In Vivo MR-Monitoring of Kidney and Renal Cyst Volume in Preclinical Mouse Model under Therapy

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Introduction:

Autosomal-dominant polycystic kidney disease (ADPKD) is a common genetic disorder frequently leading to cysts that eventually replace most of the normal renal parenchyma finally resulting in severe enlargement of the kidneys. Renal failure occurs in most cases by the age of 50. Survival depends on lifelong haemodialysis or kidney transplantation. No alternative clinical treatment is currently available.
In this study we established a MRI-Protocol for the evaluation of a novel therapy in the established PCY model for renal cysts [1]. Using a dedicated animal scanner we measured the total volume of mice kidneys and the ratio of cyst volume to renal volume in two therapeutical groups and one control group at designated time points during therapy.
The goal of this Study was detailed monitoring of a preclinical therapy in a mouse model differentiating effects on total renal volume and on cystic volume.

Materials and Methods:

So far 12 mice, 4 per group, were imaged using a 9,4T small bore animal Scanner (Biospec 94/20, Bruker, Ettlingen, Germany). They were anesthetized using Isofluran. Heart rate and respiration rate were continuously monitored and gating was used to reduce moving and blood flow artefacts during the scan. So far MRI-measurements were taken at three distinct time points of the therapy (fig.2: d28, d42 and d56).
The MRI–Protocol consisted of a T1-weighted FLASH sequence (TR/TE/FA: 350ms/5.4ms/40°) to outline the renal borders and a T2-weighted RARE sequence (TR/TE/FA: 3000ms/36ms/180°) with a field of view of 30mm x 30mm, a matrix of 256x256 pixel obtaining an in plane resolution of 117 x 117$\mu m^2$to detect renal cysts. Slice thickness and distance was 0.5mm. Slice orientation was coronal in both sequences. The number of slices was adjusted to the measured volume (approximately 25), always covering the complete kidneys. The kidney volume estimation technique involved a manual segmentation (perimeter drawing) of kidneys and a semiautomatic threshold approach, using a histogram analysis of peak densities of renal parenchyma and renal cysts. The reliability and reproducibility of this technique in quantifying renal cysts has been described [2].
Total kidney cyst volumes were calculated from sets of contiguous images by summing products of area measurements and slice thickness. The percentage of cystic volume was determined from the ratio of cyst volume versus total renal volume.

Results and Discussion:

Preliminary results were promising as we were able to show distinct changes in the different groups corresponding to their treatment. The measured total volume in the control (Placebo) group was significantly higher than the volume in the treatment group (fig.1).
During the course of the treatment the ratio of the cyst volume versus total renal volume was increasing in the untreated group, indicating that growth of the total renal volume in the untreated group was primarily due to the growth of the cysts, rather than the parenchyma (fig.2). Total renal volume and ratio of cystic versus total renal volume remained stable in the treated groups.
Fig.3 displays a regular mouse kidney (a), an untreated polycystic kidney (b) and a treated polycystic kidney (c), illustrating the therapeutic effect of the treatment and the changed structure of the polycystic kidneys.
In Conclusion we were able to show that it is possible to monitor the therapeutic effect of a novel anticystic treatment in a preclinical mouse model of PKD.

References: [1] Takahashi: J Am Soc Nephrol. 1(7) (1991**),** [2] Lee: Nephron Clin Pract 2006. c173-c180

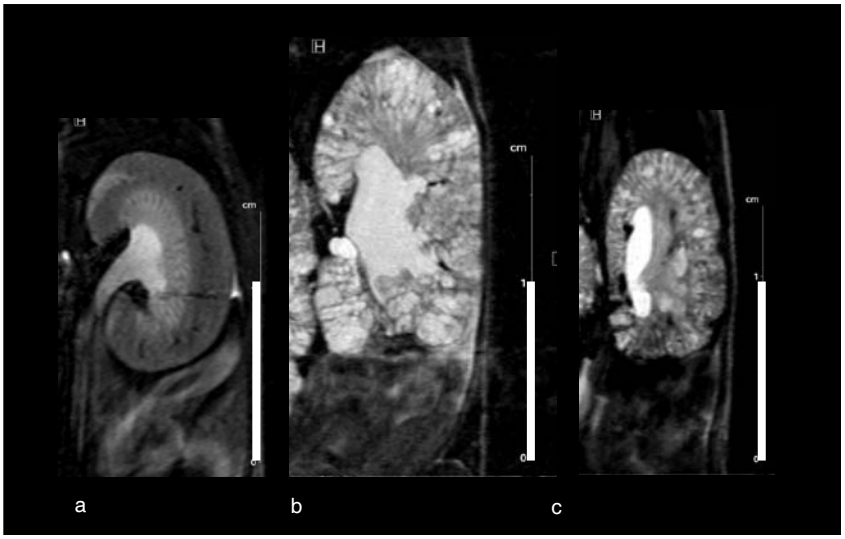

Fig.3: RARE Images with TE=36ms of normal mouse kidney (a), untreated *PCY-mouse model* (b) and treated *PCY-mouse model* (c). Bar in the picture is indicating 1cm.

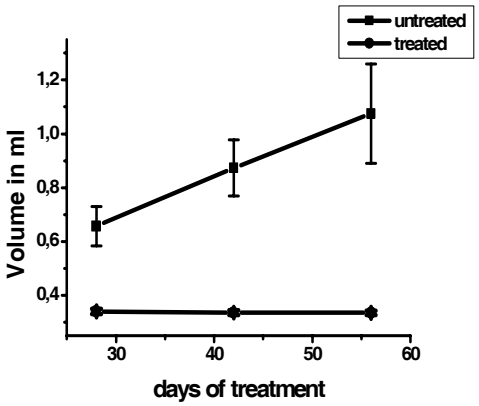

Figure 1: Total renal Volume during Therapy

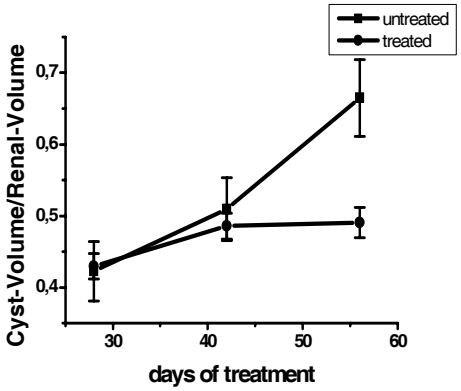

Figure 2: Cystic-Volume versus renal Volume during therapy