

Quantitative Assessment of Kidney and Liver Disease in a Rat Model of Autosomal Recessive Polycystic Kidney Disease (ARPKD)

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Introduction: Autosomal Recessive Polycystic Kidney Disease (ARPKD) is a multiorgan pediatric disease that manifests as progressively increasing renal cysts as well as liver biliary dilatation and congenital hepatic fibrosis¹. Unfortunately, no tools are currently available to effectively monitor ARPKD kidney and liver disease progression². We are currently developing quantitative MRI assessments of ARPKD kidney and liver disease using the PCK rat model that exhibits both kidney and liver diseases similar to human ARPKD³. In this study, we have developed a multiple spin echo MRI acquisition on a preclinical 7T scanner to obtain kidney and liver T2 relaxation maps with limited impact of cardiac and respiratory motion, tissue perfusion, and stimulated echoes. This acquisition reliably distinguished kidney and liver pathology from normal parenchyma in longitudinal assessments in the PCK rat.

Methods: Four PCK rats were scanned at 1-month and 2-months of age in a 7T Bruker Biospec MRI scanner (Bruker Inc, Billerica, MA). Six 2-month old Sprague-Dawley (SD) rats were scanned as controls. Multislice, sagittal kidney and liver images of each animal were obtained with a flow-saturated, respiration-gated, multiecho spin echo acquisition (TR=5000ms, TEs = 10ms-120ms, 12 echoes, resolution=391x391x2000μm). Sagittal images were acquired to limit the effects of cardiac motion on the liver images. Varying crusher gradients were used to limit the effects of spurious echoes. T₂ relaxation maps of each animal's kidney and liver were generated via a linear least squares regression of a monoexponential decay model accounting for signal noise. Manual thresholding based on T2 histograms was used to segment the cysts in the kidney and dilated bile ducts in the liver (longer T2 species) from the normal tissue parenchyma (shorter T2 species). Mean and standard deviations of the T2 relaxation times for disease and normal tissues were calculated and analyzed using 2-tailed Student's t-tests for all animals and time points.

Results: Representative T2-weighted images for a PCK (ARPKD) rat and SD control rat are shown in Figure 1. As expected, the cysts and dilated bile ducts are easily visible in T2-weighted images for the PCK rat. A plot of natural log of the signal intensity as a function of echo for each of four tissue compartments (renal cysts, liver bile ducts, kidney parenchyma, liver parenchyma) is shown in Figure 2. These data are based on manual segmentation of one PCK rat image set. Note the largely linear character and lack of oscillation in the plots indicating limited effects of perfusion and spurious echoes, respectively. Graphs of the mean T2 values for all four tissue compartments are shown in Figure 3 for 1-month/2-month PCK rats and SD controls. Most importantly, the cysts and dilated bile ducts in the PCK rats show markedly increased T2s in comparison to normal kidney and liver parenchyma (p < 0.00001).

Discussion: We have developed an effective multiple spin echo MRI acquisition to enable reliable T2 relaxation assessments of kidney and liver disease progression in an ARPKD rat model. The improved acquisition resulted in largely monoexponential decay curves with little or no effects of motion, perfusion, or spurious echoes. As a result, we were able to easily differentiate kidney and liver pathology from normal parenchyma in the PCK rat. Further, we observed increased T2 values for normal kidney and liver parenchyma for the PCK rat over time and in comparison to SD rats indicative of sub-voxel pathology. The sensitivity to pathology suggests that measuring T2 relaxation with this acquisition will provide a useful assessment of ARPKD progression.

References: [1] Dell K Adv in Chronic Kid Dis 2011 [2] Turkbey B Ped Radiology 2009 [3] Lu L. MRM 2011.

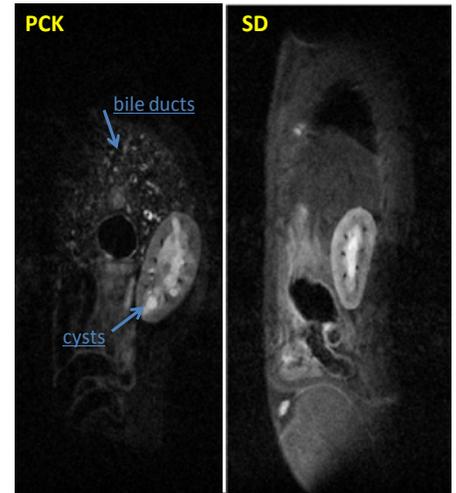


Fig. 1: T2-weighted images of PCK and SD rats. Note the obvious renal cysts and dilated bile ducts in the PCK rat.

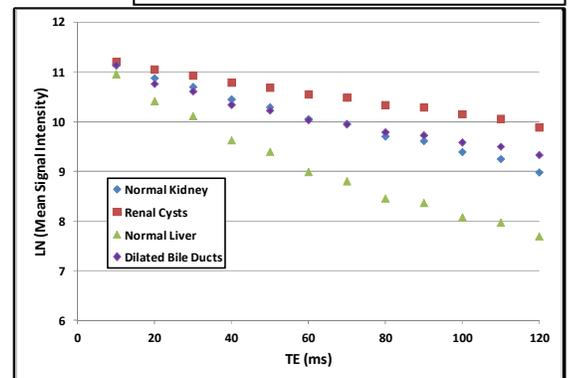


Fig. 2: ln(signal) for liver and kidney in PCK rat.

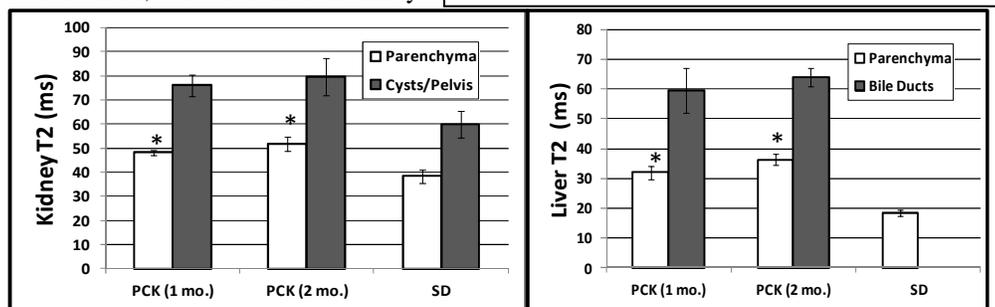


Fig. 3: Mean T2 times for kidney (left pane) and liver (right pane) of PCK and control rats. The cysts and dilated bile ducts in the PCK rats are significantly increased T2s in comparison to normal kidney and liver parenchyma (p < 0.00001). The normal kidney and liver parenchyma of the PCK rats are also elevated in comparison to SD controls (p < 0.001) indicative of sub-voxel pathology.