

Diabetic Complications Consortium

Application Title: Diffusion Tensor Imaging MRI: A Novel Biomarker for Early Diabetic Nephropathy

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1. Project Accomplishments:

The overall goal of this pilot project was to obtain quantitative MRI assessments in the kidneys of type 2 diabetes mellitus (T2DM) subjects relatively early in their DM course to test the hypothesis that diffusion tensor imaging (DTI-MRI) can be used to identify a subset of T2DM subjects with normal clinical kidney function measures (no significant CKD, no albuminuria) who have microstructural changes that may portend progression to overt diabetic kidney disease. Imaging has been completed and analysis is underway. Comparisons are also being made to an age and gender-matched control group because medullary fractional anisotropy (FA), the DTI-MRI biomarker being studied, has been shown to decrease with age and show gender differences as well. This matched approach has not been utilized previously.

A second accomplishment is the attainment renal perfusion assessments utilizing arterial spin labeling (ASL), which has not been previously studied in the T2DM population. The methodology has the advantage that it does not require use of gadolinium or other contrast agents. Data analysis for this portion of the study is also underway.

2. Specific Aims:

Specific Aim 1. To assess renal medullary FA in T2DM subjects without clinical evidence of renal disease vs. healthy controls.

Progress: We completed quantitative MRI imaging (DTI-MRI) on 8 T2DM subjects and 8 controls. Analysis is currently underway. Our original enrollment targets were 24 T2DM and 16 controls. However, recruitment was quite challenging due to difficulty in identifying T2DM subjects who met the inclusion criteria (40-60 years of age, eGFR >80ml/min/1.73m², no albuminuria and 5-10 years duration of T2DM). Recruiting otherwise healthy subjects in the age ranges needed (to approximate the ages of the T2DM subjects) was also a challenge in the population that we draw from given the high rates of hypertension (an exclusion criteria for controls). In addition, a large number of subjects (T2DM or controls) had one or more exclusion criteria, such as large tattoos, the presence of indwelling non-MRI compliant implants / devices and/or morbid obesity.

Specific Aim 2. To define the mechanism underlying medullary FA changes in DN.

Progress: As above, analysis of the subjects imaged in Specific Aim 1 is underway. For this aim, we have also obtained renal perfusion assessments using non-contrast Arterial Spin Labeling MRI. The ASL perfusion assessments are in addition to the microstructural information obtained from the DTI MRI assessments described in Aim 1. This data will be used to determine the

relationship (if any) between cortical perfusion and medullary microstructure changes in the T2DM subjects and controls

3. Publications:

None to date