Assessment of renal allograft fibrosis with magnetic resonance elastography in kidney transplantation patients

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TARGET AUDIENCE: Radiologists, nephrologists, MRI physicists

INTRODUCTION: Kidney transplantation (KT) has revolutionized the care of patients with renal failure, improving kidney function, quality of life, and survival. However, renal allograft fibrosis resulting in chronic allograft injury (incidence of 60% at 10 years post-KT) has limited the life span of transplanted kidneys, leading to reduced graft function and graft loss [1, 2]. Unfortunately, it is usually identified at an advanced and irreversible stage. The extent of irreversible fibrosis in the allograft is a critical factor that guides choice and timing of therapy. Currently, percutaneous renal biopsy is the gold standard for monitoring the progression of renal interstitial fibrosis. However, renal biopsy has many inherent problems: sampling error, low patient acceptance, and complications. Given that irreversible fibrotic injury can often coincide with other reversible diseases such as inflammation, a major challenge for clinicians has been how to estimate the extent of fibrosis to determine the value of initiating treatment for these reversible forms of injury. Accordingly, a non-invasive modality that assesses fibrosis on a kidney-wide scale would be of great clinical utility.

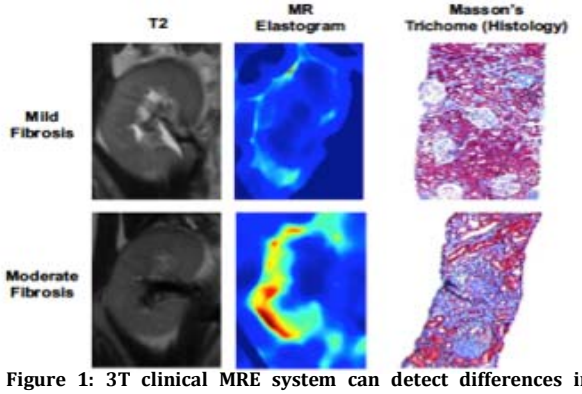

Figure 1: 3T clinical MRE system can detect differences in stiffness and fibrosis in transplanted kidneys. Two kidney-transplant patient undergoing biopsy, one with minimal and one with severe fibrosis, underwent MRE scanning prebiopsy. Representative magnitude image are shown in the left panel, and the corresponding elastogram is presented in the middle column. Note the significant heterogeneity in stiffness within the both kidneys. A representative image of the percutaneous needle biopsy sample from each kidney is presented in the right column, stained with Masson's Trichrome (blue represents fibrotic material, original magnification1.5x).

MR elastography has broadened the utility of MRI to assess microstructural changes in different organs. MRE is a non-invasive, phase-contrast technique that detects the propagation of mechanical shear waves in tissue [3]. This information is used to generate quantitative measure of tissue stiffness in kilopascals [4]. MRE was developed initially to measure liver stiffness as a surrogate measure of fibrosis severity. Since microstructural changes occur early in the time course of graft function loss and precede clinical symptoms, the validation of MRE for this purpose in renal allografts would have major impact on the clinical management of patients.

PURPOSE: To assess the relationship between MRE-derived stiffness in renal allografts and standard fibrosis scores obtained from allograft biopsy.

METHODS: This prospective study was approved by our institutional review board. Eight (8) patients were recruited from a busy outpatient transplant nephrology clinic from patients with normal and abnormal allograft function. A free-breathing flow-compensated gradient echo (TR/TE/θ=50/20.8/12) coronal MRE acquisition were performed using a passive acoustic driver placed over the transplant kidney on the lower abdominal wall on a 3.0T MRI (Siemens Skyra) over a 380 mm FOV, encoding voxels of 1.5x1.5x5mm. We used 60 Hz vibrations to derive magnitude images (Fig 1, panel 1) and corresponding stiffness map (Fig 1, panel 2) on all 8 patients. Each patient subsequently had a percutaneous ultrasound-guided allograft biopsy (3 samples) taken from the lower pole following MRI within 24 hours. Five slices were acquired and 6 uniform regions of interest (ROIs) with area of 0.25±0.02cm^2 were randomly placed on each slice in the lower (biopsied) pole renal parenchyma, yielding 30 ROI stiffness measurements from the lower pole of each allograft. The mean of 30 ROIs at the lower (biopsied) pole was calculated and compared with histopathologic renal allograft fibrosis score, as assessed by a renal pathologist using the Banff Criteria [2, 4] in each of the 8 patients.

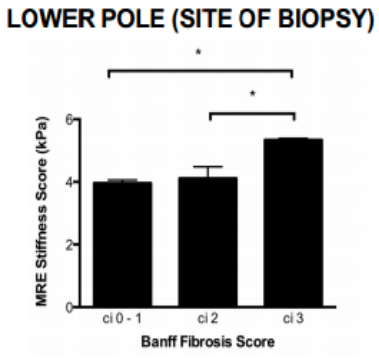

Figure 2: Biopsy-site specific stiffness quantification derived from MRE scans vs. Banff lesion interstitial fibrosis score where ci0-1= none minimal or mild interstitial fibrosis (n=4), ci2 = moderate (n=2), ci3 = severe (n=2). *p<0.05

RESULTS: The mean MRE-derived stiffness values obtained in our pilot data of 8 patients were consistent with values obtained in the only other published MRE study of renal allografts. [3]. MRE was able to detect increased stiffness (red in Fig 1, panel 2) in the parenchyma of renal allografts with histological proven fibrosis. We found a trend towards increasing MRE-derived stiffness with increasing severity of fibrotic material (amount of blue staining) seen on Masson's Trichrome (Fig 1, panel 3) (t-test: p=0.392). We also found significant increase in MRE-derived stiffness in allografts with severe fibrosis (Banff score ci3) compared to no, minimal or mild fibrosis (ci0-1) and compared to moderate fibrosis (ci2) , (one-way ANOVA: *p<0.05, respectively), as seen in Figure 2.

DISCUSSION AND CONCLUSION: MRE is a feasible non-invasive test to measure stiffness in renal allografts, and shows a trend toward increased MRE-derived stiffness in patients with increasing fibrosis measured by histopathology. Thus MRE may enable non-invasive quantitative assessment of renal allograft fibrosis and may be able to predict sites for targeted biopsy. Further study with a larger sample size is needed to assess whether MRE can accurately measure fibrosis in renal allografts.

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