Harmonic Motion Imaging – Applications in the Detection of Stiffer Masses

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Abstract - The technique of Harmonic Motion Imaging (HMI) utilizes the localized stimulus of the oscillatory ultrasonic radiation force as produced by two overlapping beams of distinct frequencies, and estimates the resulting harmonic displacement in the tissue in order to assess its underlying mechanical properties. In this paper, we studied the relationship between the measured displacement and the gel/tissue stiffness. Two focused transducers with a 100 mm focus were used at the frequencies of 3.7500 MHz and 3.7502 MHz (or, 3.7508 MHz depending on the case), respectively, in order to produce an oscillatory motion at 200 Hz in the gel (or, 800 Hz in the tissue). A 1.1 MHz diagnostic transducer (Imasonics, Inc.) was also focused at 100 mm and acquired RF signals of 5 ms in total duration (PRF =3.5 kHz) at 100 MHz sampling frequency during radiation force application. First, three acrylamide gels of 50 x 50 mm^2 were prepared at concentrations of 4%, 8% and 16%. The resulting displacement was estimated using crosscorrelation techniques between successively acquired RF signals with a 2 mm window and 80% window overlap at 1260 W/cm^2. A 1-D normal indentation instrument (TeMPeST) applied oscillatory loads at 0.5-200 Hz with a 5 mm-diameter flat indenter. Then, 12 displacement measurements in six ex vivo porcine muscle specimens (2 measurements/case) were made using 1260 W/cm^2, before and after ablation for 10s at 1260 W/cm^2. In all gel cases, the harmonic displacement was found to steadily decrease with gel concentration. The TeMPeST measurements showed that the elastic moduli for the 4%, 8% and 16% gels equaled 3.93+/-0.06kPa, 17.1+/-0.2kPa and 75+/-2kPa, respectively; demonstrating, thus, that the HMI displacement estimate depends directly on the gel stiffness. Finally, in the ex vivo tissues, the mean displacement amplitude showed a two-fold decrease between non-ablated and ablated tissue; depicting thus the stiffness dependence of the HMI response in tissues.

I. INTRODUCTION

Mechanical properties of tumor tissues are known to differ from the surrounding tissues as indicated by the use of palpation as a diagnostic tool. This is especially true in the breast [1]. Infiltrating ductal carcinoma have been found to have average moduli of 558 $\pm$180 kPa compared with 48 $\pm$ 15 and 20 $\pm$ 8 kPa for normal glandular and fat tissue in the breast (Krouskop et al. [1]). As a result, several methods have been developed to estimate tissue stiffness, or stiffness-dependent tissue responses, following a mechanical stimulus [1-6].

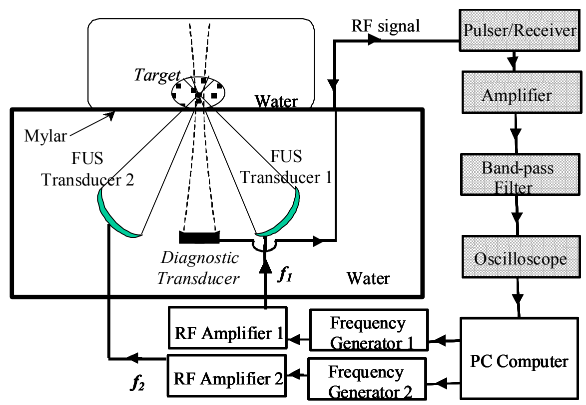

Figure 1: Harmonic Motion Imaging setup

The development of Localized Harmonic Motion Imaging (HMI) has already been described [4]. The main principle behind the proposed technique is that local harmonic motion can be precisely estimated and imaged in tissues as induced by an oscillatory, remotely applied, harmonically varying radiation force of amplitude F_0 (Fig. 2). In this study, we utilize the radiation force that is applied via using two overlapping beams radiating at slightly different frequencies, same as the method in [2]. However, the harmonic motion is estimated at different snapshots of the motion (t_1, t_2, etc.) using crosscorrelation of RF ultrasonic signals acquired at the same location undergoing vibration by a separate ultrasound beam diagnostic transducer (Fig. 3).

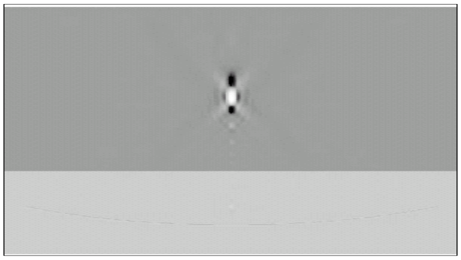

Figure 2: Localization of the radiation force in the tissue (upper block) produced by the FUS transducers radiating through the lower (water) block of the image. Image courtesy of Chris Connor [9].

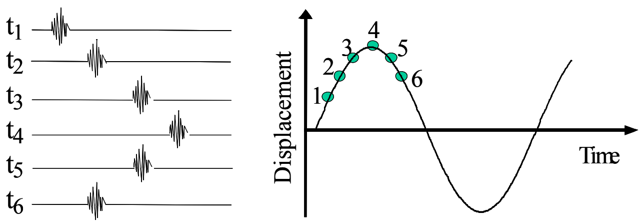

Figure 3: Harmonic Motion Imaging: RF line tracking at different time instants (t_1, t_2, etc.) acquired at the focus of the diagnostic transducer (Fig. 1) yields precise displacement estimates and identifies the characteristics of the locally induced vibration [4].

In addition, the local elastic modulus E can be directly estimated from the characteristics of the harmonic motion [1], i.e.,

$$E = \frac{2\left(1-\nu^2\right)F_0 r}{X_0 A}, \qquad (1)$$

where $F_0=2\alpha I/c$, A is the cross-sectional area of the beam at the focus, r is the radius of the beam at the focus, α is the absorption of the tissue, I is the intensity of the radiation force generating transducers and c is the speed of sound [5]. In this paper, the dependence of the HMI response on the underlying elastic modulus is examined using gel phantom and ex vivo tissue experiments.

II. METHODS

Gel experiments

First, three acrylamide gels of 50 x 50 mm^2 were prepared at concentrations of 4%, 8% and 16% following Protocol 2 in [10]. The resulting displacement was estimated using crosscorrelation techniques between successively acquired RF signals with a 2 mm window and 80% window overlap at 1260 W/cm^2. Sephadex beads were added in the gel phantoms for scattering [4]. Two focused ultrasound transducers were utilized operating at a frequency of 3.75 MHz and at slightly different frequencies (Fig. 1). A PZT composite diagnostic transducer (Imasonics, Inc.) was also operated at pulse/receive mode at a frequency of 1.1 MHz and focused at a depth of 10 cm. The focused transducers and the diagnostic probe were all focused on the same region of the tissue-mimicking gel phantoms in order to ensure highest signal-to-noise ratio of the signal to be tracked (Fig. 3). The pulse duration was equal to 0.28 ms and a PRF of 3 kHz was used. RF data was of total duration equal to 10 ms and acquired at a sampling frequency equal to 50 MHz. The data were acquired and digitized on a digital oscilloscope (Yokogawa DL 7100, Tokyo, Japan) and stored on disk. RF signal tracking was performed using cross-correlation techniques with a window on the order of 1-2 mm. Estimates of the displacement relative to the initial position (i.e., at the onset of the application of the radiation force) were obtained during the application of the radiation force that oscillated at the frequency of 200 Hz in order to maintain consistency with the mechanical testing parameters. The focused ultrasound intensity used was approximately equal to 1260 W/cm^2. Prior to displacement estimation, the signals received were filtered using a notch filter that filtered the fundamental frequency of the radiation force generating transducers (in this case 3.75 MHz) and all its harmonics. As an independent technique for measuring the tissue elastic modulus, an indentation instrument, the TeMPeST 1-D (Fig. 4 [7]), was employed to determine the tissue sample impedance from 0.1 to 200 Hz. This instrument applies a load onto the tissue sample surface with a 5 mm right circular indenter, recording the applied force and relative motion away from an initial indentation caused by an applied preload force. For special geometries and approximations regarding the behavior of the tissue, a number of closed form solutions relate impedance (compliance) to the underlying material properties. If a sample is approximately semi-infinite (i.e. the deformation and indenter are small relative to the sample), linearly elastic, homogeneous and isotropic, and the contact is frictionless, then elasticity and compliance are related as: $E=(1-v^2)/dc$, where E is Young's Modulus, v is the Poisson's ratio, d is the indenter diameter and c is the measured compliance (inverse of spring constant).

Many tissues are found to be approximately incompressible, so v is often assumed to have a value close to 0.5 (0.495 is used here). To capture the visco-elastic and inertial character of the tissue, we employ a modified Voigt model [8], which includes a lumped element to represent the density and effective volume of the tissue deformed/vibrated by the indenter. We assume that for a given preload the stiffness is locally linear (i.e. we linearize about a specific point on a non-linear force/displacement characteristic curve), which permits us to calculate the effective mass from the limiting value of the static compliance and the natural frequency of the response. The damping coefficient can be determined from the ratio between the static and peak values of the compliance [9]. From these relations, an expression for material elasticity can be determined as a function of frequency and applied mean stress.

Tissue experiments

Samples of porcine muscle were obtained from recently euthanized subjects of unrelated experiments and immediately immersed in a 0.9% saline. Within an hour post mortem, these samples were prepared by cutting them into slabs with approximately parallel upper and lower surfaces. They were placed on rigid substrates, and tested with the TeMPeST instrument using a "chirp" signal—a sinusoidal force with a monotonically increasing instantaneous frequency. The frequency range of the chirp was 0.1 to 200 Hz, and chirps of both increasing and decreasing frequency were employed to avoid any effect of tissue creep, which might be observed as a decrease in measured stiffness from the beginning to the end of a chirp—a change related to time, but not the instantaneous frequency. An 'N' of at least 3 was obtained for each preload force.Subsequent to these initial tests, HMI measurements were made using the same parameters as those used in the gel experiments and at the same location of the muscle sample as that of the TeMPeST measurement. A lesion was then created at approximately the same location (at the surface of the tissue) using the same transducers and an ultrasonic intensity of 1260 W/cm^2 for 20s. Ultrasonic signals were acquired and HMI displacements were then made using the same parameters as those used before ablation. The stiffness was evaluated using HMI, after which the indentation tests were repeated directly over the lesion location. The length scale of the lesion was approximately the same as the diameter of the indenter tip (5 mm in diameter). Finally, 12 HMI displacement measurements in six ex vivo porcine muscle specimens (2 measurements/case) were made using 1260 W/cm^2, before and after ablation for 10 s at 1260 W/cm^2 without any mechanical testing verification. All remaining parameters were identical to those used in the gel experiments.

III. RESULTS

Gel Experiments

Following the model discussed in the methods section, the TeMPeST measurements showed that the elastic moduli for the 4%, 8% and 16% gels equaled 3.93+/-0.06kPa, 17.1+/-0.2kPa and 75+/-2kPa, respectively. The variation of the HMI displacement amplitude with the measured gel modulus are shown with time in Fig. 6. A steady decrease in amplitude was noted with increasing stiffness, similar to that observed in the case of the simulations [4].

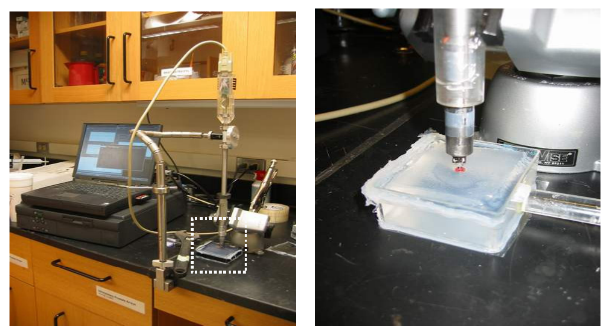

Figure 4: a) TemPesT setup; b) Gel and indentor detail.

Tissue Experiments

Figure 5 clearly shows that compliance falls (stiffness increases) with increasing preload. This is further reflected in the increase of natural frequency with preload for two reasons: natural frequency is proportional to the square root of stiffness; and with a stiffer response, the amplitude of tissue vibration will be smaller, reducing the effective volume (and mass) of moving tissue, the square root of which is inversely proportional to the natural frequency.

Figure 6 shows the variation of the HMI displacement amplitude between normal and ablated tissue. The mean displacement amplitude showed a two-fold decrease between non-ablated and ablated tissue; depicting thus the stiffness dependence of the HMI response in tissues.

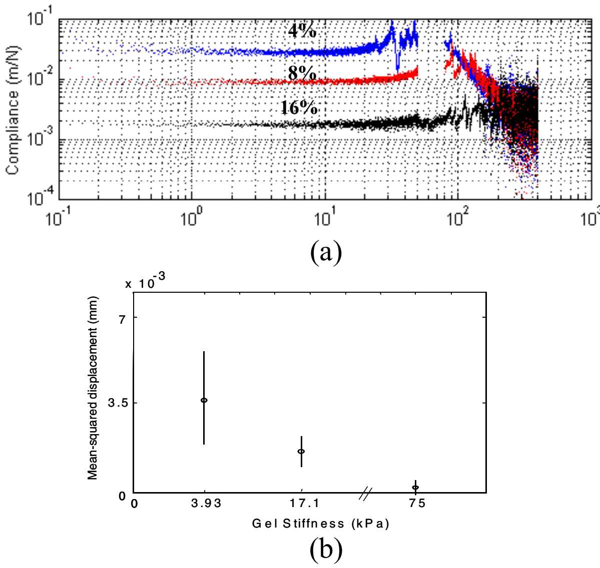

Figure 5: a) Acrylamide gel compliance magnitude vs. frequency (Hz). Compliance under varying preload and comparison of compliance for the different gels.; b) Mean-squared displacement at different acrylamide gel stiffnesses. The errorbars correspond to one standard deviation obtained from two independent locations in each gel.

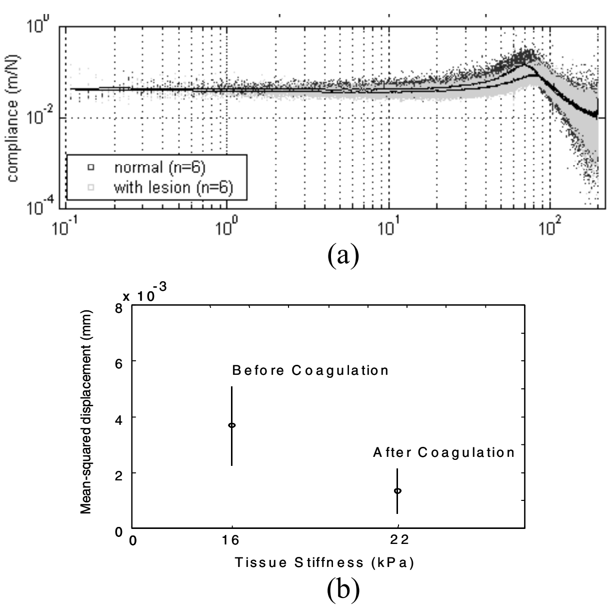

Figure 6: a) Porcine muscle compliance Bode (magnitude-phase) plots. Compliance under varying preload and comparison of compliance with and without lesion.; b) Mean-squared displacement before and after coagulation. The errorbars correspond to one standard deviation obtained from two independent locations in each sample.

IV. DISCUSSION

Harmonic Motion Imaging is a new technique that applies an oscillatory radiation force at large depths in tissues using two focused ultrasound transducers and estimates the resulting motion using a diagnostic ultrasonic transducer. It was previously shown using simulations that the estimated HMI amplitude decreases with tissue modulus. In this paper, this observation was verified experimentally. A 1D indentation system (TeMPeST) was employed to measure the modulus of gels at different acrylamide concentrations, and porcine muscle tissue ex vivo before and after coagulation. In both cases, the HMI displacement amplitude was shown to decrease with the measured modulus; reinforcing, thus, the premise of HMI for direct tissue modulus estimation.

V. ACKNOWLEDGMENTS

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VI. REFERENCES

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