MR DIFFUSION TENSOR IMAGING OF ISCHEMIC BRAIN IN VIVO

Peter J. Basser*, James Mattiello*, Carlo Pierpaoli^, and Denis LeBihan°
*Biomedical Engineering and Instrumentation Program, NCRR; ^Neuroimaging Branch, NINDS;
°Diagnostic Radiology Department, The Warren G. Magnuson Clinical Center; National Institutes of Health, Bethesda, MD, 20892 USA

Abstract

Diffusion *tensor* imaging[1] (DTI) provides intravoxel microstructural and microdynamic information about tissues that reflects their physiological state. We use DTI to assess changes in water mobility in an *in vivo* model of cerebral ischemia in cats. We use four estimated scalar quantities: the three principal diffusivities (λ_1, λ_2, and λ_3) and the T_2-weighted NMR signal (A(0)), as features with which to segment both normal and pathological tissues. While we can use these parameters to discriminate between normal and ischemic white and gray matter in cats, we are evaluating their use to distinguish between reversibly and irreversibly damaged tissues during stroke and other white matter diseases.

Introduction

The apparent diffusion coefficient (ADC) measured by diffusion imaging decreases during acute cerebral ischemia[2]. However, the effective diffusion tensor ($\underline{D}^{eff}$) measured by diffusion *tensor* imaging (DTI) [3], provides additional information with which to characterize physiologic state than the ADC. We use DTI to assess changes in water mobility in an *in vivo* model of cerebral ischemia in cats, specifically the three principal diffusivities (λ_1, λ_2, and λ_3) and the T_2-weighted NMR signal (A(0)), as features with which to segment normal and pathological tissues.

Theory

Diffusion tensor imaging consists of estimating an effective diffusion tensor, $\underline{D}^{eff}$ in each voxel from a series of diffusion-weighted images, and deriving useful quantities from $\underline{D}^{eff}$, such as the local fiber directions (and mean diffusion distances parallel and perpendicular to them), the scalar invariants, and indices of diffusion anisotropy.

The tissue's three *principal axes* coincide with the eigenvectors of $\underline{D}^{eff}$; the eigenvector of the largest eigenvalue is the tissue's fiber-tract direction .

The principal diffusivities of $\underline{D}^{eff}$, λ_1, λ_2, and λ_3 are the eigenvalues of $\underline{D}^{eff}$. They are invariant to rotations of the tissue within the NMR magnet, and characterize diffusion anisotropy of water within a voxel. They reflect changes in material properties that affect molecular transport (e.g., compartmental diffusivities and viscosities) and in microscopic organization and anatomy (e.g., the spacing and dimensions of membranes, macromolecules, fibers, and other subcompartments within heterogeneous tissues).

The T_2-weighted scalar, A(0), is also rotationally invariant, but contains *functional* information[4] that is independent and complementary to $\underline{D}^{eff}$.

Scalar invariants [5] of $\underline{D}^{eff}$, such as its Trace,

$$\mathrm{Tr}(\underline{D}^{eff}) = D^{eff}_{xx} + D^{eff}_{yy} + D^{eff}_{zz} = \lambda_1 + \lambda_2 + \lambda_3, \quad (1)$$

reflect microstructural and microdynamic changes independent of the tissue's orientation within the NMR magnet [1].

Three scalar *anisotropy ratios*[1], λ_2/λ_3, λ_1/λ_2, and λ_1/λ_3, measure the relative diffusivities in the three principal directions (e.g., the degree of rotational symmetry about the longest (fiber-tract) axis, and the relative diffusivities parallel and perpendicular to the fiber-tract axis).

Diffusion ellipsoid images display the tissue's principal axes and its mean diffusion distances along them (with the longest principal axis parallel to the fiber-tract direction).

Materials and Methods

We induced global cerebral ischemia in cats by inflating vascular occluders around the left subclavian and innominate arteries. We used a 2.0-T CSI-Omega imaging system with a quadrature head coil to acquire 14 multislice 128x128 axial 2-D FT spin-echo diffusion-weighted images. Images were acquired during pre- and post-occlusion, reperfusion, and post mortem periods. We applied gradients in 7 oblique directions[6]. From the measured T_2-weighted signal, A(TE), and the b-matrix calculated from each spin-echo sequence[7] we estimated $\underline{D}^{eff}$ and A(0) optimally in each voxel[1, 6] using weighted multivariate linear regression of [6]

$$\ln\left(\frac{A(TE)}{A(0)}\right) = -\sum_{i=1}^{3}\sum_{j=1}^{3} b_{ij} D^{eff}_{ij} \quad . \quad (2)$$

Eigenvalues and eigenvectors of $\underline{D}^{eff}$ were calculated, the former were sorted by size. Scalar invariants were also calculated.

Classification and clustering were performed with MultiSpec©, treating images displaying A(0), λ_1, λ_2, and λ_3 as a four-dimensional multi-spectral data set.

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Supervised and unsupervised clustering were performed to identify distinct classes of tissues. Feature extraction was performed to identify combinations of the four parameters that are optimal in separating the clusters in parameter space.

Results and Discussion

Diffusion ellipsoid images (Figs 1a,b) show that the principal diffusivities decrease in both gray and white matter (and ventricles) during ischemia (and following death), however, fiber direction does not change significantly.

$Tr(\underline{D}^{eff})$, a scalar measure of water mobility *independent of tissue orientation*[1], is similar in gray and white matter *in vivo*, but decreases significantly in both tissues (and ventricles) following ischemia and death. Note: $Tr(\underline{D}^{eff}) \neq ADC_{xx} + ADC_{yy} + ADC_{zz}$, contrary to recent claims[8].

Anisotropy index images are useful in identifying white matter fibers and change during ischemia. However, other measures of anisotropy may be more useful and more noise immune.

Functionally segmented images (e.g., Fig 2) show brain tissues classified by parameters $A(0)$, λ_1, λ_2, and λ_3. Membership in the white matter class requires one eigenvalue to be much larger than the other two; the gray matter class has all its eigenvalues more nearly equal, while the fluid compartment class has all its eigenvalues nearly equal but larger than gray matter. In parameter space clusters appear smeared primarily because partial voluming mixes their elements. To mitigate this artifact one should perform clustering on high resolution images.

In this parameter space, 2-D projections of clusters migrate during global ischemia. This effect is also observed using combinations of the four parameters, (e.g., the scalar invariants, and anisotropy ratios).

Conclusion

Diffusion tensor imaging subsumes diffusion imaging. The effective diffusion tensor ($\underline{D}^{eff}$) estimated from diffusion-weighted images reflects physiological changes in tissues. The principal diffusivities λ_1, λ_2, and λ_3, and T_2-weighted signal, $A(0)$, should further improve our assessment of the physiological state of tissues, owing to their unique invariant properties and sensitivity to microstructural and microdynamic changes. Clustering and segmentation may improve our ability to assess, measure, and monitor pathophysiological changes in tissues, and ultimately may help us to distinguish between reversibly and irreversibly damaged tissues during stroke and other white matter disorders.

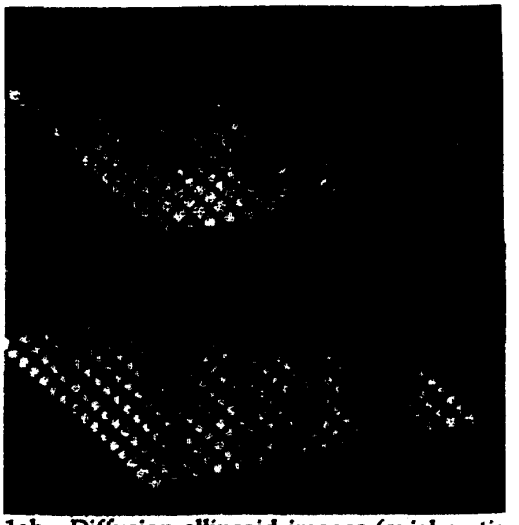

Fig 1a,b: Diffusion ellipsoid images (axial section) of ROI in cat brain a) preocclusion, and b) post-mortem.

Fig 2. Axial image of normal cat brain.

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