

**PhD Thesis Title:** “Bubble Wavelet Decorrelation based Ultrasound Contrast Plane Wave Imaging and Microvascular Parametric Perfusion Imaging”

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## **ABSTRACT**

Due to the strong decorrelation characteristics of microbubbles under insonation, ultrasound contrast imaging can sensitively detect the perfusion information of microvessels, and parametric perfusion imaging (PPI) can accurately depict the spatial distribution of perfusion details and features. However, the ultrasound contrast imaging and PPI in musculoskeletal, heart disease, and intratumoral vascularity were limited by the disturbances from guided waves, the low contrast-to-tissue ratio (CTR) of plane wave imaging, and the low resolution and contrast of intratumoral PPI, respectively. According to the imaging theory of acoustic driven decorrelation characteristic of microbubbles, these limitations were clarified and overcome in this study.

The pure guided waves in tibia were detected and reconstructed through transmitting-air gap-receiving method. The guided waves with individual modes S0 (1.23 MHz) and A1 (2.06 MHz) were accurately obtained. The influences of guided waves on decorrelation characteristics of microbubbles, particularly the nonlinear scattering, were illustrated through the Marmottant model derived from measured guided waves, and then verified by continuous infusion experiments in a vessel-tibia flow phantom. Due to the individual modes S0 and A1 in the tibia, the peak values of the microbubble backscattered echoes were enhanced by  $83.57\% \pm 7.35\%$  and  $80.77\% \pm 6.60\%$  in the microbubble subharmonic frequency and subharmonic imaging, respectively. However, corresponding resolutions were  $0.78 \pm 0.07$  and  $0.72 \pm 0.12$  times of those without guided wave disturbances, respectively. Such enhancement of backscattered echoes were beneficial to improve the CTR of contrast images near the cortex, but the decrease in resolution prejudiced the identification of perfusion details and outlines.

An ultrasound contrast plane wave imaging method based on pulse inversion bubble wavelet decorrelation imaging (PIWI) was developed to improve the CTR of contrast images. Compared with those obtained in pulse inversion harmonic imaging, the CTR and detection sensitivity of microbubbles were improved by the PIWI technique up to  $10.09 \pm 2.96$  dB and  $12.52 \pm 2.10$  dB in *in vitro* experiments, respectively. The disruption rate and infusion time of microbubbles in PIWI-based plane wave imaging were then quantified using two perfusion parameters of area under curve and half transmit time estimated from denoised time-intensity

curves (TICs), respectively. The area under curve and half transmit time in plane wave imaging were 55.94% and 20.51% higher than those of conventional focused imaging, respectively. Due to its high CTR and low disruption of microbubbles, PIWI-based plane wave imaging has long infusion time and is therefore beneficial for transient monitoring and perfusion assessment of microbubbles circulating in vessels.

PPI of microvessels with single-pixel resolution and high contrast was proposed in this study. The single-pixel TICs were first extracted to ensure PPI with the highest resolution. The signal-to-clutter ratio of single-pixel TICs was enhanced by  $4.71 \pm 0.31$  dB using respiratory motion compensation and detrended fluctuation analysis; and the disturbances from respiratory motion and tissue clutters were removed effectively. Then, the disturbances from no-MBs regions and adjacent tissue were suppressed by using the filtration of valid TICs and targeted perfusion parameters. Compared with the conventional PPI with  $3 \times 3$  pixel resolution, the resolution of the proposed PPI was improved to single-pixel resolution; compared with the PPI with single-pixel resolution, the imaging efficiency and average contrast were improved by 49.6% and  $3.97 \pm 0.88$ , respectively. The edge, morphostructure, inhomogeneous hyper-enhanced distribution, and ring-like perfusion features in intratumoral vascularity were finally accurately distinguished by the proposed PPIs with high resolution and contrast.

#### KEY WORDS:

Ultrasound contrast imaging; Parametric perfusion imaging; Contrast; Resolution; Guided waves

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