Ultrasound Elastomicroscopy using Water Beam Indentation: Preliminary Study

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Abstract. This study is aimed to develop a novel non-contact ultrasonic indentation system for measuring or imaging quantitative mechanical properties of soft tissues, which are increasingly important for tissue assessment and characterization. The key idea of this method is to use a water beam as an indenter to stimulate the soft tissue. The water beam also serves as a medium for an ultrasound beam propagating through. The application of water beam benefits the system to use focused high frequency ultrasound without any additional attenuation. The indentation deformation was estimated from the ultrasound echoes using cross-correlation algorithm and the indentation force was calculated from the measured pressure and an overall force. Experiments were performed on tissue-mimicking phantoms whose Young's moduli and Poisson's ratio were measured using uniaxial compression and the indentation pressure/deformation curves were obtained. This system shows good ability in measuring the phantoms with different stiffness. It is expected that this novel water beam indentation method can be used to construct an ultrasound elastomicroscopy for imaging tissues elasticity in a high resolution.

Keywords: ultrasound; high-frequency ultrasound; indentation; ultrasound indentation; water beam; elastomicroscopy; elastography

1. Introduction

To measure or image the mechanical properties of tissues has been attracting increasing research efforts during the recent decades as changes in tissue stiffness are often related to pathological changes in tissue. In pathological situation, soft tissues, such as sclerous cancer, edema, degeneration, and pressure sore, posses different stiffness. Normal tissues may also have different stiffness, which is important information for tissue characterization. The tissue mechanical properties can even take on different values depending on whether measured *in vivo* or *in-vitro*, *in situ* or as an excised specimen. For the lack of quantitative tools for *in vivo* assessment of living tissue, manual palpation has been the primary technique for tissue stiffness assessment for many years in clinic. However, it strongly relies on personal experiences and cannot provide a quantitative measurement of changes in tissue stiffness.

Indentation has been the most frequently used approach to measure the mechanical properties because it does not require special specimen preparation techniques. Moreover, it has the added advantage that the material properties of soft tissues are determined *in situ* or *in vivo*. It also provides a method to determine the variation of tissue properties over a relatively large surface because it can perform multiple tests at several different sites conveniently and does not affect the ultra-structure or composition of the tissue [1]. Theoretical analysis of general indentation problems, with various idealizations of the physical model, has been conducted for about a century. Some mathematical solutions have also been solved for thin-layer soft tissues and materials [2-7]. The indentation depth, the shape and size of the indenter, and tissue thickness are critical factors in the calculation of tissue mechanical properties [8-11].

Several generations of indentation instruments have been developed for tissue mechanical properties assessment, especially for articular cartilage [4, 12-14]. These mechanical indentation apparatuses employ a load cell to measure the loading force, and a displacement transducer (LVDT) to record the tissue deformation in concert with the displacement of the indenter. A cylindrical flat-ended, or a spherical, rigid indenter is used to perform contact loading on soft tissues. The structures of these mechanical indentation instruments are quite complicated which cannot be used for *in vivo* measurement in clinic. On the other hand, they employ a needle probe to penetrate into the tissue to measure the tissue thickness, which is important information for indentation stiffness estimation. Destruction of the tissue structure at the site of measurement restricts the further use of the specimen. For clinical application, similar but portable indentation instruments have been developed for the quantification of cartilage stiffness under arthroscopic control [15], *in vivo* analysis of residual limb tissues [16], plantar tissue stiffness measurement in patients with diabetes mellitus and peripheral neuropathy [17], stiffness estimation of spinal tissues [18] etc. These indentation apparatuses use the obtained force/ deformation (F/D) curves to estimate the tissue stiffness; however, they are limited in the lack of tissue thickness.

During recent decades, ultrasound has been introduced to measure or image the mechanical properties of soft tissues [19-22]. The development of ultrasound indentation apparatuses improves the indentation technique quite a lot because it can measure the tissue deformation and meanwhile obtain the tissue deformation *in vivo* non-invasively [23-24]. A load cell or a strain gauge is used to collect the force loading on the tissue. A flat-ended ultrasound transducer is used as indenter, meanwhile it can estimate the indentation depth and tissue thickness by the time delay of the ultrasound echoes reflected from the interested soft tissues. The accuracy of ultrasonically derived measures of displacement during indentation has been investigated [25]. Compared with other methodology in tissue thickness measurement, like using optical [26] and needle probe [4], ultrasound-based techniques have been proved to be most suitable for *in vivo* tissue thickness measurement because of its noninvasiveness. Ultrasound indentation is easy to use for *in vivo* stiffness measurement, and it has been widely used for assessment of residual limb tissues, diabetic foot tissue, fibrotic neck tissue with radiotherapy, and spinal tissues [25-30]. It has also been demonstrated that the proposed ultrasound indentation technique can be used to accurately identify the abnormality of articular cartilage [21, 31].

Present ultrasound indentation techniques utilize an unfocused transducer as an indenter to stimulate the soft tissue. The direct contact way makes it difficult for them to properly stimulate the small specimens of soft tissue and biomaterial due to the relative large size of the transducer. Moreover, for these developed techniques, ultrasound frequency typically operated in the range from 2MHz to 10MHz, which can obtain tissue deformation at the resolutions in the order of several millimetres. It’s obvious that the resolution is not sufficient for the mechanical properties measurement of the structural organs, like articular cartilage, corneal tissues or thin skins with a higher demand of resolution. To achieve ultrasound indentation measurement at a microscopic level, focused high frequency ultrasound transducers have to be used. However, it remains challenge for the present techniques, say contact ultrasound indentations, because of the increased signal attenuation for high frequency ultrasound when passing through tissues.

Accordingly, it is very necessary to develop a new method to achieve non-contact ultrasound indentation so that we can 1) perform proper loading on small specimen, 2) use high frequency ultrasound without the problem of high attenuation to achieve high resolution elasticity imaging. The main idea in our approach is to use a water beam serving as an indenter and as the medium for ultrasound propagating through. The potential of this non-contact ultrasound indentation system to measure phantoms with different stiffness has been demonstrated.

2. Materials and Methods

2.1 System description

A non-contact ultrasound indentation system was constructed (Fig. 1) using a water beam as an indenter. As shown in Fig. 1, the system consisted of a focused, high-frequency (20 MHz) ultrasound transducer, a water ejector and a pressure sensor. The pressure sensor was used to monitor the water pressure within the water pipe. The transducer with a nozzle was installed to a three dimensional translating device which is easy to adjust the distance from the nozzle to the specimen surface and later is used to perform one-dimensional or two-dimensional scanning over tissue surface. Specimens were placed on a rigid platform within a water container. An outlet was used to monitor the water level inside the container. A load cell that located under the platform could sense the overall force applied on the platform.

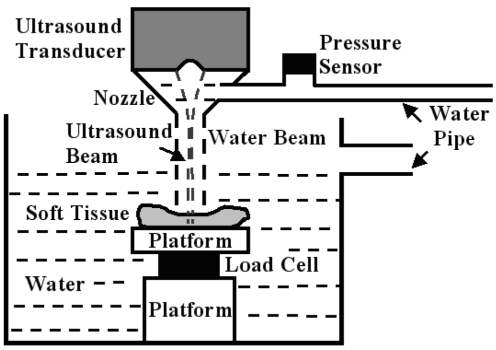


Fig. 1. Diagram of the noncontact ultrasound indentation system using water beam compression.

An ultrasound pulser/receiver was utilized to drive the ultrasound transducer and to amplify the received signal. The ultrasound echoes reflected from the specimen were digitized by a high speed A/D converter. The pressure and the force were sampled by a data acquisition card. Fig. 2 shows the system architecture. A software has been developed in Microsoft VC++ to process and display the ultrasound signal together with the force and the pressure in real time during the indentation process. The code is multithread with separate threads acquiring A-mode ultrasound, force and pressure data synchronously. All the data could be recorded in a file for further off-line study. The deformation of the specimen under water beam indentation was estimated from the ultrasound echoes using a cross-correlation algorithm. With the high-speed A/D converter, when sampling frequency 500 MHz was selected, the accuracy of the time measurement was 2 ns. The accuracy of the deformation determined by the water indentation system was better than 2 μm. By using the 24-bit A/D converter to digitize the force and pressure signal, the accuracy of force was better than 1 e-6N within the 10 N range and the accuracy of pressure was better than 0.05 Pa within the 350 kPa range.

2.2 Phantom preparation

Tissue-mimicking phantoms made from some kinds of silicones or gels have similar mechanical properties with soft tissues while their shapes, sizes and compositions are easier to control. In our experiments, three kinds of silicones were used to make phantoms with different stiffness for experiments (Fig. 2). The uniform phantom was made from one kind of silicones and was supposed as homogeneous. They were labeled as type A, B and C according to their material. Each type has three groups of samples, named 1, 2 and 3, with different height. Each group has three pieces, labelled as a, b and c. The combined phantom was made by two or three kinds of silicones, which had different stiffness distribution. The sizes of the phantoms were about (width×length×height) 1cm×1cm×0.5cm, 1cm×1cm×1cm, 1cm×1cm×1.5cm for the uniform phantoms and o.5cm height with radius 1.1cm for the combined phantoms, respectively.

2.3 Experiment design for the uniform phantoms

To demonstrate the feasibility and the function of the non-contact ultrasound indentation system, experiments were performed on phantoms and the pressure/deformation curves were obtained. As Galbraith and Bryant [32] indicated that the results of the indentation analysis were unaffected if the radius of the tissue was at least three times the radius of the indenter, in our experiments, the area of the phantom was more than twenty-five times the area of the water indenter, such a geometry could be accepted. For each test, the phantom was placed on the centre of the platform and was slightly fixed by four organic screws. The distance from the ultrasound transducer to the phantom surface was modified according to the height of the phantom to keep a constant initial distance. The focal point of the transducer was placed approximately at the surface level of the phantom. We calibrated the relationship between the pressure measured within the water pipe and the overall force applied on platform and found a linear relationship between them. Later this calibration result was used to calculate the pressure applied on the phantom by assuming a uniform stress distribution in the interface between the water beam and phantom surface. The container was full of water before loading to keep a constant water level. In each loading and unloading cycle, the water pressure within water pipe ranged from 0 to 180 kPa at a rate of 45 kPa/s. This was repeated for 3 cycles in each test. Each phantom was indented by three times. Twenty-seven pieces of uniform phantoms were measured in total.

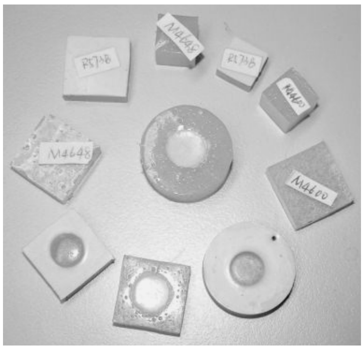


Fig. 2. Phantoms made from different kinds of silicones were prepared for the experiments.

2.4 Measurement of mechanical properties of phantoms

As a reference of the experimental result of the water indentation, the compressive properties of the phantoms were measured by a material testing machine as shown in Fig. 3 [33]. The axial displacement was monitored by a displacement transducer- linearly variable differential transformer (LVDT), and the lateral displacement of the phantom was measured by an unfocused ultrasound transducer during the uni-axial compression. Ultrasound coupling gel was used between the ultrasound transducer and the phantom for ultrasound beam propagation. It was also used in the interface between the phantom and the compressor together with that between the phantom and the platform, serving as lubrication. The test phantom was placed at the centre of the platform and kept perpendicular to the ultrasound transducer. The ultrasound echoes were tracked using the cross-correlation algorithm to estimate the lateral displacement of the phantom during compression. The uni-axial force applied on the phantom was measured by a load cell. The axial displacement, force and ultrasound echoes could be recorded synchronously.

Each phantom was compressed one time in each test. Such test repeated three times for every phantom. The compression rate was kept at 45 μm/s and the total deformation was up to 10%. The compressive Young's modulus and Poisson's ratio of the phantoms could be thus obtained.

2.5 Experiment design for scanning on combined phantoms

One-dimensional scanning experiment was conducted on the combined phantom using the three-dimensional translating device. The phantom was first scanned by the ultrasound transducer at a moving rate of 1 mm/s when the pressure kept as a constant. Then it was scanned again along the same line when the pressure changed to another value. The deformation at each site along the scanned line could be thus obtained. When two-dimensional scanning was performed, the same area of the phantom was scanned under different pressure and the surface position distributions of the phantom under two different pressures were compared to obtain the deformation distribution image.

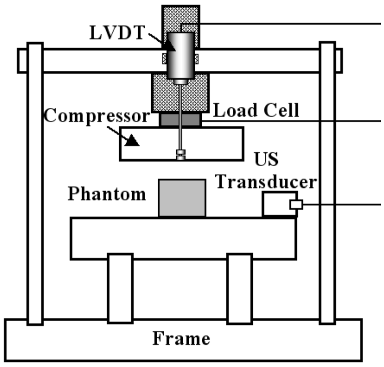
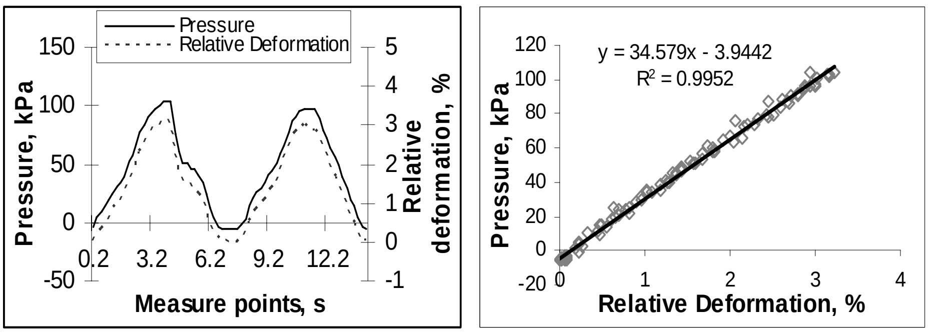


Fig. 3. Diagram of the system which was used to measure the compressive Young's modulus and Poisson's ratio of the phantom. A load cell was used to measure the uni-axial force. A US transducer was used to estimate the lateral deformation of the phantom, while the LVDT was used to measure the axial deformation.

3. Preliminary results

3.1 Experiments on uniform phantoms

Fig. 4a shows the pressure/deformation curves during the loading and unloading applied on the test phantom, and Fig. 4b shows the relationship between the pressure and the surface deformation of the phantom derived from the ultrasound echoes. The ratio of pressure/ relative deformation was used as an index of the stiffness of the phantom. The tests on each phantom showed a good repeatability.



(a) (b)

Fig.4. (a) The pressure and relative deformation curves on one uniform phantom; (b) the relationship between the pressure and the relative deformation.

3.2 Measurement of mechanical properties of phantoms

The strain–dependent Young's moduli and Poisson's ratios are calculated at the strain according to the indentation depth on each phantom by using the non-contact water indentation system. The test results also show a good repeatability. The slopes of pressure/ relative deformation obtained from water indentation were compared with the compressive Young's modulus. They demonstrated a good correlation with R^2 =0.75 (Fig. 5).

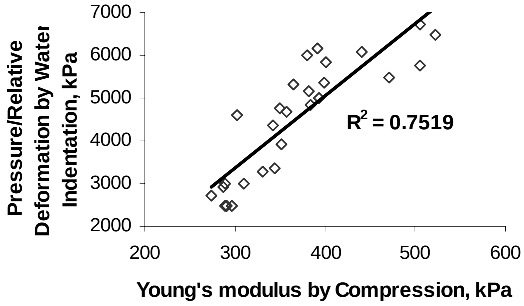
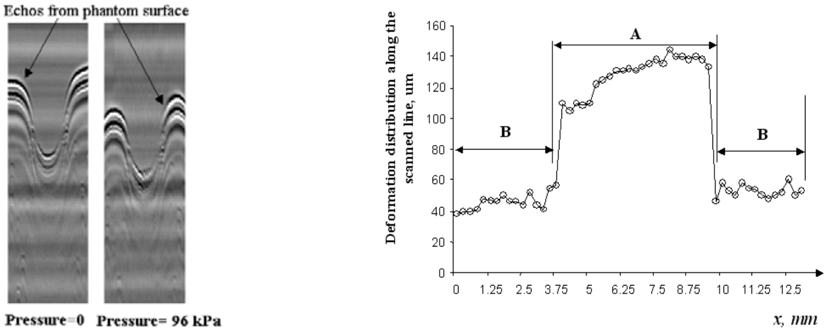


Fig.5. The correlation between the slopes of Pressure/ Relative deformation obtained from water indentation and the compressive Young's modulus of the uniform phantoms.

3.3 Scanning on the combined phantoms

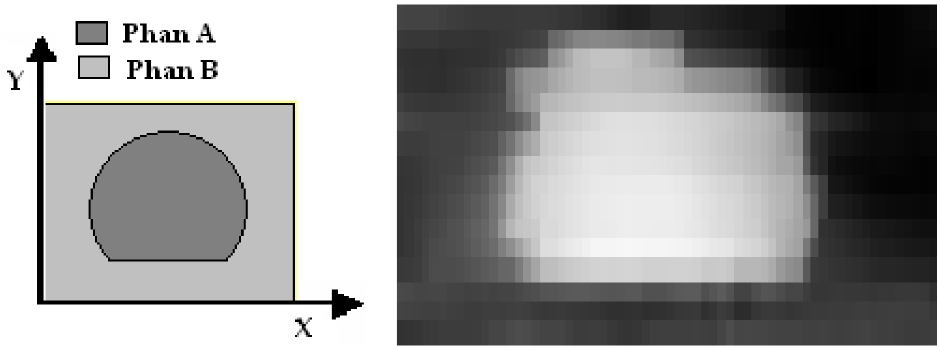
One- and two-dimensional scanning were performed when the pressure within water pipe was kept as 0 and 96 kPa respectively. Fig. 6a shows the comparison of the M-mode ultrasound images obtained under two different pressures. Fig. 6b is the deformation distribution along the scanned line derived from Fig. 5a. It indicated that under a certain pressure, the deformation of the region made from material A was larger than that made from material B, i.e. the region made from material A was softer than that made from material B.



(a) (b)

Fig.6. One-dimensional scanning result: (a) comparison between the M-mode ultrasound images obtained under two pressure values; (b) the deformation distribution along the scanned line.

Fig. 7a shows a schematic of the two dimensional-scanning, and Fig. 7b is the grey image of the deformation distribution of the scanned area. This result agreed with that obtained from the one-dimensional scanning.



(a) (b)

Fig.7. Two-dimensional scanning result: (a) schematic of the scanning area; (b) the grey image of the deformation distribution of the scanned area.

4. Discussions

A non-contact ultrasound indentation system using water beam has been developed for the assessment of tissue mechanical properties. Preliminary results have demonstrated that this novel system was feasible to measure phantoms with different stiffness. Because of its use of water beam as an indenter, it could conduct proper loading on small specimen, and there was no additional attenuation when high frequency ultrasound was used. This new system has an added advantage that it could conduct fast scanning on phantoms with various surface conditions. The deformation distribution under a certain pressure could be obtained quickly, which indicated the stiffness distribution for the interested area of soft tissues.

There were many factors to affect the system steadiness as water flow was used. The effect of the water temperature on the pressure measurement and on the ultrasound speed was investigated. Experimental results suggested that when the temperature in the water pipe kept accordance with that in the container, the effects were quite slight. Since the medium for ultrasound propagation was flowing, the effect of the flow rate on the ultrasound speed has also been studied. For a fixed distance from the ultrasound transducer to a rigid platform, when the water pressure within the water pipe ranged from 0 to 180 kPa, the maxim change of the ultrasound speed through water beam was less than 0.04%, i.e. if ultrasound speed in stagnant water was 1520 m/s, it varied 0.6 m/s when the pressure ranges from 0 to 180 kPa. Such a result suggested that the effect of water flow for ultrasound speed could be neglected.

In our experiments, a focused ultrasound transducer was used and the system could achieve high axial resolution of the measurement because the deformation of phantom under water indentation was determined from ultrasound echoes. For 20MHz ultrasound, two cycles of damping period and an ultrasound speed of 1520 m/s, the theoretical axial resolution was approximately 75 μm [34], which was much higher than those obtained using the contact indentation apparatuses. This resolution could be improved by using higher frequency ultrasound.

During our experiments, the ratio of the pressure/ relative deformation curves was used as the index of the material stiffness, however, the extraction of the mechanical property from the non-contact water indentation needs further investigation. As previous research suggested, the Young's modulus derived from indentation test are related to the Poisson's ratio of the material, the stress distribution, the indentation depth, and aspect geometry of the indentation. The measured Young's modulus and Poisson's ratio of all the tested phantoms will help much to understand the indentation stiffness. In the future work, finite element analysis will also be used to simulate the process of the water indentation to well understand the interaction between the water beam and the tested phantoms.

This non-contact ultrasound indentation system has lots of potential applications. It could be used to quantitatively assess the stiffness of body tissues for clinical diagnosis, such as skin cancer, burn status, cornea condition, blood vessel stiffening, articular cartilage degeneration, etc. It also could perform indentation on small specimens in microscopic levels for tissue and material characterization for small animal tissues, bioengineered tissues, semiconductor materials, thin films, and so on. Moreover, its fast scanning function makes it easy to conduct scanning on tissues with large area for clothing design, such as bra, swimsuit.

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