	456.29±40.21	560.08±53.78	41.34±8.04
R_D	857.65±329.74	1601.21±93.00	1807.04±73.89	308.38±33.80

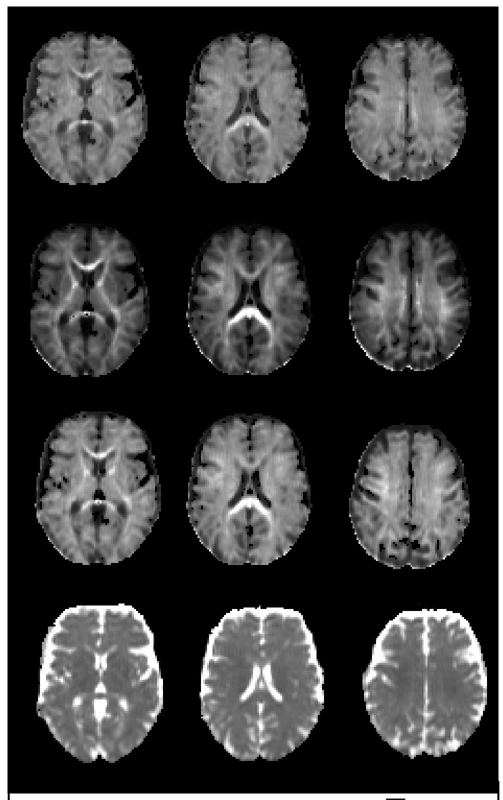

Figure 1. $R_{D,G}$, $R_{D,NG}$, R_D , and $\overline{D}$ maps (top to bottom) for three axial slices.

Discussion: Robust metrics to describe microstructural organization are essential for interpreting diffusivity measurements in both healthy and pathological tissues. Diffusional restrictivity should prove valuable in describing smaller scale structures and thus is potentially more sensitive to pathological tissue alterations. In particular, it is expected to be substantially less affected than the mean diffusivity by the CSF contamination resulting from partial volume averaging.

References: 1. Jensen JH, Helpern JA, et al. MRM 2005;53:1432. 2 Lu H, Jensen JH, et al. NMR Biomed 2006; 19:236.