Ultrasound super-resolution imaging of the renal microvasculature changes in mouse acute kidney injury model

Qiyang Chen[1, 2], Jaesok Yu[1, 2], Brittney Rush[3], Sean D Stocker[3], Roderick J. Tan[3], and Kang Kim[1, 2, 3]

[1] Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA, USA. [2]Center for Ultrasound Molecular Imaging and Therapeutics, Department of Medicine & Heart and Vascular Institute, University of Pittsburgh School of Medicine and University of Pittsburgh Medical Center, Pittsburgh, PA, USA. [3] Department of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

Background, Motivation, and Objective:

Episodes of acute kidney injury (AKI) can lead to the permanent loss of renal function known as chronic kidney disease (CKD). One mechanism by which this occurs is via AKI-induced renal microvascular rarefaction. Ultrasound super-resolution (USR) imaging, which can identify microvessels with high spatial resolution beyond acoustic diffraction limit, can be a promising method to assess renal microvascular changes during AKI-to-CKD progression. In this study, the changes of renal microvasculature of the mouse kidney with AKI were quantitatively evaluated by USR and verified by histology to examine the feasibility and accuracy of USR for noninvasive assessment of the progressive kidney disease.

Statement of Contribution/Methods

AKI was induced on six mice by a unilateral ischemia-reperfusion injury under an approved animal protocol. Ultrasound scan was performed in vivo on contralateral healthy kidneys, 21 days and 42 days post-injury kidneys (n=3 for each group). A 0.1 mL bolus of 10% microbubbles (Definity) was intravenously injected. Ten seconds after injection, multi-angle plane wave imaging was applied using Verasonics Vantage system with a L22-14v probe (15.6MHz) to acquire the raw data of 1000 frames (250 frames/s). The raw data were processed through beamforming, motion compensation, SVD filter, Richardson-Lucy deconvolution, and frame summation to reconstruct the final USR images. Renal cortical size, relative blood volume (rBV), vessel density, and vessel tortuosity were quantitatively assessed based on the USR images. CD31 stain on the harvested kidney sections was performed to correlate with USR assessment.

Results/Discussion

The overall microvasculature rarefaction with the progression of AKI at different time points was observed in the USR images shown in Fig.1A with a spatial resolution of 32 μm. The decrease in cortical size, rBV, and vessel density of injured kidney, and increase in vessel tortuosity at 42 days compared to control were quantitatively evaluated by USR with statistical significance. The reduction of renal vessel density (Fig. C) around corticomedullary junction was evidenced by histology (Fig. 1B). A significant correlation with R^2 of 0.76 between USR and histology measurement of vessel density was demonstrated (Fig 1.D).

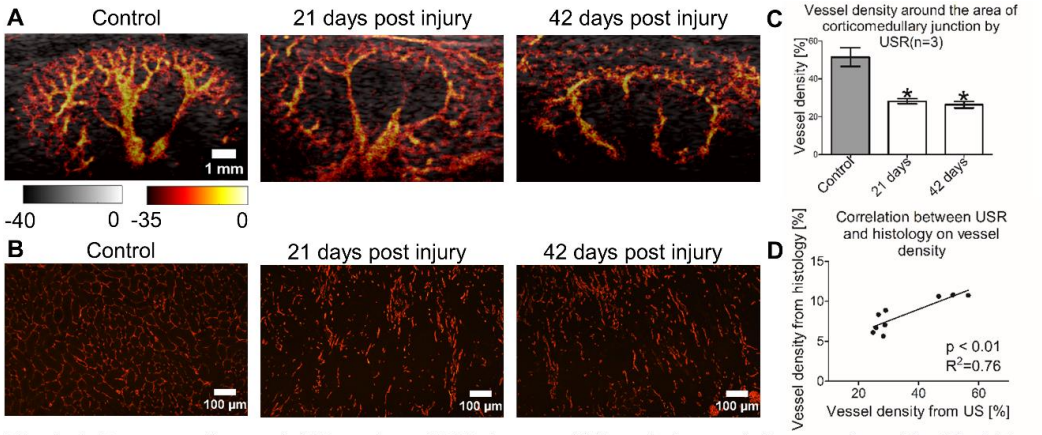

Fig. 1. A. Representative overlaid B-mode and USR images of kidney in long axis for contralateral healthy kidney, injured kidney at 21 days, and 42 days post injury. **B.** Representative CD31 stain for renal vasculature for corresponding groups. **C.** Vessel density around the area corticomedullary junction measured by USR. (ANOVA, n=3, *P<0.001) **D.** Correlation between USR and histology on vessel density. (Pearson's correlation p<0.01, R^2=0.76)