Imaging of Single Transducer – Harmonic Motion Imaging (ST-HMI)-derived Displacements at Several Frequencies Simultaneously: Experimental Demonstration in a Breast Cancer Mouse Model and Breast Cancer Patients

Md Murad Hossain[1], Niloufar Saharkhiz[1], and Elisa E. Konofagou[1], [1]Department of Biomedical Engineering, Columbia University, New York, NY, USA.

Background, Motivation and Objective.

ST-HMI interrogates the mechanical properties of tissues at the "on-axis" to acoustic radiation force (ARF) by transmitting tracking pulses in-between the discrete excitation pulses. By modulating excitation pulse duration, harmonic oscillation at a particular frequency is generated in ST-HMI. While "off-axis" shear wave speed at different frequencies was investigated previously, the impact of frequency on the "on-axis" displacement was not explored. We hypothesize that the frequency of oscillation in ST-HMI can be optimized to delineate the different size and stiffness inclusions. Towards the goal of generating ST-HMI-derived displacements at several frequencies simultaneously, this study investigates a new excitation pulse composed of a sum of sinusoids with different frequencies.

Statement of Contribution/Methods.

A continuous excitation pulse (cEP) was generated by summing sinusoids with 100:100:1000 Hz and then, normalized to have a range of values from 15-100 µs. The cEP was sampled to generate 6 discrete excitation pulses per period (1/100 Hz) to interleave tracking pulses with PRF of 10 kHz. The new excitation pulse was implemented using a Verasonics Vantage system and L7-4 (phantom and Human) or L22-14vxLF (Mouse) arrays with (excitation, tracking) pulses' center frequency of (4.0, 6.1) or (15.63, 20.8) MHz. ST-HMI and ARFI imaging of 6, 9, and 70 kPa inclusions with 10.4 mm diameter (D) and the 36 kPa inclusions with D=10.4, 6.5, 2.5, and 1.6 mm were performed and compared using CNR. In vivo, ST-HMI imaging with the novel excitation pulse was also performed in a breast cancer patient (F, 65 years with invasive ductal carcinoma) and 4T1 breast tumors in mice (N=2).

Results/Discussion.

The ST-HMI at 900 and 1000 Hz but not ARFI detected 36 kPa inclusion (D=1.6 mm) (Fig. 1(a)). The highest CNR was achieved at frequencies (300, 300, 600) Hz for (6, 9, 70) kPa inclusions (D=10.4 mm) and (300, 400, 1000, 1000) Hz for 36 kPa inclusion (D=10.4, 6.5, 2.5, 1.6 mm). The ST-HMI-derived maximum CNR was higher than ARFI irrespective of inclusions' size and stiffness (panel (b)). The maximum CNR was achieved at 500 and 1000 Hz for mouse and human tumors, respectively (panels (c, d)). The range of P2PD ratio of healthy versus tumor was 0.87-1.72, 1.78-2.78, and 1.81-1.96 in mouse # 1, 2, and human, respectively. These results suggest the importance of using a multi-frequency excitation pulse to simultaneously generate displacement at several frequencies to better delineate smaller and stiffer inclusions or lesions at higher frequencies and vice versa.

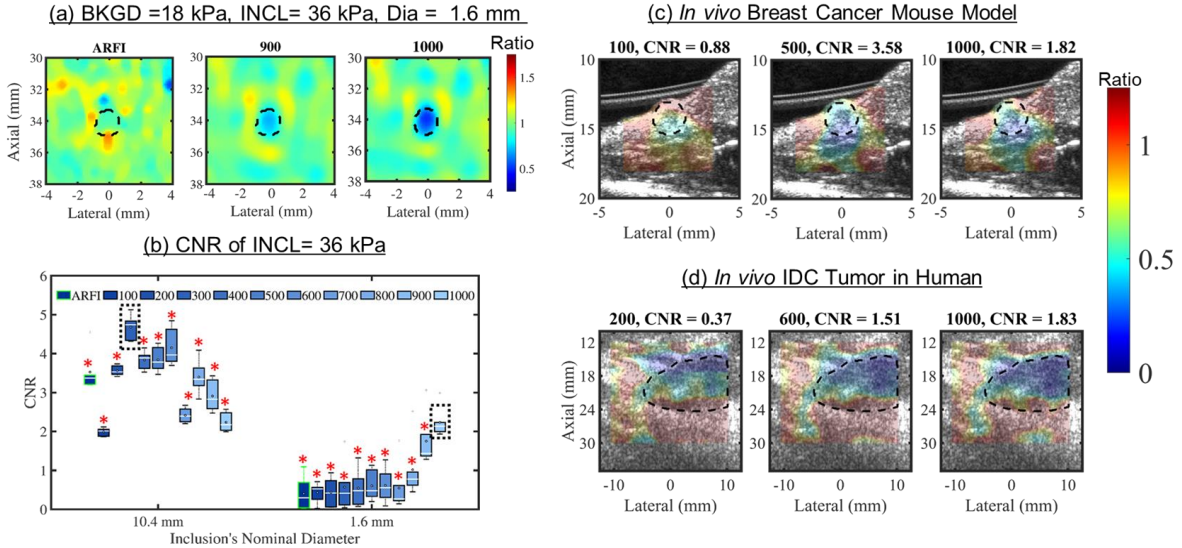

Fig. 1: (a) ARFI normalized peak displacement and ST-HMI normalized peak-to-peak displacement at 900 and 1000 Hz images of 1.6 mm, 36 kPa inclusion (INCL) embedded in an 18 kPa background (BKGD). (b) CNR of ARFI (green box) and ST-HMI derived images at 100:100:1000 Hz (shade of blue) of 36 kPa inclusions with 10.4 and 1.6 mm diameters. Data are plotted as median ± 0.5*interquartile range over 6 repeated acquisitions. Red asterisks represent when Kruskal–Wallis test suggests a statistical difference ($p < 0.05$) and median CNR were statistically different (Sign Ranksum, $p<0.05$) from the highest median CNR (dotted black box). (c) Representatives normalized P2PD images of a mouse (#2) tumor (diameter = 2.2 mm) at 100, 500, and 1000 Hz after 3 days of tumor cell injection with corresponding CNR at the title. (d) Representatives normalized P2PD images of Human invasive ductal carcinoma (IDC) tumor at 200, 600, and 1000 Hz with corresponding CNR at the title. Normalized P2PD was lower at tumor for both mouse and human indicates tumor is stiffer than the surrounding non-cancerous tissue. All boundaries (dotted black contour) of either inclusions or tumors were derived from the B-mode ultrasound image.