
Ge Zhang¹, Sevan Harput¹, Hanyu Hu¹, Kirsten Christensen-Jeffries², Jiaqi Zhu¹, Jemma Brown², Chee Hau Leow¹, Chris Dunsby³*, Robert J. Eckersley²*, Meng-Xing Tang¹*

¹Department of Bioengineering, Imperial College London, London, UK, SW7 2AZ, United Kingdom
²Biomedical Engineering Department, School of Biomedical Engineering and Imaging Sciences, Kings College London, London, SE1 7EH, UK
³Department of Physics and Centre for Pathology, Imperial College London, London, SW7 2AZ, UK

* These authors contributed equally to this work

Corresponding author: MengXing.Tang@Imperial.ac.uk

Introduction

Ultrasound super-resolution imaging techniques have shown the capability of breaking the diffraction limit in spatial resolution [1,2]. However, these current localization-based ultrasound super-resolution imaging techniques rely on a low concentration of active flowing microbubble signals. This means that, for slow flows associated with the micro-vasculature, a longer acquisition time is required for the microbubbles to replenish. During this long acquisition time, motion is very likely to be introduced to lower the imaging quality of super-resolution imaging. Therefore, there is a need to develop a super-resolution imaging technique to acquire images sufficiently rapidly in order to avoid motion artefacts. We have recently developed Acoustic Wave Sparsely Activation and Localisation Micriscopy (AWLSALM) [3], which is able to achieve super resolution in no-flow condition using activataion and deactivation of phase change nano-droplets. While this method has great potential to achieve fast super-resolution imaging, the relatively high boiling point droplets used mean that separate ultrasound transmissions are required for droplets activation and for imaging, leading to extra acquisition time. In this study, fast acoustic wave sparsely activated localization microscopy (fast-AWSALM) is developed to simultaneously image, activate and deactivate octafluoropropane nanodroplets during high-frame-rate plane-wave ultrasound imaging to achieve ultrasound super-resolution images on a sub-second timescale.

Methods

Octafluoropropane nanodroplets consist of octafluoropropane liquid cores encapsulated by lipid shells. A 200 µm cellulose tube (Hemophan®, Membrana) phantom was fixed and immersed in a water tank where the walls were covered with acoustic absorbers. A L11-4v transducer equipped with ultrasound research platform (Verasonics Vantage 128, Kirkland, USA) was held 20 mm above the center of the tube. The water temperature was maintained at 24 °C. A concentration of diluted nanodroplet solution (~1.35×10⁷ PCCAs/mL) was prepared. A customised ‘Imaging/Activation’ sequence was implemented on an ultrasound research platform (Verasonics Vantage 128, Kirkland, USA) with a L11-4 38-mm linear array probe (ATL, USA). Briefly, a 1-cycle single-angle plane-wave pulse at 3.5 MHz with a peak-negative-pressure (PNP) of 1.42 MPa was transmitted in order to simultaneously image, activate, and deactivate the octafluoropropane nanodroplets. The frame rate was 5000 Hz and 1000 frames were acquired in 200ms. Singular value decomposition (SVD) processing was used to obtain the changing contrast signals. The SVD thresholds were automatically determined from the location of the largest gradient on the energy versus singular value order curve. After SVD processing, super-localization was performed to reject the noise and detect potential vaporized droplets [3]. The location of single isolated vaporized droplets was calculated by the “centroid” method. The resulting super-resolution map was created from all the localizations detected over all the imaging frames.
Results

Figure 1 shows three representative successive image frames after SVD filtering. It can be seen that the octafluoropropane nanodroplets were sparsely activated or deactivated by plane-wave pulses in the tube without any flow. Acoustic droplet vaporization has only been performed using focused single element transducers or linear-array probes with focus-wave transmissions in previous literature. The activation of nanodroplets via plane-waves without the need of using focus-wave enables a faster imaging and activation acquisition. Figure 2 shows the comparison between the summation of 1000 conventional B-mode image frames acquired in 200 ms and the corresponding super-resolution image which superimposes all the localization events in these 1000 frames. It can be seen that, in the super-resolution imaging, it not only has a better resolution but also help to remove some imaging artefacts appeared on the B-mode image. Figure 3 shows the resolution measurement of the B-mode and super-resolution image at the same lateral ROI from -8.6 to -8.4 mm. According to the measurement, the super-resolution image gives a FWHM of 190 µm whereas the B-mode image shows a FWHM value of 550 µm.

Figure 1. Three representative successive SVD-filtered image frames shows that octafluoropropane nanodroplets were sparsely activated or activated octafluoropropane nanodroplets were sparsely deactivated. Images were acquired with no flow in the tubes.
Figure 2. The summation of 1000 conventional B-mode image frames acquired in 200 ms (b) Super-resolution image superimposes all the localization events in 1000 frames acquired in 200 ms. Note that there is no flow in the tube.

Figure 3. Full-width-half-maximum (FWHM) resolution measurement of the B-mode and super-resolution images at same lateral region of interest (ROI) from -8.6 to -8.4 mm.

Conclusions

In summary, this study demonstrates sub-second temporal resolution super-resolution can be achieved using the proposed fast-AWSALM – using high-frame-rate plane-wave transmit pulses to simultaneously image, activate and deactivate the octafluoropropane nanodroplets. The imaging frequency used in this study (3.5 MHz) indicates that this technique can be used for deep-tissue imaging. The acoustic pressure of the plane-wave pulses was well within the FDA-approved safety range. This study shows fast-AWSALM, a faster version of AWSALM, which is also flow independent and does not require a precise control on contrast agent concentration.

References