Journal of Magnetic Resonance **139,** 1–7 (1999)
Article ID jmre.1999.1752, available online at http://www.idealibrary.com on IDEAL®

Comparison of Scalar Measures Used in Magnetic Resonance Diffusion Tensor Imaging

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Received April 6, 1998; revised October 14, 1998

The tensors derived from diffusion tensor imaging describe complex diffusion in tissues. However, it is difficult to compare tensors directly or to produce images that contain all of the information of the tensor. Therefore, it is convenient to produce scalar measures that extract desired aspects of the tensor. These measures map the three-dimensional eigenvalues of the diffusion tensor into scalar values. The measures impose an order on eigenvalue space. Many invariant scalar measures have been introduced in the literature. In the present manuscript, a general approach for producing invariant scalar measures is introduced. Because it is often difficult to determine in clinical practice which of the many measures is best to apply to a given situation, two formalisms are introduced for the presentation, definition, and comparison of measures applied to eigenvalues: (1) normalized eigenvalue space, and (2) parametric eigenvalue transformation plots. All of the anisotropy information contained in the three eigenvalues can be retained and displayed in a two-dimensional plot, the normalized eigenvalue plot. An example is given of how to determine the best measure to use for a given situation by superimposing isometric contour lines from various anisotropy measures on plots of actual measured eigenvalue data points. Parametric eigenvalue transformation plots allow comparison of how different measures impose order on normalized eigenvalue space to determine whether the measures are equivalent and how the measures differ. These formalisms facilitate the comparison of scalar invariant measures for diffusion tensor imaging. Normalized eigenvalue space allows presentation of eigenvalue anisotropy information. © 1999 Academic Press

Key Words: **diffusion tensor imaging; anisotropic diffusion; magnetic resonance imaging.**

INTRODUCTION

In some tissues of the body, such as the gray matter of the brain, diffusion is nearly directionally uniform in space. This spatially uniform diffusion is referred to as isotropic diffusion and can be described by a simple scalar quantity. Diffusion that varies with direction is termed anisotropic. The complex nature of anisotropic diffusion has been described by a diffusion tensor that contains information about the magnitude of diffusion in different directions. This information is often depicted as a diffusion ellipsoid oriented in space with the major axis in the direction of greatest diffusion (*1, 2*). The major, intermediate, and minor axes are mutually orthogonal. The lengths of the axes are proportional to the square of the diffusion coefficient in the direction along the axis. This complete tensor description of diffusion cannot be fully characterized by a simple scalar quantity. However, scalar quantities can be used to convey information about various attributes of the tensor, including the magnitude of the diffusion coefficient, the orientation of diffusion directions, and the degree of anisotropy. Summarizing attributes of the tensor in a scalar quantity is important both for quantification of the attributes of the tensor and for display of parametric images of the diffusion attributes.

Many measures of diffusion anisotropy and the magnitude of diffusion have been introduced (*1, 3–7*). It is often difficult to compare and contrast these measures and to determine which measure is best suited for a particular application. This determination involves three steps. First, many candidate measures must be considered. To this end, the first part of the manuscript details a method of constructing scalar invariant measures. Secondly, these measures must be compared to determine which has the proper theoretical characteristics for the intended task. The constructs introduced in this manuscript are designed to perform this step. The normalized eigenvalue plot demonstrates how measures map eigenvalues into scalar quantities. These two-dimensional plots retain *all* the information about the anisotropy of the eigenvalues. The only information that is removed when normalizing the eigenvalues is a scale factor for the absolute magnitude of the eigenvalues. This allows all of the information about eigenvalue anisotropy to be plotted and compared on two-dimensional plots. An example will demonstrate the application of these plots. A construct for determining whether two measures are equivalent is also introduced; these are the parametric eigenvalue transformation plots. Third, before using a measure for clinical applications, the effect of measurement noise on the value needs to be determined. This last step might be based on statistical calculations or Monte Carlo simulation. The sensitivity to experimental error for the various measures is not discussed in the present manuscript.

THEORY AND DEFINITIONS

A set of eigenvalues of a diffusion tensor are λ_1, λ_2, λ_3. If they are ordered according to magnitude they become λ_{min}, $\lambda_{intermediate}$, λ_{max}. (This manuscript is concerned only with the theoretical characteristics of different eigenvalue measures. Measurement error in the eigenvalues is not a factor in this consideration. The eigenvalues here are considered to be noise-free.)

Definition: A *scalar measure* for a set of eigenvalues is a function that maps a set of eigenvalues into a scalar value.

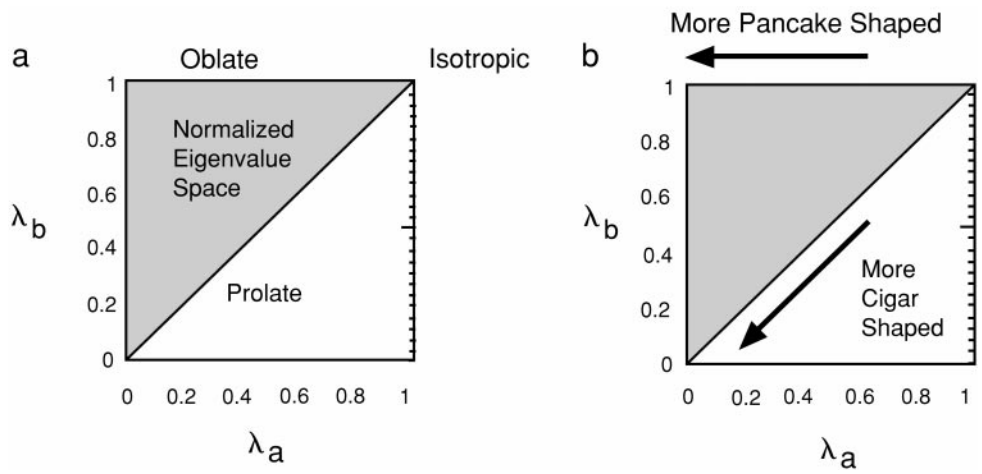


FIG. 1. (a) Normalized eigenvalue space (shaded region). Perfect isotropic diffusion maps onto (1, 1). Prolate diffusion ellipoids map along the line of identity. Oblate diffusion ellipsoids map along $\lambda_b = 1$. (b) This demonstrates the regions of normalized eigenvalue space where the diffusion ellipsoid tends toward either a pancake shape or a cigar shape.

Definition: An *invariant measure* for a set of eigenvalues is one that does not depend on the frame of reference in which the diffusion tensor was measured. Alternatively, the value of an invariant measure does not depend on the order of the eigenvalues or the names of the eigenvalues used in the calculation.

Definition: A *scalar invariant measure* is a scalar-valued invariant measure.

Definition: A *normalized eigenvalue* is a point, (λ_a, λ_b), in two-dimensional space onto which a set of eigenvalues, $(\lambda_1, \lambda_2, \lambda_3)$, is mapped by normalizing the two smaller components with respect to the largest eigenvalue:

$$(\lambda_{\min}, \lambda_{\text{intermediate}}, \lambda_{\max}) \rightarrow \left(\frac{\lambda_{\min}}{\lambda_{\max}}, \frac{\lambda_{\text{intermediate}}}{\lambda_{\max}}\right) = (\lambda_a, \lambda_b). \quad [1]$$

This can also be thought of as a point on a plane in three-dimensional space:

$$\Lambda = (\lambda_a, \lambda_b) \equiv (\lambda_a, \lambda_b, 1). \quad [2]$$

Definition: A *normalized eigenvalue plot* is a plot of λ_a versus λ_b. All of the allowable values of λ_a and λ_b fall in the region bounded by $\lambda_a = 0$, $\lambda_b = 1$, and $\lambda_a = \lambda_b$ (Fig. 1). This region is termed *normalized eigenvalue space.* In perfect isotropic diffusion, normalized eigenvalues map onto the point (1, 1). In anisotropic diffusion, when λ_a and λ_b are equal, the diffusion ellipsoid is said to be prolate (in the extreme case it has the shape of a cigar). When $\lambda_b = 1$, the ellipsoid is said to be oblate (in the extreme case it has the shape of a pancake). The boundary of normalized eigenvalue space where $\lambda_a = 0$ corresponds to the degenerate case when the diffusion ellipsoid is an ellipse.

Definition: The *order of normalized eigenvalues:* Given two sets of normalized eigenvalues, Λ_1 and Λ_2, and a particular scalar measure, $S(\Lambda)$, then $\Lambda_1 > \Lambda_2$ if $S(\Lambda_1) > S(\Lambda_2)$.

Definition: Two scalar-valued eigenvalue measures, $S_1(\Lambda)$ and $S_2(\Lambda)$, are *equivalent* if the order of the normalized eigenvalues is identical for both measures. S_1 equivalent to S_2 does not imply that $S_1(\Lambda)$ equals $S_2(\Lambda)$. If two measures are equivalent, there is a function, monotonic over the range of the measures, that maps the values of one into the other.

Definition: *Parametric eigenvalue transformation plot:* Let $S_1(\Lambda)$ and $S_2(\Lambda)$ both be scalar-valued maps of the normalized eigenvalue space. Then a parametric eigenvalue transformation plot is a parametric plot of $S_1(\Lambda)$ versus $S_2(\Lambda)$ for all Λ on the *boundary* of normalized eigenvalue space. The parametric eigenvalue transformation plot demonstrates whether two scalar measures are equivalent. If they are not equivalent, the parametric eigenvalue transformation plot will be a closed region. Normalized eigenvalue space would map into this region. If the measures are equivalent, the parametric plot will be a line (a degenerate region with no enclosed area). The shape of the line demonstrates the function that maps the values of one of the measures into the other (Fig. 2).

Definition: A *Class I measure* attains its minimum value only at (0, 0) in normalized eigenvalue space (Figs. 3a, 3b). A *Class II measure* attains its minimum value whenever $\lambda_a = 0$ (Figs. 3c, 3d).

The Mathematica software package (Wolfram Research, Inc., Champaign, IL) was used on an Apple Quadra computer (Apple Computer Inc., Cupertino, CA) to prepare the plots used in this manuscript.

RESULTS AND DISCUSSION

Three rotationally invariant parameters which can be derived from the eigenvalues are (*4*)

$$I_1 = \lambda_1 + \lambda_2 + \lambda_3 \quad [3]$$

$$I_2 = (\lambda_1\lambda_2) + (\lambda_1\lambda_3) + (\lambda_2\lambda_3) \quad [4]$$

$$I_3 = \lambda_1\lambda_2\lambda_3. \quad [5]$$

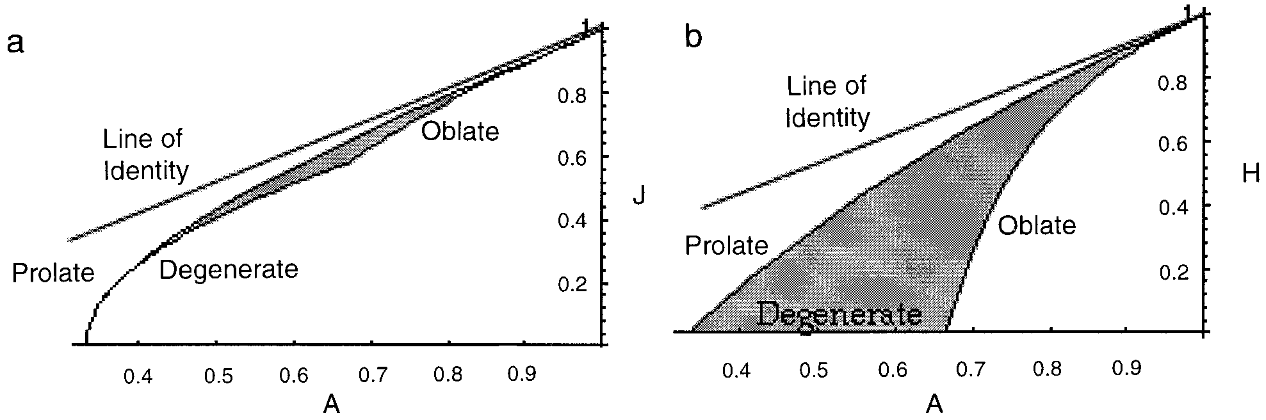


FIG. 2. (a) The parametric eigenvalue transformation plot of A versus J. The shaded region represents the map of normalized eigenvalue space. The oblate, prolate, and degenerate boundaries of normalized eigenvalue space are indicated. The entire parametric plot lies below the line of identity, since $A \geq J$ for all sets of eigenvalues. (b) The parametric eigenvalue transformation plot of A versus H.

There are other possible invariant parameters that will not be discussed here (*3*).

Measures of Diffusion Magnitude

The rotationally invariant parameters I_1, I_2, and I_3 can be put into forms that have the same units as the eigenvalues (mm^2/s):

$$A = \frac{I_1}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3} \quad [6]$$

$$J = \sqrt{\frac{I_2}{3}} = \sqrt{\frac{(\lambda_1\lambda_2) + (\lambda_1\lambda_3) + (\lambda_2\lambda_3)}{3}} \quad [7]$$

$$K = \frac{I_2}{I_1} = \frac{J^2}{A} = \frac{(\lambda_1\lambda_2) + (\lambda_1\lambda_3) + (\lambda_2\lambda_3)}{\lambda_1 + \lambda_2 + \lambda_3} \quad [8]$$

$$G = \sqrt[3]{I_3} = \sqrt[3]{\lambda_1\lambda_2\lambda_3} \quad [9]$$

$$H = \frac{3I_3}{I_2} = \frac{G^3}{J^2} = \frac{3\lambda_1\lambda_2\lambda_3}{(\lambda_1\lambda_2) + (\lambda_1\lambda_3) + (\lambda_2\lambda_3)} = \frac{3}{\frac{1}{\lambda_1} + \frac{1}{\lambda_2} + \frac{1}{\lambda_3}}. \quad [10]$$

A, J, K, G, and H are all scalar-valued invariant measures of the central tendency of the eigenvalues, or "how big" the eigenvalues are; therefore, they are in some sense measures of the magnitude of diffusion. The measures A, G, and H are the arithmetic mean, the geometric mean, and the harmonic mean of the eigenvalues, respectively. The reciprocal of H has been discussed by Basser (*4*).

In perfect isotropic diffusion the eigenvalues are identical (measurement error is not a factor in this discussion of the theoretical properties of the diffusion measures). In the perfect isotropic case, the diffusion ellipsoid is a sphere. For a given set of isotropic eigenvalues, all five measures, A, J, K, G, and H, yield identical values for the magnitude of isotropic diffusion. Therefore, the optimal choice of which measure to use in an isotropic environment is dictated by the structure of the noise in the measurement and other similar practical considerations, rather than by the theoretical properties of the eigenvalue measures.

For sets of unequal eigenvalues, the differences between the values of A, J, K, G, and H are due to the effects of disparate eigenvalues. The harmonic mean, H, is most influenced by disparate eigenvalues, J, K, and G are influenced less, and the arithmetic mean, A, is influenced the least. This relationship is reflected by the relative magnitudes:

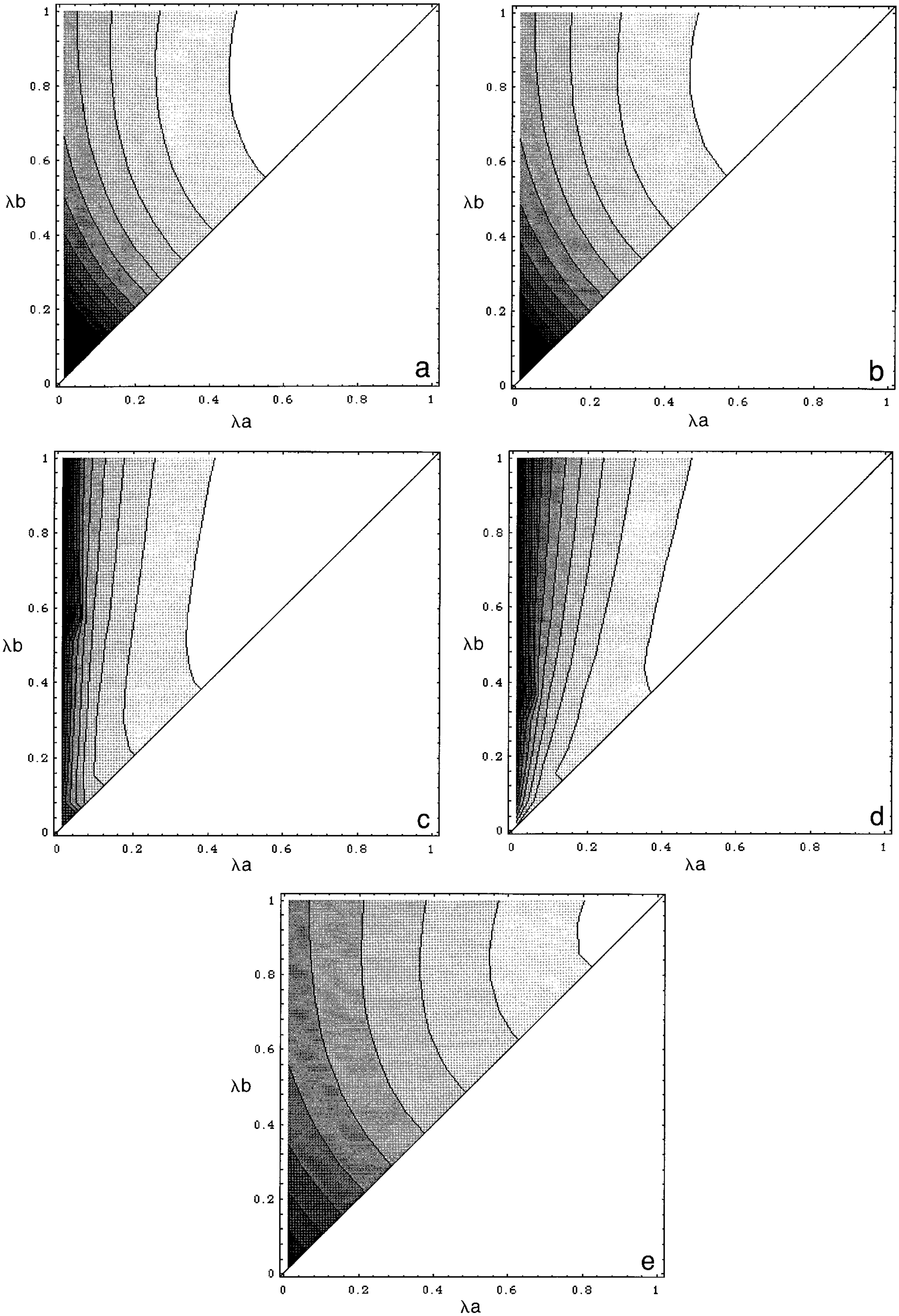
$$A \geq J \geq (K, G) \geq H \quad \text{for all sets of eigenvalues.} \quad [11]$$

The magnitude of K relative to G changes according to the specific eigenvalues under consideration. The theoretical optimal measure of the overall eigenvalue magnitude depends on the exact application of the measure and the exact meaning of overall eigenvalue magnitude for a specific application. A similar situation exists when determining how to measure "how big" a person is. Height would be a better measure when determining door heights and weight would be better for problems involving lifeboat capacity.

The differences in the values of these measures are not simply a transformation of the values by a monotonic function. There are no monotonic functions that transform A, J, K, G, or H into each other. This can be demonstrated by a parametric eigenvalue transformation plot, Fig. 2. Figure 2a defines a region with nonzero area, and therefore the measures A and J are not equivalent.

Heretofore, one the more commonly used measures of the magnitude of diffusion has been A (*1, 3, 5–9*). This might be related to the fact that A is least influenced by disparate eigenvalues and therefore has the least "anisotropy weighting."

Each measure imposes a different order on the sets of eigenvalues. Some measures may prove to have a desirable physical or physiological interpretations, and others may prove superior for demonstrating various features on parametric images. It is important to consider the theoretical property of the measure, since measures determine the order of eigenvalue


λb
1
0.8
0.6
0.4
0.2
0
0
0.2
0.4
0.6
0.8
1
λa
a
b
c
d
e

space. Use of one measure might result in an image with a lesion brighter than a certain comparison structure, whereas use of another measure might result in an image with the same lesion darker than the comparison structure.

Measures of Anisotropy

When the three eigenvalues of the diffusion tensor are not identical, there is some degree of anisotropy. Anisotropy literally means "not the same in all directions." Therefore, intuitively, a measure of anisotropy should reflect the degree of eigenvalue disparity. There are many ways in which the eigenvalues can deviate from isotropy, and the differences between the various measures of anisotropy depend on the specifics of how they map points in eigenvalue space into scalar values.

The values of the measures of central tendency, A, J, K, G, and H, differ primarily in their sensitivities to disparate eigenvalues. From Eq. [11], there is a strict ordering of the values of these measures. Because of this, ratios of these measures can be used as basic measures of anisotropy. For example:

$$R_{GA} = \frac{G}{A} \quad \text{unitless, range } [0,\ 1]. \qquad [12]$$

A, J, K, G, and H are rotationally invariant and all have the same units, so ratios of A, J, K, G, and H are also rotationally invariant and unitless. Other similar basic measures of anisotropy are R_{JA}, R_{KA}, R_{HA}, R_{GJ}, R_{HJ}, R_{HG}, R_{HK}.

Because $A \geq J \geq (K, G) \geq H$, with equality only when the eigenvalues are equal, values of these ratios near 1 occur for isotropic diffusion. Because disparate eigenvalues reduce the values of the numerators of these ratios to a greater degree than the values of the denominators, values of the ratios that are near zero correspond to more disparate eigenvalues, more anisotropic eigenvalues. It is the strict order of the magnitudes of the measures of central tendency that is the critical feature of these ratios being measures of anisotropy.

R_{KJ} is not included in the list of anisotropy measures because it is identical to R_{JA}. R_{KG} and R_{GK} are not included in this list because there is not a strict ordering of K relative to G for all sets of eigenvalues.

The normalized eigenvalue plot is a two-dimensional way of displaying all of the anisotropy information in a set of eigenvalues. Equation [13] demonstrates that normalization of the eigenvalues by any scale factor does not alter the value of the anisotropy measures:

$$R_{GA}(\lambda_1,\ \lambda_2,\ \lambda_3) = \frac{G(\lambda_1,\ \lambda_2,\ \lambda_3)}{A(\lambda_1,\ \lambda_2,\ \lambda_3)} = \frac{\lambda_{max} G(\lambda_a,\ \lambda_b,\ 1)}{\lambda_{max} A(\lambda_a,\ \lambda_b,\ 1)} = R_{GA}(\lambda_a,\ \lambda_b,\ 1). \qquad [13]$$

A similar relationship exists for all of the other anisotropy measures listed above. Because of this, the discussion of anisotropy measures can be limited to their effects on two-dimensional normalized eigenvalue space and still be completely generalizable to the entire three-dimensional eigenvalue space.

Measures of anisotropy can be compared by displaying isometric contour lines on plots of normalized eigenvalue space (Fig. 3). This convenient display would not be possible using the entire three-dimensional eigenvalue space. These plots demonstrate the desired common feature that the various measures are equal to 1 at $\lambda_a = \lambda_b = 1$ (isotropic diffusion) and decrease for points farther away from 1. The differences between the measures lie in the specific way that this decrease occurs. For example, one difference is that R_{JA} and R_{KA} tend to zero only as both λ_a and λ_b tend to zero, whereas R_{GJ} tends to zero as λ_a tends to zero. R_{JA} and R_{KA} are Class I measures, whereas R_{GJ} is a Class II measure.

The basic measures can be combined or transformed by functions that are monotonic over their range to yield more complicated measures. There are also measures of anisotropy that are not related to the basic measures defined here (*3*). An example of a transformation of the basic measures is

$$R_{AJGG} = \frac{AJ}{GG} \quad \text{unitless, range } [0,\ 1]. \qquad [14]$$

R_{GA} cubed is another transformation of the basic measures. It is equal to the familiar volume ratio, VR (*8*). VR is equivalent to R_{GA}. VR is a Class II measure:

$$\text{VR} = (R_{GA})^3 = \frac{27\lambda_1\lambda_2\lambda_3}{(\lambda_1 + \lambda_2 + \lambda_3)^3} \quad \text{unitless, range [0, 1].} \qquad [15]$$

Another measure is

$$\text{CV} = 1 - \sqrt{1 - \frac{GGG}{HAA}} = 1 - \frac{\text{standard deviation}}{\sqrt{2}A} \quad \text{unitless, range [0, 1].} \qquad [16]$$

This is proportional to the coefficient of variation of the eigenvalues and has also been used as a measure of anisotropy (*3, 6*) (Fig. 3e). CV is a Class I measure. CV is not quite a combination of the basic measures because it contains the term G/H, the reciprocal of a basic measure. VR and CV initially appear very similar; VR contains the term GGG/AAA and CV contains the term GGG/HAA. However, the presence of the H

FIG. 3. Normalized eigenvalue space with superimposed isometric contour lines for the anisotropy measures. White shading represents a value of one, whereas black is zero. (a) A/J, (b) K/A, (c) G/J, and (d) H/K. 3(e) A normalized eigenvalue plot of CV with superimposed isometric contour lines.

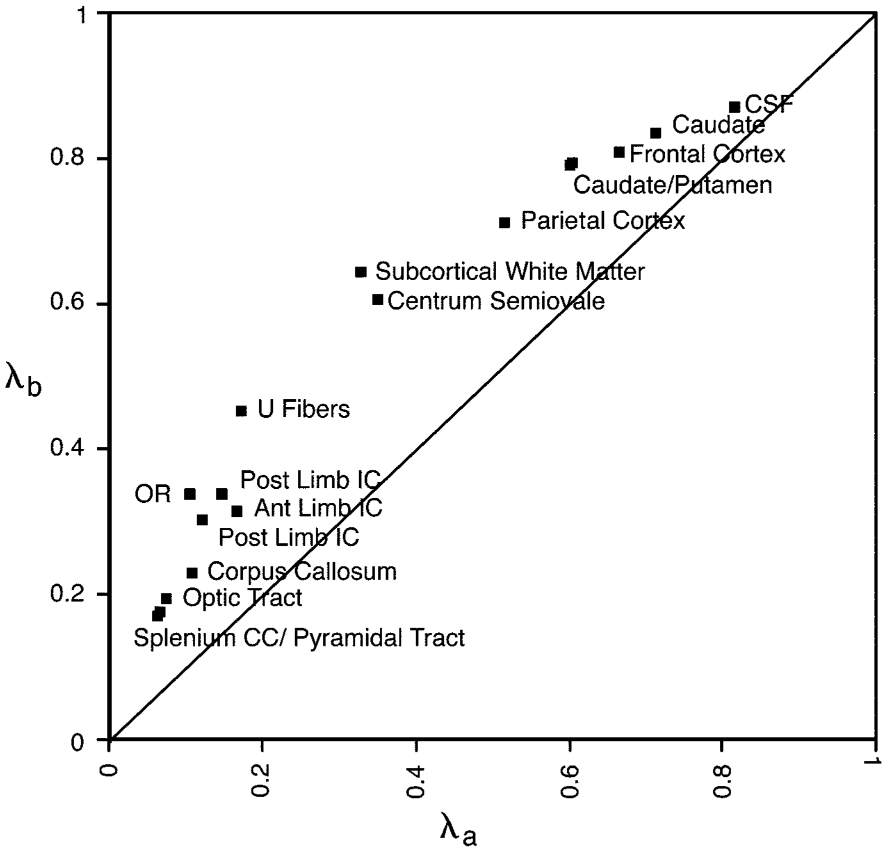


FIG. 4. Normalized eigenvalue space superimposed with the line of identity. The data points are mean eigenvalues from regions of human brain (*9*) and monkey brain (*8*). Diffusion for cerebral spinal fluid (CSF) is most isotropic: It maps nearest to (1, 1). The eigenvalues for gray matter are more isotropic than those of white matter. IC = internal capsule, CC = corpus callosum, Ant = anterior, Post = posterior, OR = optic radiations.

in the denominator of CV changes it from a Class II measure to a Class I measure.

CV and VR are clearly not equivalent because CV is in Class I, whereas VR is in Class II. Their nonequivalence can also be demonstrated by a parametric eigenvalue transformation plot.

As in the case with different measures of the overall magnitude of diffusion, the best anisotropy measure to use depends on the particular situation.

A Practical Application of the Method

Diffusion tensor imaging eigenvalues from various regions in monkey brain (*8*) and human brain (*9*) are available in the literature. These values can be plotted on a normalized eigenvalue plot, Fig. 4. If one were designing an anisotropy measure, the greatest sensitivity in discriminating two regions would be with a measure that has isometric contour lines running perpendicular to a line connecting the eigenvalue points of the structures that are under study. Figures 3a, 3b, and 3e demonstrate that the isometric contour lines of the anisotropy measure R_{JA}, R_{KA}, and CV are roughly perpendicular to the distribution of white matter points in Fig. 4. In contrast, the measure R_{GJ} might be considered to have less desirable features because its isometric lines are roughly parallel to the distribution of the more anisotropic data points (Figs. 3c and 4). Therefore, R_{JA}, R_{KA}, and CV would be candidate measures for further analysis with regard to the effects of experimental error. The distance between the isometric contour lines is not as critical a factor as the orientation of the isometric contour lines. The measures in Fig. 3 can be transformed by appropriate functions without changing the orientation of the isometric contour lines to produce images with the desired image intensity and contrast.

CONCLUSIONS

Various basic invariant measures of both diffusion magnitude and anisotropy have been introduced here. These can be added to the growing repertoire of available invariant measures. Many other measures can be made by combinations and functional transforms of these basic measures. The optimal measure to use for any specific application depends on the exact nature of the application.

The normalized eigenvalue plot allows graphic display of scalar eigenvalue measures. The visual display assists in creating an intuitive understanding of the measure. The normalized eigenvalue plot can be used to compare two different scalar measures of an eigenvalue characteristic. Moreover, this graphic display can be used to choose between various anisotropy measures by demonstrating how the measure changes relative to the eigenvalues under study.

The parametric eigenvalue transformation plot allows visual assessment of whether two measures are equivalent. The measures are equivalent if the parametric eigenvalue transformation plot is a line.

In actual applications the influence of eigenvalue measurement error on these measures must be considered when choosing a measure for any particular application.

ACKNOWLEDGMENTS

The author acknowledges Dr. Joshua Shimony and Dr. Pratik Mukherjee for their helpful comments and discussion of the manuscript.

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