Early Imaging Biomarkers of ADPKD – Quantitative MRI and Texture Analysis in a Murine Model

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INTRODUCTION Currently, only a small amount of the wealth of information that could be made available by radiological imaging is used to assess disease status and follow progression of ADPKD. Advanced MR imaging techniques can be used to measure functional properties such as tissue perfusion, renal blood flow, and tissue oxygenation, as well as structural properties such as kidney volume, fibrotic and cystic load, and vascular geometry. We hypothesized that advanced MRI acquisitions and image analysis methods can go beyond currently utilized imaging features and illuminate renal tissue changes preceding changes in total kidney volume (TKV) in mice of different background.

METHODS *Pkd1*$^{RC/RC}$ model mice (seven C57BL/6 and seven *C57Bl6 × 129s6Svev/Tac* 'F1' background), as well as wild-type (five C57BL/6 and five 'F1' background) were imaged at 3, 6, and 12- weeks. Mice were anesthetized and imaging was performed with a 16.4T Bruker Avance™ 700 MHz vertical bore NMR spectrometer equipped with mini-imaging accessories. Measurement of TKV and texture was performed on axial T2-weighted images, and assessment of quantitative pa rameters were obtained for T1, T2, and T2* relaxation properties, as well as magnetization transfer. The quantitative acquisitions are acquired in the coronal plane, and regions-of-interest are drawn to cover cortical and medullary regions.

RESULTS Quantitative MR parameters and texture features were found to be early biomarkers of PKD. Shown in Figure 1 is the volume progression for the four groups, as well as boxplot results at baseline/3- weeks for TKV, T1 relaxation, and entropy texture feature. In the fast progressing group ('F1'), a significant increase in TKV was observed, whereas the C57BL/6 model did not show a significant increase in TKV at 3-weeks. In contrast, T1 relaxation properties and texture were found to well differentiate the model mice from corresponding wild-type.

CONCLUSIONS We found that quantitative MR parameters and texture features: (i) correlate with subsequent disease progression, and (ii) are early biomarkers of ADPKD. These parameters could be useful for pre-screening in trials as they inform on early disease. In addition, they may afford more parameters to evaluate treatment benefits, which may be assessable over shorter study durations.

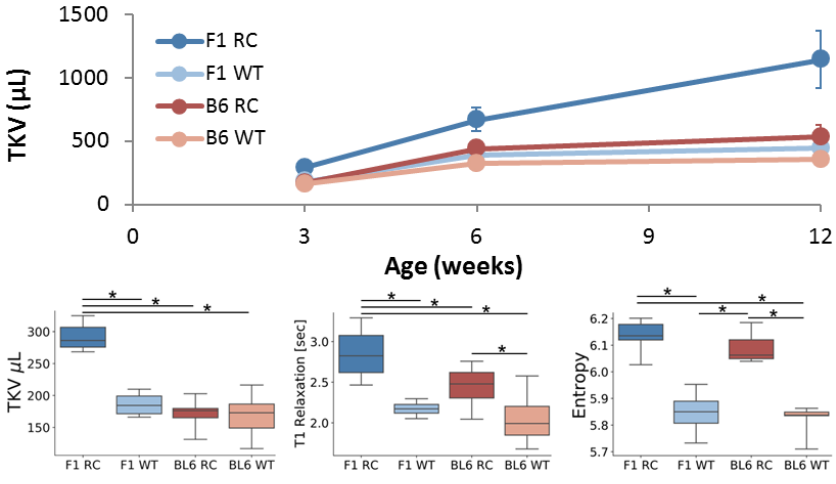

Figure 1. Top panel – volume progression of the four groups in this study. Bottom panel – boxplot comparisons of TKV (left), T1 relaxation (middle), and Entropy texture feature (right) at three week time point. Quantitative parameters, and texture features were found to distinguish RC model from corresponding wild type suggesting their suitability as early imaging biomarkers of PKD.