USING ULTRASOUND IMAGING FOR QUANTIFYING KIDNEY FIBROSIS

SUMMARY: A signal analysis technique using raw ultrasound radiofrequency (RF) data is proposed as a non-invasive method for the detection of kidney fibrosis for kidney transplants.

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Chronic Kidney Disease (CKD) affects ~10% of the world population and currently has no cure [1]. Kidney transplantation remains the only option for treatment, however, the donor pool is very small compared to the number of patients on the waiting list [2]. This small donor pool consequentially leads to patients receiving older, less healthy kidneys with pre-existing fibrosis. Fibrosis is characterized by the accumulation of extracellular matrix proteins, which impairs kidney function [3]. Biopsies are considered the gold standard of assessment but have limitations as they are invasive and are not representative of the total fibrotic burden on the kidney.

In this project, we are working towards exploring whether ultrasound (US) imaging can detect and quantify kidney fibrosis. US imaging is a non-invasive alternative to a renal biopsy, can assess the full kidney, and it is also widely accessible. Using signal analysis techniques on B-mode US images of murine kidneys, this work aims to find differences in US imaging for varying degrees of kidney fibrosis verified by histological results.

METHODS

EXPERIMENT

Fibrosis was induced in the left kidneys of 15 mice by obstructing the left ureters via Unilateral Ureteral Obstruction (UUO) surgery. The right kidneys were left unobstructed as controls. On days 0, 7, and 14, five mice were sacrificed, and their kidneys were imaged *ex vivo* using B-mode US in a saline bath at 4°C to mimic the conditions of a transplanted kidney. After imaging, histology slices were taken from the top, middle and bottom regions of the kidneys for histological analysis.

SIGNAL ANALYSIS

The signal analysis technique employed compares the signal amplitude (SA) values for each pixel in the kidney ROI for a series of B-mode images. The comparisons were made by taking the absolute differences in individual pixel SAs for each imaging frame relative to the first acquired frame. These changes are shown in Fig. 1 using coloured parametric maps of B-mode images to localize the areas of significant changes, and histograms to show the distribution of pixels experiencing a change in SA. All figures were generated using MATLAB.

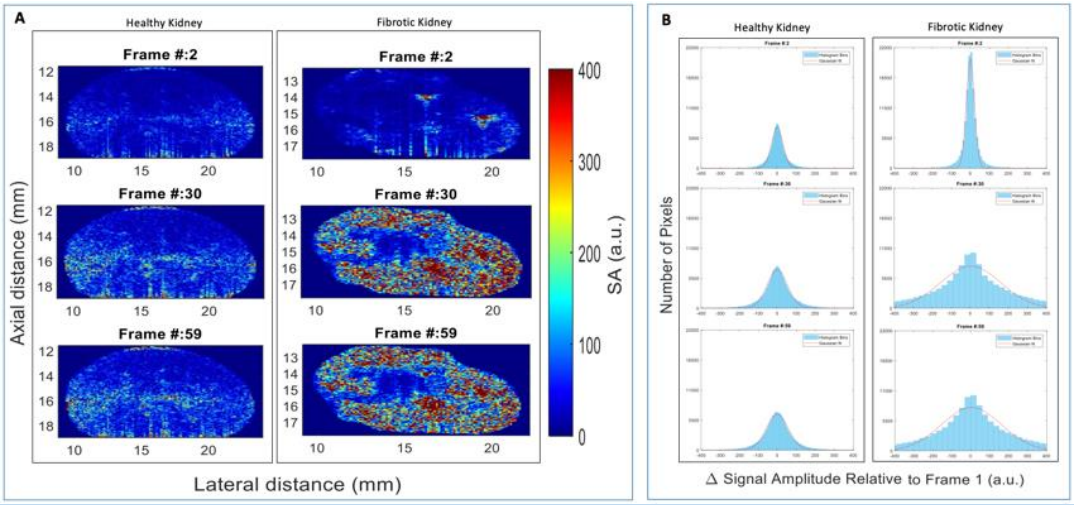

Figure 1. Changes in SA during a single 59-frame acquisition are shown for healthy and fibrotic kidneys as coloured parametric maps (A) and histogram distributions (B). 59 frames of B-mode images were taken using a frame rate of 5 frames per second, therefore frames 2, 30 and 59 correspond to imaging time-points of 0.4 s, 6.0 s, and 11.8 s, respectively.

In addition, a Gaussian fit was applied to each histogram, and the full width at half maximum (FWHM) for each Gaussian fit was plotted as a function of imaging time, where every 0.2 seconds corresponds to the next US frame (Fig. 2).

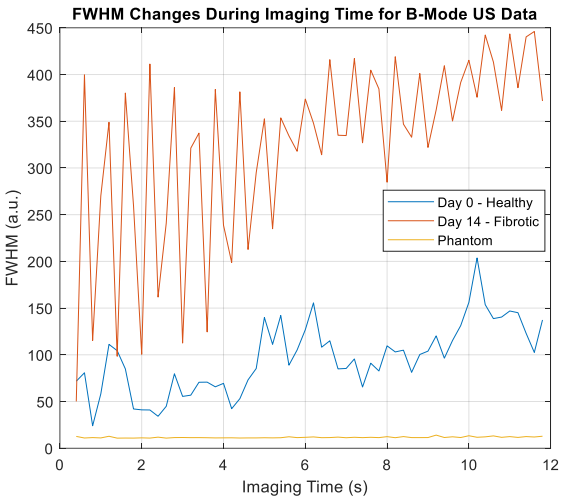

Figure 2. FWHM as a function of imaging time for histograms of healthy and fibrotic kidneys and a phantom.

DISCUSSION

From Fig. 1A, it is noted that SA values from *ex vivo* murine kidneys change over time in various locations, with the greatest changes corresponding to red pixels. Healthy kidneys show small changes in SA at an axial distance of ~16 mm and near the edges of the kidney, whereas fibrotic kidneys exhibit large changes in SA throughout the kidney. These observations can also be explained using Fig. 1B, where healthy kidneys give similar distributions throughout imaging time, while fibrotic kidneys have narrow histogram distributions at the beginning of imaging, which become broader as imaging time progresses.

When comparing the FWHM for the kidneys and the phantom in Fig. 2, the FWHM increases over imaging time for both kidney conditions but has very minimal changes over imaging time for the phantom. Fibrotic kidneys show the largest increase in FWHM over time.

CONCLUSIONS

These temporal changes in pixel signal amplitudes during US image acquisition suggest that this method, with further development, could be the new standard for the non-invasive quantification of kidney fibrosis. Larger changes in FWHM for kidneys compared to phantoms may indicate biologically induced motion in the kidneys during imaging. Furthermore, the larger increase in FWHM over time for fibrotic kidneys compared to healthy kidneys suggests that the FWHM to a fit of the distribution of SA changes could possibly be used as an indicator of kidney fibrosis.

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