T_2 Relaxation Assessments of Kidney and Liver Disease in the PCK 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 fibrosis. ARPKD kidney disease results in kidney failure in 40-50% of ARPKD children [1]. With improved care of the kidney disease, an increasing number of ARPKD children are now experiencing liver dysfunction which may eventually require transplant. Unfortunately, no tools are currently available to effectively monitor ARPKD kidney and liver disease progression which directly limits therapeutic trials[2]. 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 ARPKD[3,4,5]. In this study, we are exploring the potential of T_2 relaxation assessments to assess renal cystic burden and hepatobiliary dilatation while also limiting the potentially variable effects of tissue perfusion.

Materials and Methods: Three 4-month-old male PCK rats were anesthetized with isoflurane and positioned at isocenter in a 7T Bruker Biospec MRI scanner. Axial kidney and liver images of three 4-month old male PCK rats were obtained with a respiratory-gated, multiecho RARE acquisition (TR=820ms, TE = 10ms-60ms, 6 echoes, resolution = 312 x 312 x 1500µm). T_2 relaxation maps of each animal's kidney and liver were generated via linear least squares fitting of conventional monoexponential decay models using either 1) all 6 echo images (TE=10-60ms); or 2) last 4 echo images (TE = 30-60ms). An ROI analysis was used to identify potential biexponential decay effects suggestive of tissue perfusion. A histogram analysis was then performed to establish consistent thresholds and to generate separate compartments for the kidney (cysts vs. normal kidney parenchyma) and liver (bile ducts vs. normal liver parenchyma) based on these T_2 estimates. Diseased and normal tissues were then segmented and mean T_2 values of each tissue compartment were calculated for each animal.

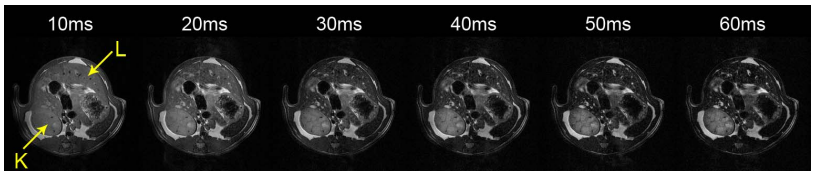

Fig. 1: Axial multiecho RARE images (6 echoes) from PCK rat liver and kidneys.

Results: Representative T2-weighted RARE images of PCK rat kidney and liver are shown in **Fig. 1**. As expected, biexponential characteristics suggestive of tissue perfusion were observed for the PCK rat liver and kidney data (**Fig. 2**). Based on these results, a histogram analysis (data not shown) was performed on the T_2 maps from the TE = 30-60ms data to establish consistent segmentation thresholds of 100ms (liver) and 130ms (kidney) for all imaging slices. Mean T_2 values for each tissue compartment are shown in **Fig. 3**. Mean T_2 values for all animals / slices are: liver parenchyma / bile ducts = 51ms / 175 ms; kidney parenchyma / cysts = 83ms / 184ms.

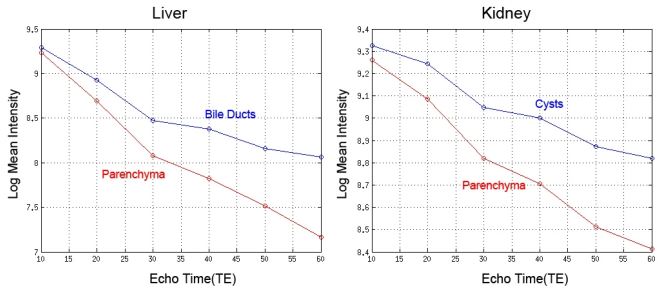

Fig. 2: T2 decay curves for PCK rat liver and kidney. Note the rapid decay observed for the 10-30ms data suggestive of tissue perfusion effects.

Discussion and Conclusions: We have developed an initial MRI methodology to characterize ARPKD kidney and liver disease progression in PCK rats in vivo using T_2 relaxation assessments. These preliminary results suggest that elimination of early echoes (TE=10-30ms) can reduce the biexponential characteristics of the T_2 decay curves thereby limiting the impact of tissue perfusion. As a result, these T_2 relaxation assessments may provide a consistent assessment allowing semiautomatic segmentation of diseased regions of both kidney and liver in ARPKD. Further studies are needed to confirm that the biexponential characteristics are indeed due to tissue perfusion. In addition, histological verification of the cystic burden and biliary dilatation obtained from this T2 methodology are pending.

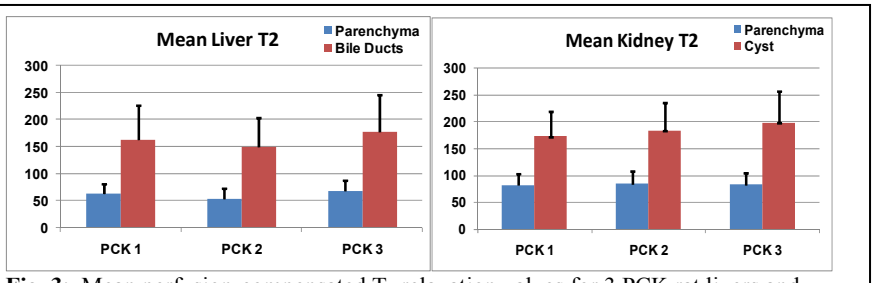

Fig. 3: Mean perfusion-compensated T_2 relaxation values for 3 PCK rat livers and kidneys. Note the consistent T_2 values for normal and diseased tissues.

References: [1] Dell K Adv in Chronic Kid Dis 2011 [2] Turkbey B Ped Radiology 2009 [3] Goto M Ped. Nephrology 2010 [4] Ward CJ Nat Genetics 2002 [5] Lu L. MRM in press.

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