

# Fractional Anisotropy in Subcortical White Matter Regions of Interest Among Cardiovascular Patients

D. F. Tate<sup>1</sup>, J. Gunstad<sup>2</sup>, R. Paul<sup>2</sup>, S. Zhang<sup>3</sup>, D. H. Laidlaw<sup>3</sup>, R. Cohen<sup>2</sup>

<sup>1</sup>Medicine, Brown Medical School, Providence, Rhode Island, United States, <sup>2</sup>Behavioral Medicine, Brown Medical School, Providence, Rhode Island, United States,

<sup>3</sup>Computer Science, Brown University, Providence, Rhode Island, United States

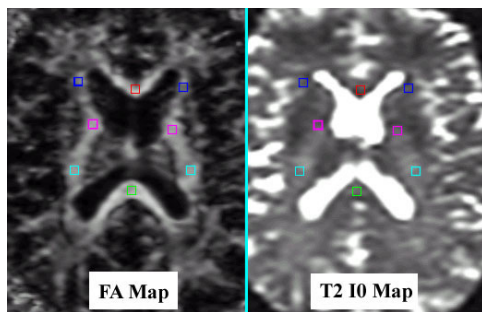
## Background

Persons with cardiovascular disease (CVD) exhibit neurocognitive impairment long prior to onset of stroke or dementia, with particular difficulty on tasks tapping executive function, psychomotor speed, and memory (1-3). Recent studies demonstrate that cognitive deficits vary as a function of CVD severity, with poorer health associated with greater impairment (4). One possible explanation for this relationship that has not been examined is reduced white matter tract integrity. Recent studies demonstrate fractional anisotropy (FA) measured using diffusion tensor imaging (DTI) is closely related to cognitive performance in persons with cerebrovascular disease (5). No study to date has examined whether persons with more severe CVD show reduced FA relative to those with milder CVD.

## Method

Participants included 6 older adults enrolled in a prospective study of the neurocognitive consequences of CVD. For enrollment into the parent study, participants are required to have documented history of CVD, a total score on the Mini Mental Status Examination (MMSE) above cutoff for dementia, and no history of neurological or severe psychiatric disorder. Participants included in the present study averaged  $70.50 \pm 8.24$  years of age and had an average MMSE of  $29.50 \pm 0.55$  and ejection fraction of  $62.85 \pm 10.11$ .

All patients were scanned using a standardized protocol for structural and diffusion weighted imaging on a 1.5 Siemens scanner. The following sequence was used to collect the diffusion images: TR=7 s, TE=150 ms, b=1000s/mm<sup>2</sup>, d=25ms, and D=31ms (FOV=220mm, 128x128 matrix). An acquisition with no diffusion gradients (b = 0, two averages) was followed by acquisition where gradients (b = 1000, three averages) were applied in twelve non-collinear directions. This DTI acquisition resulted in isotropic samples of 1.7 mm on a side. The DTI data was collected in sagittal slices corresponding to the same thickness, spacing and location of the MPRAGE T1 sequence. Mean diffusivity (MD) and fractional anisotropy (FA) maps were calculated for each participant in the study from diffusion images using proprietary software and an experimenter blind to participant diagnosis. The FA maps were then analyzed using the region of interest tool in ANALYZE<sup>®</sup>. Measures of anisotropy were taken from the genu and splenium of the corpus callosum, as well as left and right measurements of the anterior, genu, and posterior limbs of the internal capsule were identified as regions of interest (see figure below).



## Results

Two sets of analyses were conducted. First, given the known effects of age on FA, we compared younger (<70) and older (>70) participants. No significant differences emerged in the analyzed regions, though there is clearly a decline in FA values in the older group for the internal capsule (see graph below). Non-significant, though moderate effect sizes (> .40) were noted for age effects in FA. We then examined the possible effects of CVD severity on FA by comparing persons with mild CVD (e.g. atrial fibrillation) to those with severe CVD (e.g. heart failure, CABG). Persons with severe CVD showed reduced FA in the splenium of the corpus callosum ( $t=7.15$ ,  $p=0.006$ ). No other significant differences were noted, though effect sizes were large (>.75) between groups.

## Discussion

This preliminary examination suggests FA may vary as a function of CVD severity in older adults, with reduced FA found in persons with more severe CVD. These effects appear independent of the effects of age and suggest reduced white matter tract integrity may be another contributing factor to the reduced cognitive performance found in persons with severe CVD. Though significant findings were limited in the present study, the large effect size between CVD groups suggest examination in large samples would result in significant differences.

## References:

1 Cohen et al. (1999). Neurocognitive functioning and improvement in quality of life following

participation in cardiac rehabilitation. *Am J Cardiol*, 83, 1374-1378.

2 Di Legge & Hachinski (2003). Prospects for prevention and treatment of vascular cognitive impairment. *Curr Opin Investig Drugs*, 4, 1082-1087.

3 Hachinski & Bowler. (1993). Vascular dementia. *Neurology*, 43, 2159-2160.

4. Trojano et al. (2003). Cognitive impairment: a key feature of congestive heart failure in the elderly. *J Neurol* 2003; 250: 1456-1463.

5. O'Sullivan et al. (2004). Diffusion tensor MRI correlates with executive dysfunction in patients with ischaemic leukoaraiosis. *J Neurol Neurosurg Psychiatry*, 75, 441-7.