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DETERMINATION OF IN-VIVO ELASTIC PROPERTIES OF SOFT TISSUE USING MAGNETIC RESONANCE ELASTOGRAPHY

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INTRODUCTION

In-vivo measurements of the elastic properties of soft tissue have been made using a variety of direct techniques, such as indentation probes and rotary shear actuators, but they are unable to access much of the soft tissue of interest. Indirect ultrasonic methods for imaging elastic properties of soft tissue were first introduced about 15 years ago, see Ophir (1991). Although the results of ultrasonic elastography studies have been quite promising, they may not be suited for applications requiring accurate quantification of soft tissue properties. An alternative to ultrasound, magnetic resonance imaging, has the advantage of enabling precise measurement of all three components of tissue displacement. The reconstruction of elastic properties from the imaged displacement field is called magnetic resonance elastography (MRE), and is the subject of this paper.

Several MRE schemes have been introduced in recent years for reconstructing the elastic properties of soft tissue from displacement images during elastic wave propagation in the tissue. One approach is to substitute the transient displacement components directly into the discretized inverse dynamic elasticity equations (Muthupillai, 1995), but this dynamic method suffers from the relatively low frame rate of MR images unless planar wave motion can be obtained. Alternatively, quasi-steady wave motion is simpler to produce, but reconstruction of the elastic properties is more difficult. Strain-based reconstructions have been successful in many cases (Plewes, 2000), but suffer from noise induced by the differentiation of the displacement field to obtain strain data. Iterative reconstruction techniques have proven to be more robust (Van Houten, 2000; Sinkus, 2000), and one such method is described here.

METHODS

Motion generation and displacement imaging

To produce harmonic shear waves in the soft tissue, it must be vibrated within the magnetic resonance imager in synchronization with the image acquisition. Mechanical excitation in this study was achieved with an MR-compatible piezo-electric actuator, which drives a flat plate in a steady-state, time-harmonic oscillation with an amplitude of about 40 μm. Oscillation frequency was generally 100 Hz and was phase-locked with the MR system clock. The tissue (or phantom) being imaged was compressed lightly against the flat shear plate and was imaged with a coil mounted beneath the shear plate on a 1.5 T whole body imager. The phase and amplitude of the time-harmonic, quasi-steady state displacement field were measured using a simple motion encoding pulse sequence. Images were obtained in each of the three orthogonal coordinate directions.

Reconstruction of elastic properties

Spatial variation of the shear modulus was computed using a three-dimensional nodal-based subzone inversion technique based on the finite element method with a modified Newton-Raphson iterative scheme (Van Houten, 2000). In that MRE inversion technique, the elastic parameters are determined for a set of imaged displacement vectors throughout the elastic solid. The solid is assumed to be isotropic and linearly elastic, so the displacement vector **u** is related to the shear modulus μ, Lamé's parameter λ and the density ρ (which was assumed to be that of water in this study). A finite element mesh is created over the entire tissue volume, and the mesh is then divided into overlapping subzones. In this work, a typical finite element mesh contained about 200,000 elements and 60,000 nodes. A typical spherical subzone was about 5 mm in diameter; approximately 500 subzones were used in a typical 3-dimensional tissue volume. In the iterative inversion scheme, initial guesses of μ and λ are used to determine the displacement at each nodal point in the subzone by solving the finite element equations (forward solution). The displacement error $\Delta\mathbf{u}$ is found by subtracting the calculated displacement from the measured displacement at each point. The local Jacobian matrix is constructed and it is used in computing updates to μ and λ at each point by solving the normal equations describing the least-squares problem using Marquardt's approach. Spatial filtering was performed at each iteration to suppress high frequency fluctuations in shear modulus estimates. The process is repeated multiple times until the root mean squared error between the measured and computed displacement is reduced; then another subzone is randomly selected. A global iteration was said to be completed when all subzones had been treated. In this study, all reconstructions were terminated after 35 global iterations, which was found to be sufficient to produce a stable, converged solution.

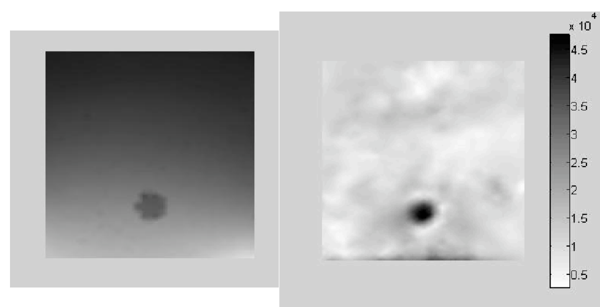

Figure 1:
Left - MR image slice showing structure of (10 cm)^3 gel phantom containing a 1 cm diameter stiff inclusion.
Right – MRE image showing shear modulus distribution within phantom (Units – Pa).

RESULTS

Gelatine-based, linearly elastic phantoms were produced in a controlled and repeatable manner from porcine skin gelatin, formaldehyde, distilled water and ethylenediamine tetra-acetic acid, as described by Doyley (2003). One such phantom was a 10 cm cube, containing a stiff 1 cm-diameter inclusion (Figure 1). Separate dynamic mechanical testing of the phantom materials using a dynamic viscoanalyzer showed that the shear modulus of the inclusion was

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about 13-15 kPa, while that of the surrounding matrix was about 38-40 kPa at 100 Hz. The location, size, and shear modulus of the matrix and inclusion are seen to be accurately portrayed in the MRE shear modulus image of the phantom (Figure 1). The error in shear modulus is less than 15%. Recent work with other phantoms has shown that inclusions as small as 5 mm diameter can be detected accurately with this method (Doyley, 2003).

Results of an MRE study of a heel fat pad on a normal foot are shown in Figure 2. The sole of the foot was pressed against the vibrating plate for the MRE study. The surface was vibrated in the heel/toe direction, with amplitude of 20 μm and frequency =100 Hz. Six homologous structures are labeled in the anatomical MR image (Fig. 2, left) and the reconstructed shear modulus image (Fig. 2, right). Those locations appear dark in the MR image, but appear as brighter, stiffer regions in the shear modulus image. Therefore, the shear modulus of the fat pad on the base of the foot can be quantified and it is related to the structure of the tissue in that region. Recent work has indicated that the structure and properties of the fat pad are affected by the onset of diabetes, so this method offers promise as a diagnostic tool for diabetic patients. One difficulty in the evaluation of the fat pad properties is that the heel fat pad tissue may be non-linearly elastic, with an increase in shear modulus associated with an increase in applied normal pressure (Weaver, 2002). The model used to evaluate the elastic properties has assumed linearly elastic behavior. A modified model for nonlinear elasticity is currently under development.

Up to now the primary application of MRE has been in the detection of breast tumors, which are known to be stiffer than the surrounding breast tissue (Plewes, 2000; Sinkus, 2000). In our application of the technique, the breast is lightly compressed against the plate and imaged while being subjected to low amplitude shear oscillations at a frequency of 100 Hz. Figure 3 shows the results of an MRE exam from a subject with a large centrally located fibroadenoma that is clearly demarked in the shear modulus image, although it is not really evident in the MR magnitude images. The pathology report characterized this fibroadenoma as 'hard and gritty'; hence it is not surprising that it has a higher shear modulus than the surrounding tissue. The case points our clearly the potential value of MRE in detecting tumors and other abnormalities in the breast non-invasively.

CONCLUSIONS

A methodology is described for measuring in-vivo shear modulus of soft tissue using magnetic resonance elastography (MRE). Results with gelatin-based phantoms have shown that the method is capable of accurately determining the shear modulus distribution, even for inclusions as small as 5 mm diameter. Clinical trials have been successful in locating breast lesions in breast cancer patients and in detecting regions of increased stiffness in the foot pads of diabetic patients.

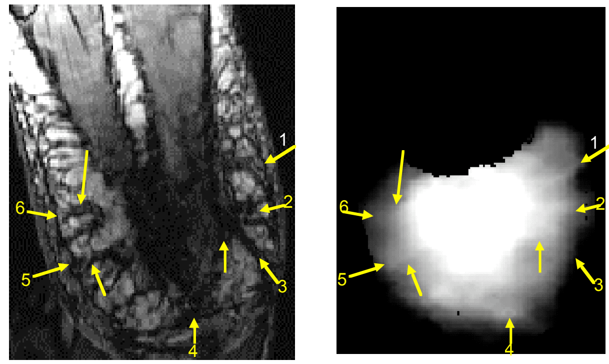

Figure 2: Magnetic Resonance Elastography study of a normal heel fat pad. The anatomical MR image is shown at the left and the reconstructed shear modulus image is on the right. Homologous structures are labeled by arrows in the two images.

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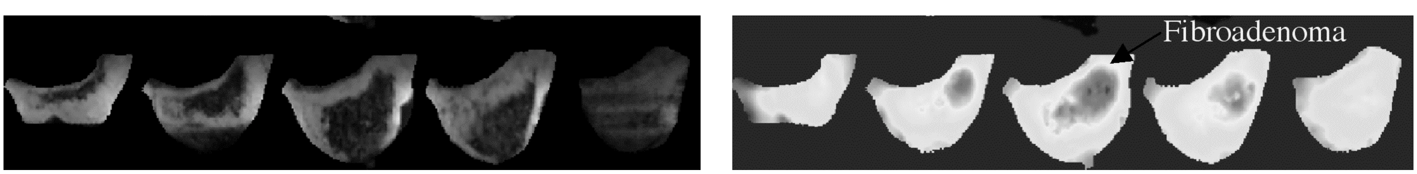

Figure 3 : MR anatomical images (left) and shear modulus images (right) from MRE study of human breast with a stiff fibroadenoma.

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