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ELUCIDATING TISSUE STRUCTURE BY DIFFUSION *TENSOR* MRI

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INTRODUCTION

We present new MRI parameters, derived from the effective diffusion tensor, $\underline{\mathrm{D}}$, and suggest their potential biomedical applications. Specifically, they characterize a material's structure, (i.e., its diffusion anisotropy, structural similarity, and fiber-tract organization). Like the scalar invariant, Tr($\underline{\mathrm{D}}$), which we proposed previously (1), these new parameters are independent of a) the position and orientation of the sample within the MR magnet, b) the direction of the applied diffusion gradients, and c) the choice of the laboratory coordinate system.

THEORY

We derive these parameters from $\underline{\mathrm{D}}$ by decomposing it into isotropic and anisotropic tensors:

$$\underline{\mathrm{D}} = \underbrace{\langle D\rangle \underline{\mathrm{I}}}_{\text{isotropic}} + \underbrace{\left(\underline{\mathrm{D}} - \langle D\rangle \underline{\mathrm{I}}\right)}_{\text{anisotropic}} \quad [1]$$

The isotropic tensor is the product of the (isotropic) identity tensor, $\underline{\mathrm{I}}$, and the (scalar) mean diffusivity, $\langle D\rangle$ (2):

$$\langle D\rangle = \frac{\mathrm{Tr}(\underline{\mathrm{D}})}{3} = \frac{D_{xx}+D_{yy}+D_{zz}}{3} = \frac{\lambda_1+\lambda_2+\lambda_3}{3}, \quad [2]$$

where λ_1, λ_2, and λ_3 are the eigenvalues (principal diffusivities) of $\underline{\mathrm{D}}$. We call the anisotropic part of $\underline{\mathrm{D}}$ the *diffusion deviation tensor,* $\underline{D}$, since it measures how much $\underline{\mathrm{D}}$ *deviates* from being isotropic.

An invariant (scalar) measure of the magnitude of a tensor is obtained by taking its generalized tensor product--a generalization of the vector dot product (3). The magnitude of the anisotropic part of $\underline{\mathrm{D}}$ is:

$$\underline{D} : \underline{D} = \sum_{i=1}^{3}\sum_{j=1}^{3} D_{ij}^{\,2} = \sum_{i=1}^{3}\sum_{j=1}^{3}\left(\underline{\mathrm{D}} - \langle D\rangle \underline{\mathrm{I}}\right)_{ij}^{2} \quad [3]$$

which is the sum of the squared deviations between the components of $\underline{\mathrm{D}}$ and of the isotropic tensor $\langle D\rangle \underline{\mathrm{I}}$. We also write $\underline{D} : \underline{D}$ as the sum of the squared deviations between the *principal* diffusivities of $\underline{\mathrm{D}}$ and its mean diffusivity, $\langle D\rangle$:

$$\underline{D} : \underline{D} = (\lambda_1 - \langle D\rangle)^2 + (\lambda_2 - \langle D\rangle)^2 + (\lambda_3 - \langle D\rangle)^2 \quad [4]$$

We obtain a dimensionless diffusion anisotropy index by normalizing $\underline{D} : \underline{D}$ by $\underline{\mathrm{D}} : \underline{\mathrm{D}}$.

A measure of macrostructural similarity between tissues in different voxels is given by the generalized tensor product of their diffusion tensors, $\underline{\mathrm{D}} : \underline{\mathrm{D}}'$:

$$\underline{\mathrm{D}} : \underline{\mathrm{D}}' = \sum_{k=1}^{3}\sum_{s=1}^{3} \lambda_k \lambda'_s \left(\varepsilon_k^{T} \varepsilon'_s\right)^2, \quad [5]$$

where $\varepsilon_k^{T}\varepsilon'_s$ is the dot product of the k^{th} and s^{th} eigenvector of D and D', respectively. Geometrically, $\underline{\mathrm{D}} : \underline{\mathrm{D}}'$ measures the likeness of the diffusion ellipsoids constructed from $\underline{\mathrm{D}}$ and $\underline{\mathrm{D}}'$. We obtain a macrostructural similarity index by normalizing $\underline{\mathrm{D}} : \underline{\mathrm{D}}'$ by $\sqrt{(\underline{\mathrm{D}} : \underline{\mathrm{D}})\,(\underline{\mathrm{D}}' : \underline{\mathrm{D}}')}$.

To measure the degree of fiber-tract organization we form the generalized tensor product between *anisotropic parts*, $\underline{D}$ and $\underline{D}'$: of different diffusion tensors:

$$\underline{D}' : \underline{D} = \sum_{k=1}^{3}\sum_{s=1}^{3} \lambda_k \lambda'_s \left(\varepsilon_k^{T} \varepsilon'_s\right)^2 - \frac{1}{3}\left(\sum_{k=1}^{3} \lambda_k\right)\left(\sum_{s=1}^{3} \lambda'_s\right). \quad [6]$$

We obtain a correlation index of fiber-tract organization by spatially convolving Eq. [6] with an isotropic kernel.

MATERIALS AND METHODS

Using a 2-T CSI animal imaging system and a birdcage quadrature coil, we acquired 14 (128 x 256) axial DW 2D-

Diffusion gradients were applied in 7 non-collinear, oblique directions (4). (Imaging para-meters: TE=80ms, Δ=40ms, δ=19ms, TR=2sec, na=2, FOV=80mm, st=2mm, max. gradient=3.25 G/cm). From the measured T_2-weighted signal and the calculated b-matrix for each sequence(5), we estimated $\underline{\mathrm{D}}$ in each voxel (4) from which these scalar invariant parameters were calculated.

RESULTS AND DISCUSSION

In the image of the anisotropy index (Eq. [4]), white matter fibers appear bright while isotropic grey matter and ventricles appear dark. Unlike Eqs. [3] or [4], the (SD) anisotropy index proposed by van Gelderen et al.(6) (whose numerator contains the sum of squares of the deviation between ADCs measured in three mutually perpendicular directions: ADC_x, ADC_y, and ADC_z; and their mean value, $\langle ADC\rangle$) introduces a significant orientational artifact (7). The *fiber-tract organizational index* image shows high contrast in the corpus callosum where nerve fiber-tracts run parallel to each other, lower contrast in regions containing white matter where fiber patterns are known to be less well-defined, and virtually no contrast in gray matter and in CSF-filled ventricles, where there is effectively no macroscopic organization.

A quantitative "stain" must be invariant with respect to laboratory coordinate system in which it is measured. To characterize diffusional anisotropy (8) (as well as structural similarity or fiber-tract organization in anisotropic media), we must know *all* elements of $\underline{\mathrm{D}}$, (i.e., both its diagonal and off-diagonal elements) or its eigenvalues and eigenvectors.

The transformation of biological structures from a less ordered to a more ordered state is an essential characteristic of development. Conversely, the loss of organization and structure is an essential characteristic of aging. These noninvasive, nondestructive, and quantitative imaging parameters are potentially sensitive to these changes. Potential physiological and pathophysiological applications for characterizing macroscopic fiber organization include detection of scarring following cardiac ischemia, and of demarcating tumors in white matter or skeletal muscle. In general, an objective measure of fiber-tract organization may represent an important contribution to the assessment of normal function and disease.

CONCLUSION

We have proposed new and useful quantitative MRI parameters that "stain" for normal or pathological structural features. Due to the inherently high sensitivity of molecular diffusion to a change in microstructure, their potential biomedical applications include measuring and monitoring structural or physiological changes (at macromolecular, cellular, tissue, and organ length scales) in development, aging, and disease.

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