

## **White matter damage in end-stage renal disease: assessment with diffusion-tensor imaging**

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Figure 1: Axial images of a fractional anisotropy (FA) map in a control subject. The FA values were obtained from the (a) bilateral parietal white matter, (b) bilateral frontal white matter and genu and splenium of the corpus callosum, (c) bilateral occipital white matter, and (d) bilateral temporal white matter.

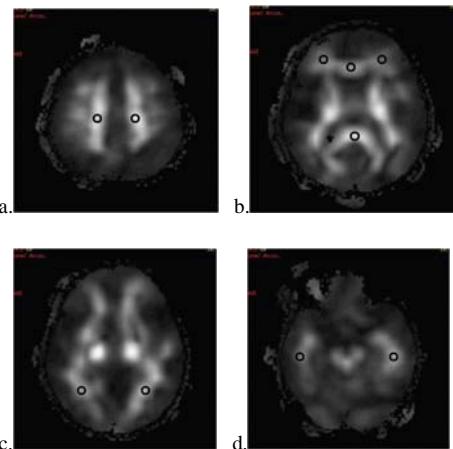


Figure 2: Scatterplots showed distributions of FA values between ESRD and control groups.

### **Synopsis:**

In patients with end-stage renal disease (ESRD), the causes of neurologic complications are complex and a non-invasive, subjective method to predict the occurrence of these complications is needed. The aim of our study was to prospectively determine regional differences of anisotropy between ESRD patients and normal controls and the effect of dialysis on microstructure changes of the white matter.

### **Introduction:**

ESRD is characterized by multi-organ dysfunction and patients with ESRD frequently

present with central nervous system abnormalities. Prevention and early diagnosis of these complications play an important role in assuring optimal care for ESRD patients. Conventional magnetic resonance imaging (MRI) for structural imaging shows focal white matter lesions that are more common in hemodialysis patients (56%) than in the normal population (27%). However, these structural changes noted by conventional MRI are mostly irreversible and the ability to predict these complications is important. Diffusion tensor imaging (DTI) can measure an effective diffusion tensor of water in tissues and can be potential for examining the microstructures of the white matter. Fractional anisotropy (FA) is an index that is extracted from the DTI and can quantify the maps of isotropy and anisotropy in tissues. The usefulness of FA measurements for the investigation of ultrastructural brain changes was demonstrated in several studies and FA measurements are considered to have a causative role in cognitive decline.

### **Materials and Methods:**

Institutional review board approval and informed consents were obtained. We recruited 42 ESRD patients undergoing regular hemodialysis three times weekly at the hemodialysis center at our hospital and 42 gender and age-matched ( $\pm 3$  years) healthy volunteers with normal renal function. In order to avoid possible confounding effects, all participants were less than 50 years old. Conventional MRI and DTI (TR, 8000 ms; TE, 82.8 ms; field of view, 240 mm  $\times$  240 mm; matrix, 128  $\times$  128; section thickness, 4.4 mm; no gap; with Asset) were obtained using a 1.5-T scanner. Image post-processing is performed to FA maps and the fields of interest, including bilateral parietal, frontal, occipital and temporal white matter (WM) and genu and splenium of corpus callosum, were defined (Figure 1). Cognitive function testing (CASI) was obtained just before MR examination.

### **RESULTS:**

Totally, 42 patients with ESRD and 42 healthy volunteers were enrolled in this study. There were no significant differences in gender ( $p=1.000$ ) or age ( $p=0.544$ ) between the two groups. In the patient group, the mean duration was  $5.7 \pm 4.6$  years. As expected, the CASI scores of the patients with ESRD ( $121.2 \pm 9.5$ ) was significantly lower than those of the controls ( $125.5 \pm 5.2$ ) ( $p=0.025$ ). All of the FA data in the patient group showed significantly lower than that in the control group at the same region (all  $p<0.001$ ) (Figure 2). Most of the FA data show negative correlations with age and dialysis duration. The distributions of gender and age had no difference between the patients and volunteers.

### **Discussion:**

In this present case-control study, we evaluated the associations of ESRD with brain white matter changes that were characterized *in vivo* using whole brain DTI. The patients with ESRD had a significantly lower FA than the controls. A negative relationship between the duration of dialysis and anisotropy changes of the white matter was of interest. There was a diffuse decrease of FA in normal-appearing white matter in patients with ESRD undergoing hemodialysis compared with that in healthy subjects, indicating abnormalities in diffusion anisotropy of water diffusion in the white matter; this result has never been reported. The exact mechanisms underlying the changes in diffusion anisotropy are not yet fully understood, but likely reflect changes in the underlying microscopic structure of the tissue being examined. In ordered structures, such as the myelin sheaths of densely packed white matter tracts, a loss of order or structural integrity of the tissue results in a reduction of FA.

### **Conclusion:**

This study investigated the relationship between ESRD and FA, a measure of microstructural integrity in the brain. Decreased FA was found to be associated with uremia. The negative correlations between FA and dialysis duration here suggests that FA may be a useful follow-up index of white matter change.

**References:** 1. Brouns R, De Deyn PP. Neurological complications in renal failure: a review. *Clin Neurol Neurosurg* 2004;107:1-16. 2. Agildere AM, Kurt A, Yildirim T, Benli S, Altinors N. MRI of neurologic complications in end-stage renal failure patients on hemodialysis: pictorial review. *Eur Radiol* 2001;11:1063-1069. 3. Nucifora PG, Verma R, Lee SK, Melhem ER. Diffusion-tensor MR imaging and tractography: exploring brain microstructure and connectivity. *Radiology* 2007;245:367-384.