Ultrasound in Med. & Biol., Vol. 41, No. 12, pp. 3216–3232, 2015

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2015.07.018

● *Original Contribution*

OPTICAL QUANTIFICATION OF HARMONIC ACOUSTIC RADIATION FORCE EXCITATION IN A TISSUE-MIMICKING PHANTOM

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(*Received* 3 *March* 2015; *revised* 18 *June* 2015; *in final form* 16 *July* 2015)

Abstract—Optical tracking was used to characterize acoustic radiation force-induced displacements in a tissue-mimicking phantom. Amplitude-modulated 3.3-MHz ultrasound was used to induce acoustic radiation force in the phantom, which was embedded with 10-μm microspheres that were tracked using a microscope objective and high-speed camera. For sine and square amplitude modulation, the harmonic components of the fundamental and second and third harmonic frequencies were measured. The displacement amplitudes were found to increase linearly with acoustic radiation force up to 10 μm, with sine modulation having 19.5% lower peak-to-peak amplitude values than square modulation. Square modulation produced almost no second harmonic, but energy was present in the third harmonic. For the sine modulation, energy was present in the second harmonic and low energy in the third harmonic. A finite-element model was used to simulate the deformation and was both qualitatively and quantitatively in agreement with the measurements. (E-mail: visa.suomi@eng.ox.ac.uk) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Acoustic radiation force, Optical tracking, Harmonic displacement, Amplitude modulation, Tissue-mimicking phantom, Tissue deformation, Finite-element analysis.**

INTRODUCTION

Ultrasound elastography is an emerging technique used in diagnostic clinical applications in medicine to detect contrast in tissue stiffness (Parker et al. 2011). Areas of application include: cancer screening, assessment of vascular pathology and monitoring of high-intensity focused ultrasound (HIFU) therapy. In many implementations, tissue displacement is induced by acoustic radiation force (ARF), which is dependent on both ultrasound intensity and tissue properties. The work reported here is motivated by a desire to better quantify the ultrasound-induced displacement in tissue.

The majority of ARF-based ultrasound imaging techniques, such as acoustic radiation force impulse (ARFI) imaging (Nightingale et al. 2002), harmonic motion imaging (HMI) (Maleke et al. 2006), supersonic shear imaging (SSI) (Bercoff et al. 2004) and electromagnetic acoustic (EMA) imaging (Zhang et al. 2013), rely on quantification of tissue deformation under ultrasound excitation. The magnitude of this deformation is generally tracked with ultrasound-based methods, which use time delays to estimate the dynamic response of tissue from pulse-echo data (Pinton et al. 2006). Although these ultrasound methods can track the displacement at a submicrometer scale in the axial direction, they have several limitations. First, the displacement estimation accuracy in the lateral direction is significantly lower compared with that in the axial direction. Although it is possible to derive lateral displacement estimates on the basis of axial strain, it has been found that the variance of the lateral displacement estimate is 40 $\times$ F-number^2 worse than that of the axial direction (Lubinski et al. 1996). Second, real-time tracking of displacements is limited by the interference from the ARF pulse, because the echo signal from the excitation pulse has to be sufficiently attenuated before the pulse-echo tracking data are acquired, which prevents estimation of tissue deformation during the excitation phase. Third, the depth of the region of interest (ROI) creates physical limitations for the temporal resolution because of the sound speed in tissue ($\approx$1540 m/s). For example, in theory a point located at a focal depth of 7.7 cm in tissue would only allow temporal resolution of 10 kHz, which is within the limit for short-duration ARFI pulses. In reality, however, the temporal resolution would be even lower because of the interfering

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echo signals, which would have to be attenuated before starting the next pulse-echo acquisition. Furthermore, ultrasonically derived displacement estimates in solid media are also affected by the so-called shearing artefact (McAleavey et al. 2003), which is caused by the averaging of individual scatterer amplitudes in displacement calculation. This has been found to lead to underestimation of tissue peak displacement at the focal point (Czernuszewicz et al. 2013). Although ultrasound-based tracking methods can be easily implemented in a clinical setting by using the same transducer to push and track the displacement, the limitations mentioned do not favor their usage in accurate characterization of tissue dynamics.

Bouchard et al. (2009b) were the first to demonstrate the feasibility of an optical tracking method utilizing a high-speed camera to measure the dynamics of tissue deformation under ARF excitations. They used a phantom with embedded steel markers and tracked the displacement of these markers under both impulsive and harmonic excitations. The impulsive excitations were conducted using pulse lengths from 0.5 to 50.0 ms, and the harmonic excitations, using 50- to 300-Hz amplitude modulation. These tracking data were then compared with tracking data acquired using a conventional ultrasound-based tracking method. They found the mean peak displacements differ from 2.8% to 30.7% for impulsive pulses and from −4.3% to 25.3% for harmonic excitations between the two tracking methods. Bouchard et al. (2009a) also performed another study in which they used the same tracking technique to characterize the deformation dynamics in a tissue-mimicking phantom. They used short-duration impulsive pulses (0.1–0.4 ms) and tracked the induced displacements in both the axial and lateral directions with frame rates up to 36 kHz. The displacements were tracked using several individual markers located on- and off-axis, and the results were compared with finite-element method (FEM) models.

Later, Czernuszewicz et al. (2013) used the same optical tracking method to experimentally validate the displacement underestimation in ultrasound-based techniques (McAleavey et al. 2003). For ultrasound excitation and tracking, they used a clinical ultrasound scanner with linear ultrasound probe. The probe was used with *F*-numbers 1.5 and 3.0 to excite tissue-mimicking phantoms whose Young's moduli were 6.6, 19.8 and 30.2 kPa. They found the displacement underestimation to decrease with higher *F*-number because of the larger cross-sectional area which the force is affecting. Similarly, stiffer phantoms exhibited smaller underestimation error because of faster shear wave spreading, which makes the scatterer movement at the focal point more uniform. Therefore, the maximum underestimation error (35%) was found using the *F*-number 1.5 and the softest phantom. These experimental results were in accordance with the FEM simulations of Palmeri et al. (2006).

Several studies have characterized mechanical tissue response to impulsive ultrasound excitation using optical (Bouchard et al. 2009a, 2009b; Callé et al. 2005; Czernuszewicz et al. 2013) and ultrasound (Palmeri et al. 2005; Wang et al. 2014) tracking methods, but there has been little focus on the tissue dynamics under harmonic excitations. Konofagou and Hynynen (2003) reported the feasibility of HMI with simulations and experimentally by using ultrasound tracking in tissue-mimicking phantoms. In the experimental part, they used three different transducer configurations with ultrasound modulation frequencies ranging from 200 to 800 Hz and four agar phantoms with Young's moduli between 7.1 and 94.6 kPa. The effect of stiffness on the harmonic displacement amplitude was determined, and the results were compared with simulations. The experimental results indicated that the oscillation displacements varied from −300 to 250 μm, whereas in the simulations, the estimated harmonic displacement spanned from −800 to 600 μm. An exponential decrease in the harmonic displacement amplitude with phantom stiffness was observed both in simulations and experimentally. Later, Konofagou et al. (2012) established the correlation between ultrasonically measured harmonic displacement amplitudes and Young's moduli of tissue-mimicking gel phantoms. They also reported that the harmonic displacement amplitude decreases with increasing Young's modulus of the phantom.

Apart from the effect of tissue stiffness on harmonic displacement amplitude, some research has been done on the effect of modulation frequency on oscillation magnitude. Curiel et al. (2009) used HMI to monitor HIFU ablation in rabbit muscle and measured the average normalized harmonic displacement amplitudes as a function of modulation frequency. They used modulation frequencies from 50 to 300 Hz and found the displacement amplitude to decrease with modulation frequency within this range. A similar relation was also observed in simulations performed later by Heikkila et al. (2010). Furthermore, because of the viscoelastic properties of soft tissues, Liu and Ebbini (2007) used ultrasound amplitude modulation for viscoelastic characterization of tissue properties. They studied the changes in harmonic displacement amplitudes using modulation frequencies from 200 to 1300 Hz in two different phantoms. It was found that the relative displacement amplitude is dependent on the frequency response of the target material, which can be related to the corresponding stiffness. In addition to displacement amplitude, the relative phase of the displacement was also found to vary with modulation frequency.