Tract Based Spatial Statistics in Persons who Will Develop Alzheimer’s Dementia: A Study from the Alzheimer’s Disease Neuroimaging Initiative

Cyrus A. Raji, MD PhD
Assistant Professor of Radiology
Division of Neuroradiology
Mallinckrodt Institute of Radiology
Washington University in St. Louis
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• None
Take Home Message

• Quantifying abnormal white matter structure with diffusion tensor imaging (DTI) on MRI identifies persons who will develop Alzheimer’s dementia on average 2.6 years before onset of symptoms.
Introduction

• Alzheimer’s disease (AD) is the most common cause of dementia [1].

• Recommended clinical use of imaging has been limited to visual evaluations of MRI scans for the purposes of ruling out “organic” causes of dementia such as stroke or tumor [2].

• These American Academy of Neurology guidelines have remained without update since 2001.
No role of imaging currently exists for identifying mild cognitive impairment (MCI), a proposed prodromal phase of AD \[^3\]
Summary: In this article, the underlying theory of clinical diffusion MR imaging, including diffusion tensor imaging (DTI) and fiber tractography, is reviewed. First, a brief explanation of the basic physics of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping is provided. This is followed by an overview of the additional information that can be derived from the diffusion tensor, including diffusion anisotropy, color-encoded fiber orientation maps, and 3D fiber tractography. This article provides the requisite background for the second article in this 2-part review to appear next month, which covers the major technical factors that affect image quality in diffusion MR imaging, including the acquisition sequence, magnet field strength, gradient amplitude and slew rate, and multichannel radio-frequency coils and parallel imaging. The emphasis is on optimizing these factors for state-of-the-art DWI and DTI based on the best available evidence in the literature.

Since water moves along direction of white matter tracts, DTI provides important information about white matter structure. [4]
Grey matter = site of neurons

White matter = the brain’s wiring, connecting neurons to each other.

While both grey and white matter degenerate in Alzheimer’s disease, much less is known about how this disorder influences white matter.
Purpose

- To evaluate the discriminative ability of DTI to identify persons who will develop AD compared to controls who remain cognitively normal.
Methods

• All subjects ($n = 61$) were drawn from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) Cohort

• Average age $73.5 \pm 5.8$ years; 48% women).
  
  – Controls who remained normal ($n = 31$)
  
  – Controls who declined to either mild cognitive impairment or AD ($n = 30$)
  
  – Average time to conversion: $2.6$ years
DTI Scalars

• **Fractional Anisotropy (FA)** - the amount of diffusion asymmetry in a voxel.

  - FA is between 0 and 1
  - 0 = Random diffusion
  - 1 = diffusion along one axis
  - Higher FA generally suggests better White matter structure.

Source: [http://mriquestions.com/dti-tensor-imaging.html](http://mriquestions.com/dti-tensor-imaging.html)
DTI Scalars

- **Mean diffusivity (MD)** - the total amount of diffusion in a voxel. Increases in MD generally suggest reduced white matter integrity.

- **Axial diffusivity (AD)** - the amount of diffusion along a main direction.

- **Radial diffusivity (RD)** - the amount of diffusion along minor directions.
Image Analysis

- 3.0T ADNI MRI brain scans were obtained using standard DTI protocols [5].

- Tract Based Spatial Statistics (TBSS) were done to calculate global DTI scalars in all 61 subjects and more detailed anatomical tract analysis in a subgroup of 40 (20 converters and 20 non-converters).

- Area under the curve (AUC) was generated for converters and non-converters and feature selection used to identify predictive regions.
## Overview of TBSS

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*Diffusion tensor imaging in Alzheimer's disease: Insights into the limbic-diencephalic network and methodological considerations*
Genetic and Cognitive Data

• APOE4, an Alzheimer’s risk gene, was also collected.

• Overall cognitive function was evaluated with the mini-mental state examination.

• ROC curves for converters and non-converters were computed for each of these metrics.

• Separate ROC curves for full sample (n = 61) and subgroup analysis with TBSS (n = 40)

• Automated linear regression was done to extract the most predictive imaging features from TBSS
Results

DTI Scalars: Sensitivity = 87%, Specificity = 81%, Accuracy = 89%

MMSE: Sensitivity = 70%, Specificity = 71%, Accuracy = 78%

APOE4: Sensitivity = 73%, Specificity = 61%, Accuracy = 71%
Results of TBSS Analysis

This image shows areas of reduced fractional anisotropy - a diffusion MR imaging marker of white matter damage - in 20 persons who develop Alzheimer's dementia compared to 20 who remain cognitively normal. These areas show up as blue colored voxel overlaid onto a white matter skeleton (yellow colors) overlaid onto a standard template brain.
Tract Specific Results

(n = 40)

Sensitivity = 94%
Specificity = 93%
Accuracy = 95%
- **Anterior corpus callosum:** attention and visual spatial function. [7]
- **Uncinate Fasiculus:** Connects the temporal and frontal lobes. Functions in procedural memory. [8]
- **Forceps Minor:** Functions in working memory. [9]
Conclusions

- Quantified DTI metrics provide good diagnostic delineation of converters from non-converters.
- These metrics performed better than MMSE and APOE4.
- Specific tracts from TBSS are predictive of future dementia.
- Deep learning algorithms applied to DICOM images can potentially produce improved accuracy.
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