Changes in kidney volume in experimental PKD quantified by a clinical 3T MR scanner

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Introduction

Polycystic kidney disease (PKD) is the most common inherited cause of kidney failure in the world. PKD is characterized by numerous fluid filled cysts resulting in massive enlargement of the kidneys. Proliferation is a key feature of cyst formation and growth. A number of studies have utilized MRI as a non invansive technique in studying structural changes with PKD disease progression in both humans and animal models of PKD. Although animal imaging is usually performed using high field animal MR scanners for the most throughput, availability of a dedicated animal scanner maybe a limitation at most clinical research institutions.

The goal of this study was to assess the feasibility of using a 3T whole body clinical scanner along with a conventional available wrist coil in a longitudinal drug treatment study in small rodents. We were able to study longitudinal kidney volume changes in rats with PKD; and the effect of sirolimus (an immunosuppressant drug with anti-proliferative properties and currently undergoing clinical trials in humans with PKD) during early disease on the progression of kidney enlargement in these animals.

Methods

Lewis polycystic kidney disease (LPK) rat is a novel hypertensive rodent model of autosomal recessive PKD (ARPKD). In this study, groups of LPK rats (n=18) and Lewis control rats (n=8) received either sirolimus (0.2 mg/kg/weekday by intraperitoneal injection) or the vehicle (90% saline / 10% ethanol) from postnatal weeks 3 to 10. Five rats were subanalysed for the MR study, four of which were LPK rats and one was a Lewis control. Two of the LPK rats received sirolimus and the remainder received the vehicle. MR scanning was performed at weeks 6 and 10 for all animals. Prior to the MR scan, rats were anaesthetised with isofluarane. Imaging was then performed using a wrist coil (Mayo Clinic Medical Devices) on a GE Twin Speed SIGNA HDX 3T Scanner. All animals were scanned tail first using a coronal and axial T2 3D FIESTA sequence. The scan parameters for the two sequences were as follows - Coronal: FOV=10, TE/TR= 4.1/12.1, Flip=45°, 352*256 acq. matrix, R/L Freq direction, 32 contiguous slices with slice thickness 0.8 and 2 NEX; Axial: FOV=9, TE/TR= 4.3/13.7, Flip=45°, 352*256 acq. matrix, R/L Freq direction, 32 contiguous slices with slice thickness 0.8 and 2 NEX.. Both the left and right kidneys were segmented from the coronal images. Segmentation was performed using a semi-automatic fast marching segmentation [1] algorithm implemented in the 3D SLICER toolkit (www.slicer.org) blinded to the categorization of the animals. Kidney volumes were computed from the segmented images.

Results

MR images for LPK rat with vehicle and LPK rat with sirolimus at week 6 & 10 are shown in Figure 1 & 2. Figure 3 and Table 1 summarizes the kidney volumes for all rats at postnatal weeks 6 and 10. In Lewis control, the kidney volume increased by a factor of 1.7. LPK rats receiving the vehicle had a 5.2x increase in kidney volume, whereas LPK rats receiving sirolimus only showed a 1.65x increase in volume, similar to the control animal.

Discussion

In this study we have shown that longitudinal structural changes in small rodents can be observed and quantified using a conventional whole body clinical 3T MR scanner and a wrist coil. We developed this method to quantify kidney volume in a small animal model of PKD. This method will be useful as a non-invasive marker of disease progression in experimental PKD and other drug-intervention studies.

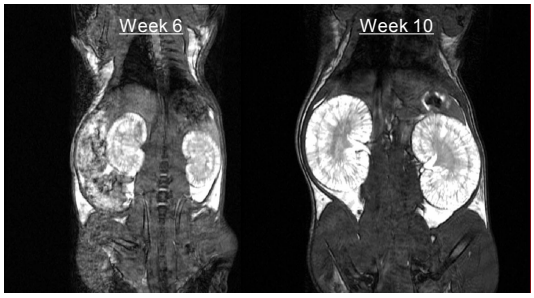

Figure 1: Coronal images from the 3D FIESTA sequence for Rat 2 (LPK rat with vehicle) at week 6 (left) & week 10 (right). A 5.4x increase in kidney volume was observed.

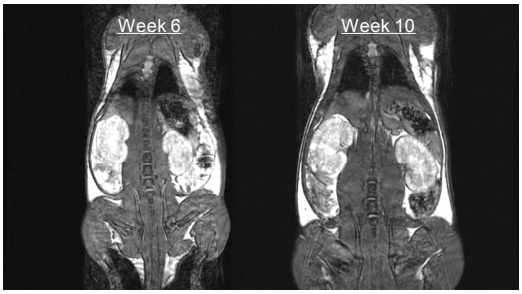

Figure 2: Coronal images from the 3D FIESTA sequence for Rat 4 (LPK rat with sirolimus) at week 6 (left) & week 10 (right). A 1.8x increase in kidney volume was observed.

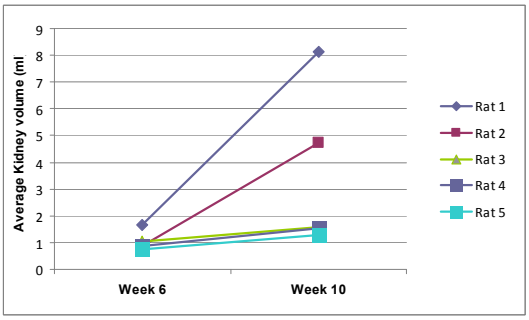

Figure 3: Changes in kidney volumes at week 6 and week 10 for all rat measured from MRI. Rat 1 & 2: LPK (vehicle); Rat 3 & 4: LPK (Sirolimus) & Rat 5: Lewis control (vehicle).

Table 1: Summary of the kidney volumes for all rodents.

	Average Kidney Volume (ml)		Factor of increase in volume from week 6 to 10	Increase in volume compared to Lewis control
	Week 6	Week 10		
LPK rat (Vehicle)				
Rat 1	1.65	8.12	4.9	2.9
Rat 2	0.88	4.74	5.4	3.2
LPK rat (Sirolimus)				
Rat 3	1.03	1.57	1.5	0.9
Rat 4	0.86	1.54	1.8	1.1
Lewis Control (Vehicle)				
Rat 5	0.75	1.30	1.7	1

References: 1. Pichon *et al. Med Image Anal.* 2004 Sep;8(3):267-74