INTRODUCTION

• Significant number of renal transplant patients experience at least one episode of parenchymal allograft dysfunction
• Definitive diagnosis is made by percutaneous biopsy, which is invasive, prone to sampling error and inter-observer variability
• Multiparametric MRI (mpMRI) has the capability to quantify renal function using advanced sequences

Objectives:
1. Compare advanced MRI parameters reflecting diffusion and hypoxia in functional renal allografts vs. renal allografts with established fibrosis.
2. Assess the association of (mp)MRI with histopathologic scoring of renal allograft fibrosis

METHODS

Patients
• Prospective IRB-approved single center study
• Study group: 27 initial patients

Functional allografts (n=15, M/F 9/6, mean age 56 y, estimated CKD-EPI serum eGFR 71.5±15.9 ml/min/1.73 m²): <25% change in creatinine in over 3 months, GFR>45 ml/min/1.73 m², n=4 had no fibrosis on biopsy

Chronic dysfunction with established fibrosis (n=12, M/F 6/6, mean age 51 y, estimated CKD-EPI serum eGFR 30.1±15.3 ml/min/1.73 m²): <25% change in creatinine in over 3 months, GFR<45 ml/min/1.73 m², interstitial fibrosis present on percutaneous biopsy

Percutaneous biopsy performed 150 ± 48 days before MRI in 16 patients

MRI Protocol (Table 1):

<table>
<thead>
<tr>
<th>Orientation</th>
<th>IVIM-DWI</th>
<th>DTI</th>
<th>BOLD</th>
<th>T₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronal</td>
<td>Coronal</td>
<td>Coronal</td>
<td>Coronal</td>
<td>Coronal</td>
</tr>
<tr>
<td>Sequence type</td>
<td>2D EPI</td>
<td>2D EPI</td>
<td>2D GRE</td>
<td>3D SPGR</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>4700</td>
<td>4100</td>
<td>311</td>
<td>4.3</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>75</td>
<td>74</td>
<td>2.8,14,20,26,32,38,44, 50, 56,68,79</td>
<td>1.28</td>
</tr>
<tr>
<td>FA (deg)</td>
<td>90</td>
<td>90</td>
<td>35</td>
<td>2.10</td>
</tr>
<tr>
<td>b-values (s/mm²)</td>
<td>0.10,30,50, 80,120,200</td>
<td>50,500</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>400,800</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diffusion directions</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FOV (mm²)</td>
<td>315 x 360</td>
<td>360 x 360</td>
<td>348 x 369</td>
<td>380 x 380</td>
</tr>
<tr>
<td>Slices</td>
<td>20</td>
<td>40</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>6</td>
<td>4</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Matrix</td>
<td>268 x 384</td>
<td>256 x 256</td>
<td>300 x 384</td>
<td>308 x 384</td>
</tr>
</tbody>
</table>

Data analysis:
• Signal curves for IVIM-DWI and BOLD were measured from circular ROIs placed at the upper, middle and lower renal allograft poles, in the cortex (C) and medulla (M)
• Fitting of ROI-averaged signal curves was performed in MATLAB:
  - IVIM-DWI parameters (true diffusion D, pseudodiffusion D*, perfusion fraction PF and ADC) were obtained by Bayesian fitting (4)
  - DTI fractional anisotropy (FA) maps, computed on the system from DWI data.
• Cortico-medullary differences in ADC (ΔADC) and T₁ (ΔT₁) were calculated (7)
• MRI parameters, compared between functional and fibrotic allografts using the Mann-Whitney test.
• Spearman correlations between cortical MRI parameters and cortical biopsy score for interstitial fibrosis/tubular atrophy (Banft, cl, and iIFTA) (8).

REFERENCES

4. Feji et al. Scientific Reports 2016. DOI: 10.1038/srep10908

RESULTS

• Qualitative assessment of advanced diffusion parametric maps (Fig. 1) shows decreased values in fibrotic vs. functional allografts, which is confirmed by the quantitative polar ROI analysis.
• Cortical ADC (Functional/ fibrotic: 2.1±0.1/1.9 ±0.2 10⁻³ mm²/s , p=0.007) and true diffusion coefficient D (Functional/ fibrotic: 1.8±0.2/1.6 ±0.2 10⁻³ mm²/s , p=0.016) decreased in patients with fibrosis; medullary ADC decreased in patients with fibrosis (functional/ fibrotic: 2.1±0.1/1.9 ±0.1 10⁻³ mm²/s , p=0.016)
• Cortical T₁ increases in fibrotic allografts (functional/ fibrotic: 1149.3±185.1/1349.6±215.9 ms, p=0.017), and there is loss of cortico-medullary differences in T₁ (functional- fibrotic: -37±15.1/-11.2±3.8 %, p=0.016).
• Medulla ADC was moderately correlated with tissue Trichrome stained fraction for collagen (r=0.55, p=0.029).
• Cortical T₁ had a moderate positive correlation to the Banff fibrosis score (p=0.53, p=0.04) and both cortical and medullary T₁ had strong positive correlations to tubular atrophy score (p=0.58, p=0.022/p=0.58, p=0.022).
• ΔT₁ had highest diagnostic performance for discriminating between fibrosis and functional allografts, increased in combination with cortical ADC (Fig.2).

CONCLUSIONS

• DWI and T₁ parameters are sensitive to fibrosis in renal Tx patients with chronic dysfunction, as shown in previous studies (7-11)
• Decrease in DWI parameters due to architectural and vascular changes with allograft dysfunction (9,11)
• Proton T1 with tissue edema and inflammation (7,10)
• Because of the small number of patients with fibrosis, and the reduced range of pathology scores, we were unable to reproduce correlations between ΔADC and ΔT₁, and pathology observed in a larger study (7)