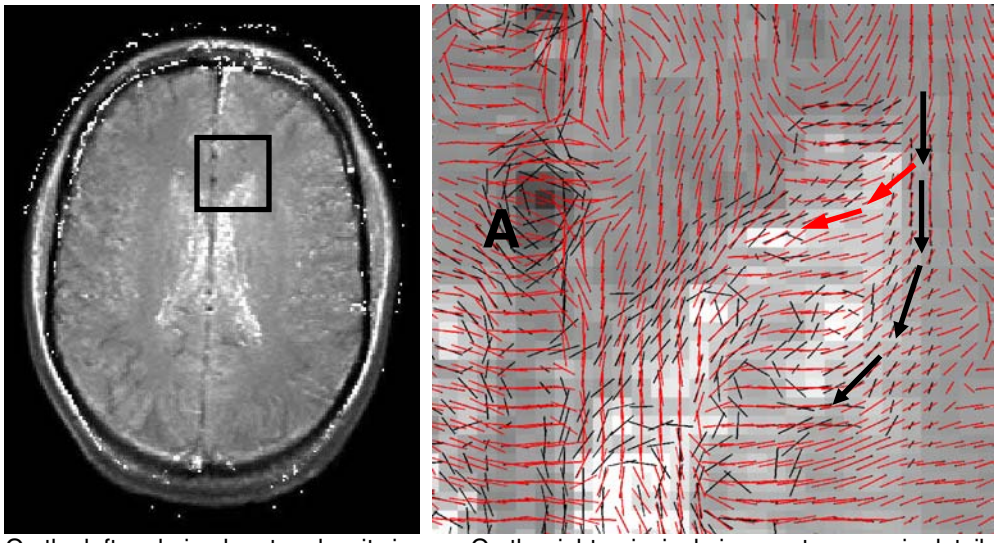
Utilization of Proton Density Gradients in the Estimation of Diffusion Tensors

S. J. Haker[1], S. E. Maier[1], R. V. Mulkern[1]
[1]Brigham and Women's Hospital, Boston, MA, United States

Introduction: Standard diffusion tensor imaging (DTI) [1] uses 6 (or more) diffusion sensitizing gradient directions and the Stejskal-Tanner [2] equation to estimate the components of a 3x3 symmetric tensor **D**. We hypothesized that proton density (PD) information may also be incorporated into the estimation of the diffusion tensor. Although the variation of proton density **ρ** in the human brain is slight, it is detectible, and persistent gradients in PD indicate low diffusion rates in the direction of this gradient. Indeed, if this were not the case, and protons were free to diffuse in the gradient direction, Brownian motion would equalize the density over time. An analysis along the lines of Torrey [3] and Stejskal-Tanner [2], relaxing assumptions to allow for spatially varying **ρ** and **D** in the diffusion term extending the Bloch equation, shows that such variations affect the angle but not the magnitude of the transverse magnetization vector. Thus, with these relaxed assumptions, the Stejskal-Tanner equation (which involves magnitude alone) still holds, and we may continue to use it while incorporating additional diffusion information provided by PD estimation.

Method: Brain images were acquired using a General Electric 3T MR imaging system and a volunteer within an approved IRB study. The diffusion images were obtained using a Line Scan Diffusion [5] sequence, with b-factor 750 s/mm^2 (b-factor 5 s/mm^2 for the baseline image), a standard set of 6 non-collinear diffusion sensitization gradient directions, and TR/TE of 2000ms/65ms. Four contiguous axial slices (allowing for 3D analysis) were obtained, having 7mm thickness and a reconstructed pixel size of .9375mm. To estimate PD, spin-echo images were obtained with TR and TE varying among all four combinations of TR={600, 1200ms} and TE={14, 28ms}. PD was then estimated using the standard MR signal decay equation $\mathbf{S=\rho\,[1-\exp(-TR/T1)]\,\exp(-TE/T2)}$, in effect extrapolating to zero echo time and infinite TR. A linear least-squares estimation of the diffusion tensor **D** was then performed, using the signals $\mathbf{S_k}$ corresponding to the 6 gradient directions $\mathbf{g_k}$, according to the Stejskal-Tanner equation $\mathbf{g_k' D g = -\log(S_k/S_0)/b}$, and a seventh equation $\mathbf{v' D v = 0}$, where **v** is a vector parallel to the PD gradient, i.e. $\mathbf{v = f(|grad\ \rho|)\ grad\ \rho}$. The length function **f** is chosen according to standard image processing methods used for edge detection, based on the histogram of $\mathbf{|grad\ \rho|}$ [4], and is constructed so that **f** is a monotone increasing function with **f(0)=0**. At locations where $\mathbf{|grad\ \rho|}$ is small, $\mathbf{f(|grad\ \rho|)}$ is nearly zero and the seventh equation becomes a superfluous **0 = 0**. The least-squares linear system then reverts to the standard 6 direction formulation. At locations where $\mathbf{|grad\ \rho|}$ is large (indicating little diffusion in the gradient direction), this extra equation comes into play as a "seventh direction," affecting **D** accordingly.



On the left, a derived proton density image. On the right, principal eigenvector maps in detail, as described in the text.

Results: The results of our initial experiment are shown in the figure. On the left is shown our estimated PD map. Contrast between gray and white matter regions is still present, after removal of T1 and T2 effects as described above. The box indicates the region of detail shown on the right. The right image shows detailed principal eigenvector maps with (in black) and without (in red) augmentation with PD. The red and black arrows indicate one visible effect of the PD addition: to prevent the stream lines defined by the principal eigenvectors from continuing into the ventricle. Near the label **A**, one sees that without PD the vector flow is through a region of decreased density, while with PD augmentation the flow is around this region.

Discussion: In this proof-of-concept work, we have shown how PD information can be utilized in the estimation of the diffusion tensor. Since PD imaging can be of higher spatial resolution than diffusion imaging, due to the latter's inherently lower signal to noise ratio, it may be of use in overcoming partial volume effects in DTI, especially near the interface between gray and white matter, or other anatomical interfaces, where a relatively large gradient in PD may be expected. A potential application is to tensor tractography, where the technique may be useful as a principled means of preventing calculated tracts from continuing from one brain region through another of differing PD. Our method may require the construction of an accurate PD map. Various effects such as coil sensitivity on PD mapping were not addressed here, but should naturally be taken into account. The robustness of our approach with respect to simpler estimates of PD is yet to be investigated.

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