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Introduction

As cancer needs nutrients and oxygen to grow and spread, it triggers angiogenesis and neovascularization. Consequently, there is growing interest in developing imaging modalities able to detect, localize, and visualize these processes. To this end, dynamic contrast-enhanced ultrasound (DCE-US) represents a valuable option. Unfortunately, performing handheld DCE-US is challenging for the breast as, unlike X-ray CT or MRI, DCE-US imaging of the breast is highly operator dependent.

Based on our recent discovery of a new marker for ultrasound contrast agents (UCAs) [1-2], we are currently developing a novel imaging technique named cumulative phased delay imaging (CPDI). CPDI could potentially lead to the development of three-dimensional contrast-enhanced ultrasound computed tomography (3D CEUS-CT), providing a radiation-free imaging modality that enables visualization of the whole breast vascular architecture in 3D. Such an imaging modality would open new horizons for the detection and localization of breast cancer.

Method

A (positive) cumulative phase delay (CPD) between the second harmonic (2H) and fundamental (F0) component is observable for ultrasound (US) propagating through UCA. This delay is dependent on agent concentration, propagation path length through UCA, pressure field amplitude, and insonating frequency. Most importantly, this delay is absent in tissue, and clearly observable at frequencies (2.5 MHz) and pressure regimes ($0.05 < MI < 0.2$) of interest for clinical application [1-2]. Consequently, variations in the total time delay between 2H and F0 can be exploited to image and detect UCAs.

Results

Numerical and *in-vitro* studies confirmed the applicability of CPDI for contrast specific US imaging [2-3], with CPDI showing superior capabilities in detecting and localizing UCA, as compared to speed-of-sound and dispersion-based US tomography [3-4]. Furthermore, phantom experiments showed how cavities of different size (filled with UCA and surrounded by tissue-mimicking material), which were down to 1 mm in diameter, could clearly be detected [3] (see Figure 1). CPD image values relate to the measured delay, which is here expressed in cycles/m.

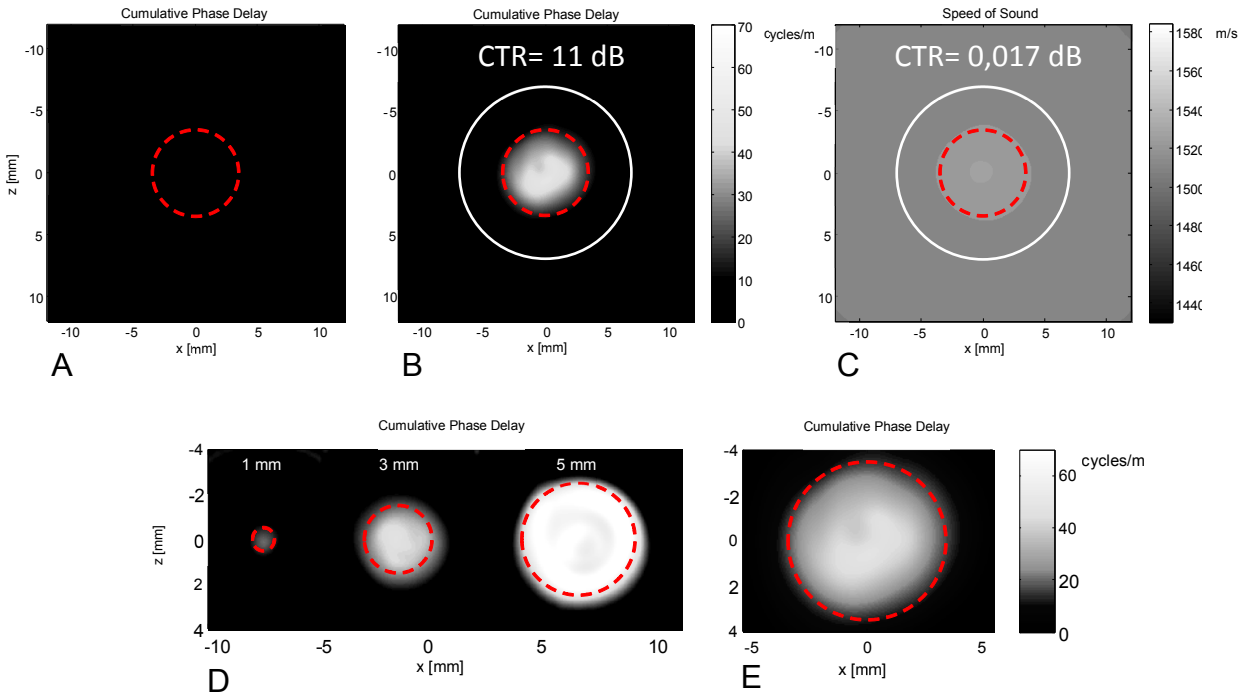

Figure 1: CPD images of a tissue-mimicking phantom containing a 7-mm cavity filled with (A) only saline and (B) SonoVue®. (C) Speed of sound tomographic image as obtained for the same intra-cavity UCA concentration. Contrast to tissue ratio (CTR) values are also shown. CPD images of tissue-mimicking phantoms containing (D) three cavities (measuring from 1 to 5 mm in diameter) and (E) a single 7-mm cavity filled with SonoVue® [3].

Conclusion and Discussion

CPDI may find relevant application to the development of contrast enhanced ultrasound tomography of the breast aimed at angiogenesis imaging for cancer detection and localization. To this end, investigating the performance of CPDI in estimating UCA flow dynamics and imaging more complex and heterogeneous targets will be the focus of future work.

References

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