Monitoring the progression of breast cancer in an orthotopic-4T1 mouse model using single transducer harmonic motion imaging

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Introduction

- Breast cancer is the second leading cause of death from cancer in women in the USA.
- Mammography and ultrasonography are used as screening tests for breast cancer.
- Collagen density is associated with increased mammographic density.
- Study found that stiffness of breast cancer tumor in mouse model was correlated to the amount of collagen.
- Ultrasound elastography (USE) is a non-invasive technique that assesses the elasticity of tissues by measuring tissue displacement when a force is applied.
- Acoustic radiation force (ARF) uses sound waves to displace tissue.
- Harmonic motion imaging (HMI) is an ARF-based method that uses a focused ultrasound transducer to generate harmonic oscillation and an imaging transducer to track the harmonic oscillation.
- Instead of two different transducers, single transducer harmonic motion imaging (ST-HMI) uses single ultrasound transducer to generate and track harmonic oscillation to facilitate data acquisitions.
- ST-HMI at single frequency indicated that the stiffness of a tumor increased over time relative to non-cancerous background tissue in a breast cancer mouse model.
- Instead of acquiring data at one frequency data at a time, ST-HMI was extended to collect 100-1000 Hz oscillation data in a single acquisition. Thus, the method is called multi-frequency ST-HMI.

Objective

- Monitor the progression of tumor in an orthotopic-4T1 mouse model using multi-frequency ST-HMI and investigate the performance of each oscillation frequency

Methods

- Multi-frequency excitation (push) pulse is a sum of sinusoids with frequencies of 100-1000 Hz and increments of 100 Hz (Fig. 2, Equ. (1)).
- Continuous multi-frequency push pulse was sampled to generate discrete push pulses (Fig. 2).
- Tracking pulses were transmitted in between the discrete push pulses to estimate the motion in the tissue (Fig. 2).
- Displacement versus time profile were generated for each pixel (Fig. 3b).
- Differential displacement (DD) was calculated for each pixel (Fig. 3c).
- Fourier Transform of DD was used to determine values of bandpass filter for the oscillation frequencies (Fig. 3d).
- DD was filtered at each oscillation frequency and pixel to generate P2PD image (Fig. 3e).

Results

- 8-10 week old female BALB/c mice were anesthetized (1-2% isoflurane in oxygen) and placed in supine position on heating pad.
- Mice were injected with 2 × 10⁶ 4T1 breast cancer cells in the 4th inguinal mammary fat pad.
- ST-HMI was performed using Verasonics Vantage Ultrasound System (Vantage, Inc., Kirkland, WA, USA) with an L11-5 linear array transducer5.
- ST-HMI-derived peak-to-peak displacement (P2PD) images were generated at oscillation frequencies of 100-1000 Hz.
- Mice were imaged 7, 12, 18, and 25 days after tumor injection5.

Discussion and conclusion

- In Mouse # 1, the P2PD ratio increased over time at each oscillation frequency.
- In Mouse # 2, the P2PD ratio stayed the same or increased depending on the oscillation frequency.
- Increase in P2PD ratio indicated that the tumor was stiffening over time relative to the background tissue.
- Tumor size increased over time. Method of calculating tumor size could be improved.
- Future work will analyze P2PD ratio in a larger sample of mice to explore why stiffness increased faster and slower in Mouse # 1 versus # 2 with histopathological validation.

References


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