

# LOCALIZED HARMONIC MOTION IMAGING: THEORY, SIMULATIONS AND EXPERIMENTS

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*Abstract* - Several techniques have been developed in an effort to estimate mechanical properties of tissues. These techniques typically estimate static or harmonic motion resulting from an externally or internally applied mechanical stimulus. In this paper, we discuss the advantages of utilizing a new technique that performs RF signal tracking in order to estimate the localized oscillatory motion resulting from the harmonic radiation force produced by two focused ultrasound transducer elements with overlapping beams oscillating at distinct frequencies. Four agar gels were utilized in order to determine the effect of stiffness on the motion amplitude. 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 frequencies ranging between 200 Hz and 800 Hz. In the simulations, an exponential decrease of the displacement amplitude with stiffness was observed at all frequencies investigated. An M-mode version to depict both the spatial and temporal variation of the locally induced displacement was used. In experiments with gels of different stiffness, the resulting amplitude of the harmonic displacement estimated oscillated at the same frequencies and an exponential decrease of the displacement amplitude with gel stiffness was also observed. In tissue experiments, the results showed that the method is feasible in tissues and that FUS ablation can be detected. These preliminary results demonstrate the feasibility of imaging localized harmonic motion as induced by an oscillatory ultrasound radiation force. Due to the highly localized and harmonic nature of the estimated response, this technique may be proven highly suitable for accurate estimation of the elastic modulus variation in tissues due to disease.

## I. INTRODUCTION

Mechanical properties of tumor tissues are known to differ from the surrounding tissues as indicated by the use of palpation as diagnostic tool. Infiltrating ductal carcinoma had 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 ([1]). As a result, several methods have been developed to estimate

tissue stiffness. In order to overcome the shortcomings of an external excitation, the remote application of the mechanical stimulus using an ultrasonic beam has been of particular interest in the last few years [2-3] with applications on artery calcifications [2] and in vivo normal breast [3]. Another method that induces vibration remotely and aims at detecting mechanical properties is Ultrasound-stimulated Acoustic Emission (USAE) by Fatemi and Greenleaf. This method uses ultrasound induced radiation force to probe tissue properties. Two ultrasound beams are operating at slightly different frequencies ( $f_1$  and  $f_2$ ), the beams overlap at the focal region where the waves interfere and generate a wave that is amplitude modulated by their difference frequency ( $f_d = f_2 - f_1$ ). An object at the overlapping zone experiences an average energy density  $\langle E \rangle$  that fluctuates at the frequency of  $f_d$ . The magnitude of the acoustic source depends on the radiation force and the mechanical frequency response of the tissue at the frequency of  $f_d$ . The stimulated acoustic signal propagates through the tissue and can be detected by an external hydrophone). The resulting acoustic signal, however, is a combination of the mechanical and acoustical properties of the tissue, the resonance characteristics of the transducer housing and its surroundings and its interaction at the hydrophone. Therefore, stiffness estimation using this method is extremely challenging.

The development of Localized Harmonic Motion Imaging is thus hereby proposed (Fig. 1). In order to avoid the artifacts and drawbacks of the overall USAE application, we propose to utilize the radiation force of the overlapping ultrasound beams, but use a separate ultrasound beam to probe the induced tissue motion (Fig. 1). Until now, techniques have either involved the estimation of motion using an external vibration or have estimated localized static motion. In this study, we propose to utilize the radiation force

that is applied via using two overlapping beams radiating at slightly different frequencies, same as the method first introduced by Fatemi and Greenleaf [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 (Fig. 1). This method is distinctly different from methods such as Remote Palpation [4], Transient Elastography [5] and Shear Wave Elasticity Imaging (SWEI) [6] that estimate motion during relaxation of the tissue *after* application of the force instead of *during* its application, such as is the case of USAE and the proposed method.

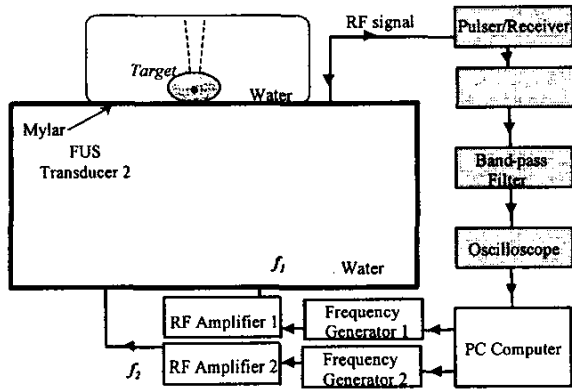


Figure 1: Localized Harmonic Motion Imaging diagram.

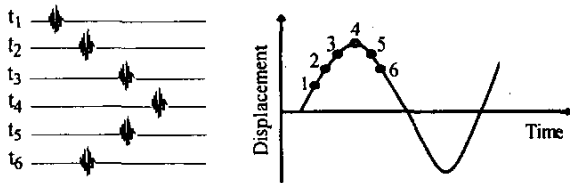


Figure 2: Concept of Harmonic Motion Imaging for displacement estimation. RF line tracking at different instants ( $t_1, t_2$ , etc.) acquired at the focus of the diagnostic transducer (Fig. 2) yields precise displacement estimates and identifies the characteristics of the locally induced vibration.

## II. METHODS

### Finite-Element Simulations

In order to assess the optimal parameters to be used with this technique, finite-element simulations and a previously developed signal generation model for the RF signal simulation were utilized. In order to model

tissues containing tumors, finite-element simulations of mechanical targets that contain inclusions of distinct stiffness from the surrounding medium were considered [7]. The normal tissue had a stiffness equal to 30 kPa and tumorous tissue varied from 30 kPa to up to 500 kPa in stiffness [7]. Loading at different nodes of the mesh occurred at frequencies ranging from 100 Hz and 800 Hz sampled at 3 kHz (same as in the experiments, see below). Four different cases were studied in order to assess the effect of loading frequency on the displacement estimate. For each one of those cases, simulated RF lines were generated by convolution of a Gaussian-modulated pulse with the random scatterer distribution based on the node distribution of the finite-element mesh. Tracking of RF lines were performed using crosscorrelation techniques [8] and the displacement were estimated at 3 kHz intervals (Fig. 2). Parameters, such as loading frequency and tissue modulus, were studied regarding their influence on the resulting estimate.

### Experiments

The method was tested on agar gel phantoms and ex vivo porcine muscle. Glass beads were added in the gel phantoms for scattering at a concentration of 0.4g/l. For the tissue experiments, fresh porcine thigh muscle tissue samples were excised from euthanized animals and immediately immersed in a 0.9% saline. They were then kept in room temperature until the measurements were made (usually 1-4 hours later). Two focused ultrasound transducers were utilized operating at a frequency of 2.27 MHz and at slightly different frequencies (Fig. 1). The transducers efficiency was equal to approximately 65%. A PZT composite diagnostic transducer (Imasonics, Inc.) were 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. 1). 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 was 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 frequencies ranging between 100 Hz and 800 Hz. The focused ultrasound intensity used was approximately equal to  $1015 \text{ W/cm}^2$ , since a preliminary study showed that displacement could be accurately estimated beyond  $900 \text{ W/cm}^2$ . 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 2.27 MHz) and all its harmonics. The displacements were also imaged in an M-mode-like fashion in order to study both their spatial and temporal variation.

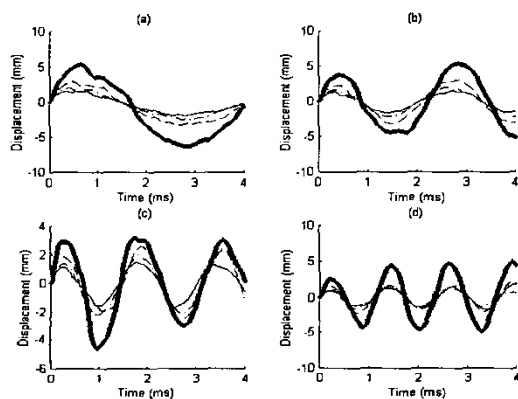


Figure 3: Displacement tracings at the inclusion with stiffness equal to 20 kPa (solid), 40 kPa (-.-), 60 kPa (-) and 80 kPa (bold solid) at frequencies of a) 200 Hz, b) 400 Hz, c) 600 Hz and d) 800 Hz.

### III. RESULTS

#### Finite-Element Simulations

In the simulations, the estimated oscillatory displacement spanned from  $-800$  to  $600$  microns (Figs. 3) and the frequencies of excitation could easily be estimated from the temporal variation of the displacement. Furthermore, an exponential decrease of the displacement amplitude with stiffness was observed at all frequencies investigated (Fig. 4). Figure 5 shows an image of the modulus distribution (Fig. 5a) and the displacement image (Fig. 5b). The inclusion is clearly depicted in the displacement (HMI) image.

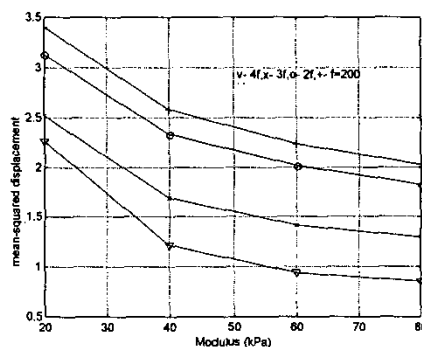


Figure 4: Mean amplitude of the estimated displacement at different frequencies and stiffnesses.

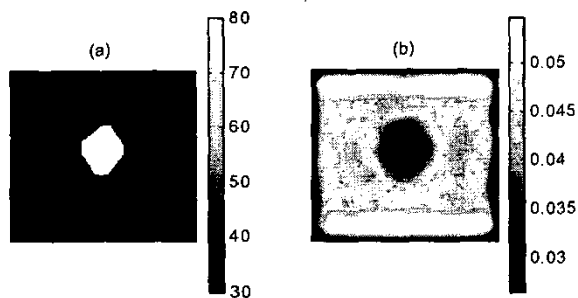


Figure 5: a) True modulus (kPa) image and b) Mean-squared estimated displacement (mm) image. The inclusion is clearly depicted.

#### Experiments

The M-mode images of the displacement at 800 Hz are shown with time in Fig. 6. At the absence of excitation frequency no harmonic motion is observed (Fig. 6b). At the onset of harmonic motion excitation as induced by the overlap of the two beams, harmonic motion is observed at 20 mm depth (Fig. 6d), confirming what was observed at simulations. Fig. 12 summarizes the results in all gels at the frequency of 800 Hz. A steady decrease in amplitude was noted with increasing stiffness, similar to that observed in the case of the simulations (Fig. 4). Figure 8 shows the M-mode RF images and displacements before and after thermal coagulation of the tissue. Before coagulation, the tissue is shown to vibrate at the depth of 21 mm. After ablation, the tissue is no longer undergoing the same amplitude of harmonic displacement at 21 mm; in fact, the displacement estimates appear to be lower.

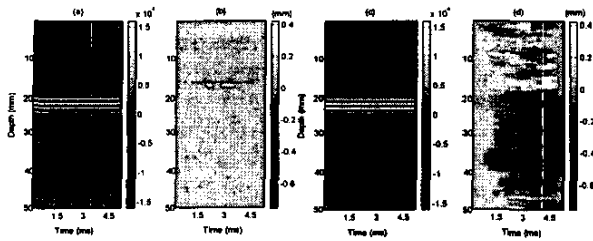


Figure 6: M-mode RF image in and outside gel 1 (ranging from 20 to 40 mm) a) before and c) during harmonic excitation at 800 Hz and at depth of 20 mm; M-mode displacement image b) before and d) during harmonic excitation at 800 Hz and at depth of 20 mm. The gel ranges from 20 to 50 mm in depth.

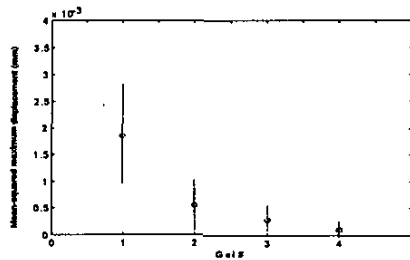


Figure 7: Mean-squared displacement at different gels (with increasing stiffness; gel 1: 7 kPa, gel2: 26 kPa, gel3: 55 kPa, gel4: 95 kPa). The errorbars correspond to one standard deviation obtained from three independent locations in each gel.

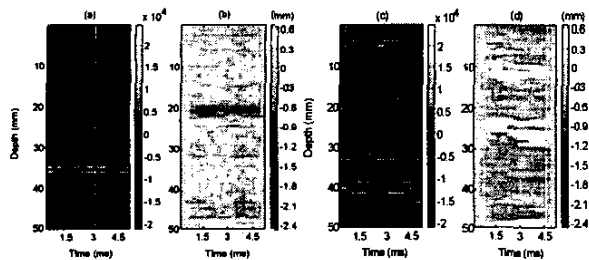


Figure 8: M-mode RF image in and outside the porcine muscle a) before and c) after FUS ablation at 20 mm; M-mode displacement image b) before and d) after FUS ablation at 21 mm. The harmonic excitation was at 400 Hz and at the depth of 21 mm. The muscle ranges between 4 and 45 mm depth.

#### IV. DISCUSSION

In recent years, there has been a multitude of techniques for the estimation of mechanical properties in order to develop new imaging modalities for the detection of cancer. In this paper, we propose a new technique that combines the precision of static

techniques with the simplicity of the harmonic excitation methods. It has been long established that remotely applied, vibratory methods are the preferred techniques for the estimation of moduli of materials [9].

Harmonic Motion Imaging applies a remote, harmonically variable radiation force deep inside the tissue and estimates the resulting harmonic displacement using crosscorrelation techniques. The high precision of the crosscorrelation techniques permits the estimation of micron-level displacements without the interference of standing waves, tank resonance and ambient noise, which may contaminate the amplitude of the signal. Most importantly, the amplitude of the displacement estimated decreases with stiffness in an exponential fashion (Fig. 4 and 7) and can yield an accurate image for lesion localization (Fig. 5), rendering this method highly sensitive for differentiation of tissues based on their stiffness. In tissue experiments, the stiffening of the muscle following FUS ablation could be detected by the substantial decrease of the displacement amplitude.

#### V. REFERENCES

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