

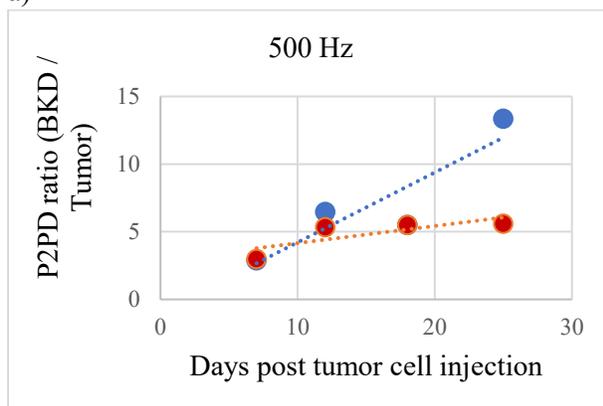
Monitoring the progression of breast cancer in an orthotopic-4T1 mouse model using single transducer harmonic motion imaging

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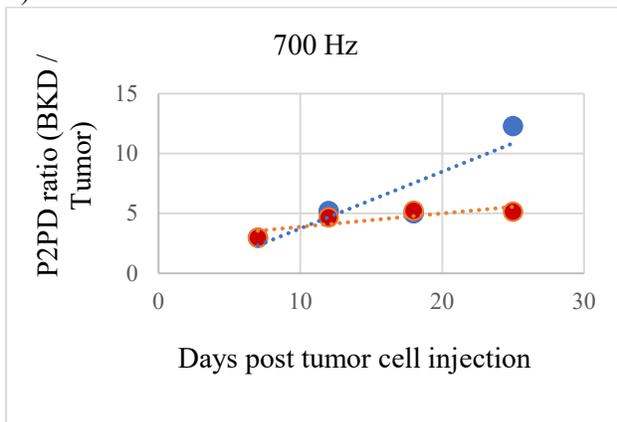
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Breast cancer is the second leading cause of cancer-related death in women in the USA¹. Mammography and ultrasonography are generally used to screen patients for breast cancers⁴. Instead of mammography and ultrasound-based morphological imaging, ultrasound elastography (USE)-derived mechanical properties like elasticity can be used to detect breast cancer as the breast tumor is generally stiffer due to increased deposition of collagen fiber. One of the USE methods uses acoustic radiation force (ARF) to displace tissue at the micron level and uses ultrasound pulse to estimate the displacement. From the estimated displacement, the elasticity of tissue is inferred. Single transducer harmonic motion imaging (ST-HMI) is an ARF-based method to assess the elasticity of tissue by using a single ultrasound transducer to generate and track harmonic oscillation⁷. Previously, ST-HMI-derived displacements at a single frequency indicated that the stiffness of a tumor increased over time relative to non-cancerous background tissue in a 4T1 mouse model⁶. Instead of collecting one frequency data at a time, multi-frequency ST-HMI was used to collect 100-1000 Hz oscillation data in a single acquisition⁷. The objective of this work is to monitor the progression of a tumor in an orthotopic-4T1 mouse model using multi-frequency ST-HMI and investigate the performance of each oscillation frequency. 8-10 week old female BALB/c mice were anesthetized and injected with 2×10^5 4T1 breast cancer cells in the 4th inguinal mammary fat pad⁶. Multi-frequency ST-HMI was performed using Verasonics Vantage Ultrasound System (Vantage 256, Verasonics Inc., Kirkland, WA, USA) with an L11-5 linear array transducer at 7, 12, 18, and 25 days post-tumor-cell injection^{6,7}. ST-HMI-derived peak-to-peak displacement (P2PD) images were generated at oscillation frequencies of 100-1000 Hz with increments of 100 Hz. In Mouse # 1, the P2PD ratio increased over time at each oscillation frequency with slope [0.33 – 0.69] and R^2 [0.80 - 0.88]. In Mouse # 2, the P2PD ratio stayed the same or increased depending on the oscillation frequency with slope [-0.045 – 0.13] and R^2 [0.014 – 0.71]. The increase in the P2PD ratio indicated that the tumor was stiffening over time relative to the background tissue. Tumor size also increased over time, but the 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 in Mouse # 1 and slower in Mouse # 2 with histopathological validation.

a)



b)



c)

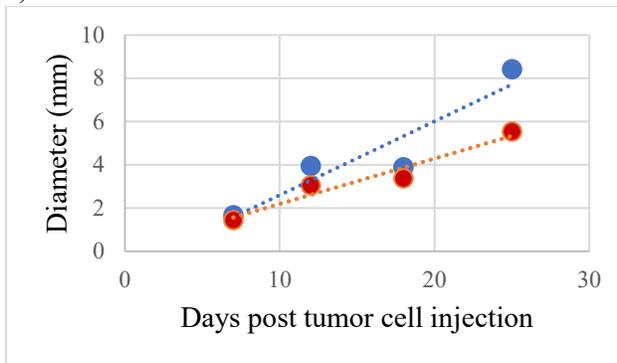


Figure 6. P2PD ratio at 500 Hz (a) and 700 Hz (b) versus time after tumor cell injection for Mouse # 1 (blue) and Mouse # 2 (red). (c) Tumor's diameter of Mouse # 1 (blue) and Mouse # 2 (red) versus time after tumor cell injection.

References

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