Quantitative MRI markers for cystic kidney disease progression in an ARPKD rat model

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Introduction
In Autosomal Recessive Polycystic Kidney Disease (ARPKD), overall kidney function diminishes only after significant disease progression. In addition, ARPKD is characterized by both macrocysts and microcysts which are not consistently delineated by conventional diagnostic imaging techniques [1-3]. Our initial results in the PCK rat model of ARPKD demonstrate that quantitative MRI techniques such as diffusion imaging overcome this obstacle and allow non-invasive monitoring of ARPKD disease progression. We have also developed a quantitative analysis methodology to provide consistent characterization of ARPKD kidneys that can be easily translated to clinical applications.

Methods
Two ARPKD-PCK rats (2,6 months old) and one Sprague-Dawley control rat (SD, 6-months of age) were euthanized, and their respective kidneys were excised for immediate ex vivo MRI scanning using a 9.4T Bruker Biospec MRI scanner (Bruker Biospin, Billerica, MA). A diffusion weighted spin echo acquisition was used to obtain ADC maps for each set of kidneys (TR/TE=3000ms/34ms, res=0.4x0.4x2mm, b=0,100,200,500, and 1000 s/mm², isotropic weighting). Histograms of the ADC maps from the 6-month PCK rat were used to determine segmentation thresholds to automatically distinguish normal renal parenchyma from microcystic and macrocystic regions in the ADC maps. The ADC thresholds were selected by determining the local minima in the ADC histograms. The total volumes of each tissue component and the percentage of normal and cystic kidneys were then calculated by summing the volumes of each ADC map.

Results
ADC maps of kidneys from 2-month and 6-month old (PCK) rats are shown in Figure 1 along with 6-month old control kidneys. PCK rats demonstrate progressive increase in large (macro)cysts as well as increased cortical hyperintense “streaks” determined by histological staining to be small (micro)cysts. The ADC histograms (not shown) demonstrated three peaks representing normal (µ_ADC=0.4x10⁻³ mm²/sec), microcystic (µ_ADC=0.9x10⁻³ mm²/sec), and macrocystic (µ_ADC=1.2x10⁻³ mm²/sec). Local minima were established between these regions and were used to calculate volumes of the respective tissue compartments. These results show that the cystic burden (both micro and macrocysts) triples from 2 to 6 months while normal parenchyma is decreased from 70% to 25% (Fig. 2).

Discussion
We have developed an initial MRI acquisition and image analysis methodology to characterize ARPKD progression in PCK rats. This methodology utilizes simple ADC maps from diffusion-weighted imaging. The ADC maps and histogram analysis demonstrate the capability to consistently distinguish regions of microcysts from both normal renal parenchyma and obvious macrocysts. Additional studies will expand the analysis to diffusion tensor imaging to account for anisotropic diffusion in the kidneys and to in vivo experiments.

References and Acknowledgements
This work was supported by NIH R24-CA110943 Northeast Ohio Small Animal Imaging Center

Fig 1: ADC maps of excised kidneys from ARPKD rats (a) 2-month PCK and b) 6-month PCK) and c) 6-month Sprague-Dawley control. Large cortico-medullary cysts are easily seen in the PCK rat kidneys. In addition, brighter streaks radiating from the inner cortex to the outer cortex are visible in the ADC map of the 6-month PCK kidneys (yellow arrows in b)). Histologic staining (c) analysis confirmed these regions to be clusters of microcysts.

Fig. 2: Results of histogram analysis of ADC maps of 2-month and 6-month PCK (ARPKD) rat kidneys. Total cystic (micro and macro) burden for PCK rat kidneys increases with age in accordance with histological results.