ACOUSTIC RADIATION FORCE IMPULSE IMAGING OF THE ABDOMEN: DEMONSTRATION OF FEASIBILITY ANDUTILITY

BRIAN J. FAHEY,* KATHRYN R. NIGHTINGALE,* RENDON C. NELSON,† MARK L. PALMERI,* and GREGG E. TRAHEY*†

Departments of *Biomedical Engineering, Duke University, Durham, NC, USA; and †Radiology, Duke University Medical Center, Duke University, Durham, NC, USA

Abstract—The feasibility of utilizing acoustic radiation force impulse (ARFI) imaging to assess the mechanical properties of abdominal tissues was investigated. The thermal safety of the technique was also evaluated through the use of finite element method models. ARFI imaging was shown to be capable of imaging abdominal tissues at clinically realistic depths. Correspondence between anatomical structures in B-mode and ARFI images was observed. ARFI images showed similar tumor contrast when compared with B-mode images of ex vivo abdominal cancers. Finite element method models and in vitro measurements confirmed the thermal safety of ARFI imaging at depth. ARFI imaging is inexpensive, safe and convenient and is a promising modality for use in abdominal imaging. (E-mail: brian.fahey@duke.edu) © 2005 World Federation for Ultrasound in Medicine & Biology.

Key Words: Ultrasound, Ultrasonic imaging, Acoustic radiation force, Abdominal imaging, Elastography, Radiofrequency ablation.

INTRODUCTION

The qualitative relationship between abdominal tissue elasticity and pathology has been well-established in recent work. The stiffness of hepatic tumors, as characterized by tissue elastic modulus, has been investigated by several groups. Hepatocellular carcinoma (HCC) and cholangiocarcinoma were shown by Yeh et al. (2002) to be softer and stiffer than healthy liver, respectively. A benign tumor (focal nodal hyperplasia) examined in the same study was shown to be stiffer than healthy liver, but considerably less stiff than the cholangiocarcinoma. Hepatic hemangioma, another benign liver tumor, has also been shown in vivo to have an increased stiffness relative to healthy liver (Emelianov et al. 1998), despite its soft and spongy internal consistency (Cotran et al. 1999).

Qualitative elasticity estimates also have an established role in the assessment of hepatic fibrosis because manual palpation is often used by surgeons intraoperatively as a crude tool in estimating liver functional reserve. More recently, several groups have demonstrated a correlation between liver stiffness measurements and the degree of hepatic fibrosis discovered after biopsy. These liver stiffness measurements were made with either invasive mechanical (Kusaka et al. 2000; Yeh et al. 2002) or noninvasive imaging-based (Sanada et al. 2000; Sandrin et al. 2003) techniques. Diagnosis of fibrosis, whether early or advanced, is significant because the incidence of HCC is increased in cirrhotic livers (Yeh et al. 2002). Cirrhotic livers also often have poor functional reserve and heptectomy procedures may be altered or abandoned if considerable fibrosis is found after laparotomy (Kusaka et al. 2000).

Recent work suggests that the relationship between tissue stiffness and pathology may also apply to the kidney (Emelianov et al. 1995, 2000; Weitzel et al. 2004). The projected half-life for renal transplants performed in 1995 was 21.6 y for living donors and 13.8 y for cadaveric donors (Hariharan et al. 2000). Although early graft loss is primarily due to acute rejection, long-term graft loss is typically associated with chronic rejection and fibrosis (Hostetter 1994; Kasiske et al. 1991). As with hepatic fibrosis, the onset of renal fibrosis may cause an increase in the elastic modulus of the organ. Weitzel et al. (2004) used ultrasonic strain imaging to compare healthy and fibrotic renal grafts, with initial results suggesting that elasticity imaging may be useful in detecting fibrosis and assessing overall graft health.

Current methods for early detection of abdominal malignancies and fibrosis are associated with fundamental limitations. Biopsy remains the “gold standard” for
identifying fibrosis in abdominal organs. However, the costs and risks involved with the procedure, coupled with factors such as patient discomfort and non-negligible morbidity and mortality rates (Ahmed et al. 2001; Murphy et al. 1988), make frequent biopsies inadvisable. The inability to perform regular biopsies on high-risk patients is a significant problem because noninvasive measurements that may call for a biopsy may not show noticeable change until damage has progressed considerably (Ader et al. 1996; de Bruijne et al. 2003). Manual palpation continues to be useful in many organs for the purpose of disease identification and diagnosis, but the diagnostic value of palpation is limited in deeper structures because they are generally obscured by overlying tissues. Although there are benefits in palpating deep-lying organs, such as the liver, as a whole, lesions situated deep in these organs will likely remain undetected. Small HCCs are difficult to palpate and pain is uncommon until the tumor is quite large, if ever. Given the commonality of late detection, the median survival time after HCC diagnosis is approximately seven months for patients in the USA (El-Serag et al. 2001).

Computed tomography (CT), magnetic resonance (MR) and ultrasound (US) imaging have been able to visualize indications of fibrosis and cirrhosis in the liver (Aubé et al. 1999; Ito and Mitchell 2000; Lucidarme et al. 2003; Tüney et al. 1998; Van Beers et al. 2001; Vignaux et al. 1999) and chronic progressive fibrosis in the kidney (Jennerholm et al. 1990; O’Neill 2000; Buturovi-Ponikvar and Visnar-Perovic 2003; Sebastià et al. 2001). However, none of these modalities has been proven to be reliable for visualizing the progression or degree of fibrosis. CT, MR and US imaging have also been employed for detection of abdominal malignancies (Choi et al. 1989; Dodd et al. 1992; Krinsky et al. 2001; Teefey et al. 2003; Yamashita et al. 1996). CT and MR imaging methods are generally considered to be more sensitive than US for the detection of primary and metastatic carcinomas in the liver and kidney, but both are associated with significant disadvantages. CT scanning is more expensive than US and includes the risks of ionizing radiation exposure and allergic reaction or kidney failure caused by the necessary iodinated contrast agent. MR scanning is considered to be safer and more efficacious than CT imaging, but it also involves the use of contrast agents, is expensive and is not suitable for all patient populations. Intraoperative ultrasound (IOUS) has been shown to be more effective than CT or transcutaneous US in detecting liver metastases (Charnley et al. 1991; Knol et al. 1993; Meijer et al. 1995), but the invasive nature of the procedure restricts its use to advanced cases.

The limitations of palpation and biopsy and the inherent drawbacks of CT, MR and US imaging demonstrate the need for a noninvasive, cost-effective, safe and accurate mechanism for detecting changes in abdominal pathology. Several groups have explored elasticity-based imaging techniques for this purpose, in the hope of exploiting the relationship between pathology and abdominal tissue mechanical properties described above. Strain and elasticity imaging techniques (Emelianov et al. 1998; Weitzel et al. 2004) have been investigated that use induced tissue compressions and ultrasonic speckle-tracking methods to interrogate tissues. The resulting images have proven to be useful in assessing abdominal organs. Disadvantages to this technique include difficulties in eliminating out-of-plane motion in vivo (Kolen et al. 2004) (which makes the technique user-dependent because visual inspection of pre- and postcompression sonograms are necessary) and limitations on the amount of compression that can be applied while retaining patient comfort. Other groups have used low-frequency vibrations to induce shear waves in abdominal tissues and then tracked the speed of the waves with US (Sanada et al. 2000) or MR (Kruse et al. 2000) techniques. Benefits of this method include the capability of extracting quantitative tissue elasticity estimates because the speed of a shear wave is proportional to the shear modulus of the tissue through which it propagates. However, diffraction and boundary effects may bias estimates (Catheline et al. 1999) and long acquisition times (10–90 s) are nonideal for organs that are displaced considerably in vivo by respiration. Transient elastography is a relatively new technique that eliminates many sources of bias when extracting elasticity measurements from analysis of induced shear waves (Catheline et al. 1999). Acquisition times with this technique are also sufficiently short (<100 ms) to be feasible for in vivo abdominal imaging (Sandrin et al. 2003). Although 1-D data collection is sufficient for the evaluation of diffuse liver disease, 2-D data acquisition with this technique requires the use of an ultrafast ultrasonic imaging system and, thus, the performance of applications requiring 2-D data is currently limited to very few institutions.

Given the heterogeneity and complexity of tissues, it is likely that they are distinguishable by their damping as well as their elasticity. All tissues are inherently viscoelastic and differences in the dynamic responses of tissues to mechanical excitation are related to their elastic, damping, inertial and structural properties. We, thus, propose the use of acoustic radiation force impulse (ARFI) imaging for investigating the mechanical properties of abdominal organs. The feasibility of using acoustic radiation force methods to detect tissue mechanical properties has been investigated by several groups (Alizad et al. 2002; Calle et al. 2003; Fatemi and Greenleaf 1998; Konofagou et al. 2001; Lizzi et al. 2003; Sarvazyan et al. 1998; Sugimoto et al. 1990; Viola and
Acoustic radiation force and ARFI imaging

Acoustic radiation force is a phenomenon associated with the propagation of acoustic waves through a dissipative medium. The force originates from a transfer of momentum from the wave to the medium, arising either from absorption or reflection of the wave (Torr 1984). The contribution of absorption is in the direction of wave propagation, whereas the contribution of reflection is dependent upon the angular scattering properties of the target. In tissue, the majority of the attenuation of an acoustic wave is caused by absorption (Christensen 1988; Parker 1983). Thus, under plane-wave assumptions, the radiation force applied to tissue can be described as (Dalecki 1993; Nyborg 1965; Starritt et al. 1991; Torr 1984):

\[ F = \frac{2\alpha I}{c}, \]  

where \( F \) is a body force or force per unit volume, \( \alpha \) is tissue attenuation, \( I \) is the acoustic beam intensity and \( c \) is the speed of sound in tissue. For a focused acoustic beam, the strongest radiation force is applied throughout the focal region of the acoustic beam and, for more attenuating media, throughout the geometric shadow of the aperture.

ARFI imaging uses short-duration (< 1 ms) focused pulses of acoustic radiation force to generate localized displacements in tissue and conventional US beams to track the tissue dynamic response. In general, tissue displacement is inversely related to tissue stiffness and tissue recovery response is related to tissue viscoelastic properties (Nightingale et al. 2003). A single transducer on a diagnostic scanner is used both to generate the radiation force and to track the resulting displacements. Because the technique is implemented via hardware and software modifications on a diagnostic US scanner, the method can provide coregistered B-mode, color Doppler and ARFI images. The tissue displacements generated by the 100–800-cycle pushing pulses used in ARFI imaging generally range from 0–15 \( \mu \)m. Tissue recovery times range from 1–3 ms so that, given the 4–8-kHz pulse-repetition frequencies (PRFs) used in abdominal imaging, the recovery can be monitored with excellent temporal resolution.

Ultrasonic thermal effects

As an acoustic wave travels through a dissipative medium, energy from the wave is transferred to the medium as a result of absorption. This absorption of acoustic energy results in heating of target tissues. The temperature rise in tissue can be estimated with the linear bioheat transfer equation (Nyborg 1988; Pennes 1948):

\[ \dot{T} = \kappa \nabla^2 T - \frac{T}{\tau} + \frac{q_v}{c_v}, \]  

where \( q_v \) is the rate of heat production per unit volume, \( T \) is the temperature, \( T \) is the rate of temperature rise, \( \kappa \) is the thermal diffusivity, \( \tau \) is the time constant for perfusion and \( c_v \) is the specific heat per unit volume for tissue. Insonification times associated with ARFI imaging are very short (< 1 ms) and, thus, cooling effects due to perfusion are typically considered to be negligible.

For a continuous linearly-traveling plane wave, the heat-source function for an US beam can be characterized by (Nyborg 1988; Thomenius 1990):

\[ q_v = \frac{\alpha p_o}{\rho c} = 2\alpha I, \]  

where \( \alpha \) is the absorption coefficient of the target tissue, \( \rho \) is the density of tissue, \( c \) is the speed of sound in tissue, \( p_o \) is the time-averaged acoustic pressure and \( I \) is the time-averaged acoustic beam intensity. The spatial distribution of the applied heat source \( (q_v) \) is dependent on transducer focal configurations and line densities used during ARFI imaging.

METHODS

Data acquisition

Experiments were performed on excised human liver tissues and in vivo on healthy human volunteers. Ex vivo images were acquired with a Siemens Sonoline Elegra™ scanner (Siemens Medical Solutions USA, Inc., Ultrasound Division, Issaquah, WA, USA) and a Siemens 75L40 linear transducer array operating at 7.2 MHz. In vivo data were acquired using a Siemens Sonol-
line Antares™ scanner and a Siemens CH6-2 curvilinear probe transmitting with a center frequency of 2.5 MHz. Both scanners were modified to provide users with the ability to specify acoustic beam sequences and intensities, as well as to access raw radio-frequency (RF) data.

ARFI image beam sequences consisted of both tracking and pushing pulses. Tracking pulses were similar to conventional B-mode US pulses (apodized, with pulse lengths of 0.3 and 0.8 μs and PRFs of 5.6 and 4.9 kHz for the 75L40 and CH6-2 probes, respectively). Pushing pulses were unapodized and had pulse lengths ranging from 0.03–0.4 ms. F number is defined as the ratio of the beam focal depth to the length of the active transducer aperture. F numbers were chosen to optimize the trade-off between lateral resolution and depth-of-field (Fahey and Trahey 2004). Dynamic focusing was used in receive so that a constant F number was maintained. Ex vivo data were acquired using an F 1.5 focal configuration in both transmit and receive, and in vivo data were acquired using an F 2.5 or F 3.5 focal configuration. Echoes from pushing pulses were not processed.

Two-dimensional ARFI images were generated using 30–80 pushing locations at various line densities. When necessary, ARFI data sets were upsampled with interpolation algorithms to obtain the same effective line density as in conventional B-mode images. In vivo focal depths ranged from 6 to 8 cm. At each pushing location, both tracking and pushing beams were fired along the same line of flight, as in typical A-line interrogation. The first beam fired was a tracking beam used as a reference to record initial tissue position. Next, one or two pushing beams were fired to generate an impulse of radiation force. Tracking beams used to record the temporal response of the tissue followed the pushing beams. The number of tracking beams determines the temporal window over which the tissue response is monitored and, thus, the duration of data acquisition. Total image acquisition times for abdominal imaging are typically < 350 ms. During in vivo scanning, ARFI beam sequences were ECG-triggered, with data acquisition taking place during diastole.

Data were processed by performing 1-D cross-correlation in the axial dimension between sequentially acquired tracking lines (O’Donnell et al. 1994; Trahey et al. 1987). Each tracking line was divided into a series of search regions and the location of the peak in the cross-correlation function between a 0.92-mm kernel in the first tracking line and a search region in the next tracking line was used to estimate axial tissue displacement in that region. The kernel regions overlapped one another by 98%. Linear motion filters were applied to in vivo data to remove artefacts stemming from physiological or transducer motion. When acquisition was performed using the Antares system, ARFI displacement images acquired at a predetermined time following the removal of radiation force were processed and displayed in real-time on a monitor next to the machine. For a more thorough description of ARFI processing methods, the reader is referred to Nightingale et al. (2002c).

Selected images were further processed off-line using time-gain control (TGC) techniques. TGC processing is implemented to normalize for gradients in applied force in the focal region of the pushing beams. This technique is used to improve contrast in the image and it also reveals details that would otherwise be lost because of strongly spatially-varying brightness. A detailed description of this algorithm has been provided previously (Fahey et al. 2005). Parametric images documenting the tissue’s dynamic response to the applied radiation force were also generated off-line.

Finite element method thermal modeling

To evaluate thermal safety, FEM were used to model the heating associated with various deeply-focused ARFI beam sequences. The details of thermal model implementation are covered thoroughly by Palmeri and Nightingale (2004). In general, acoustic intensity distributions for a given transducer and beam sequence are simulated using FIELD II, a linear acoustic field simulation software program (available for download at http://www.es.oersted.dtu.dk/staff/jaj/field/)(Jensen and Svendsen 1992). The 3-D intensity fields are computed and normalized, with values less than 5% of the maximum intensity neglected to reduce computational overhead. Normalized intensity values from the simulation (F 2.5, focal depth 8.0 cm, α = 0.7) are then scaled to a peak intensity of 820 W/cm², a value consistent with in situ values indirectly measured during ARFI imaging using a linear extrapolation of small-signal derated fields. The scaled intensity field is converted into a field of initial temperatures using:

\[ T_i = \frac{q_f}{c_v}, \]  

where \( T_i \) is the approximated initial temperature and \( t \) is insonification time. This is the solution of eqn (2) neglecting conduction and perfusion. This method is valid for our purposes because we have short insonification times relative to the thermal diffusivities of the tissues being modeled (Palmeri and Nightingale 2004). This field of initial temperatures from a single ARFI excitation is then superimposed on a curvilinear solid mesh created by a finite element mesh generation program (HyperMesh, Altair Computing, Inc., Troy, MI, USA). Plane-symmetry is assumed in both the lateral and elevation dimensions and, thus, only a quarter field is modeled to reduce computational requirements.
Tissues are modeled as thermally homogeneous isotropic solids. Hepatic tissues were modeled as having a density of 1.05 g/cm³, a specific heat of 3.6 J/g/C and a thermal conductivity of 0.57 W/m/C. Adipose tissues were modeled as having a density of 0.9 g/cm³, a specific heat of 2.3 J/g/C and a thermal conductivity of 0.19 W/m/C (Duck 1990). To simulate a continuum of tissue, the boundaries of the model are treated as insulating boundaries (Thomenius 1990). An explicit time-domain finite element analysis package (LS-DYNA3D, Livermore Software Technology Corporation, Livermore, CA, USA) is used to characterize the thermal response of the modeled tissue to ARFI interrogations. Models were validated experimentally using 36-gauge type T thermocouples (Omega Engineering, Stamford, CT, USA) and a 16-bit data acquisition system (SuperLogics, Waltham, MA, USA) (Palmeri et al. 2004).

RESULTS

Ex vivo images

Figure 1 shows B-mode and ARFI images of an excised colorectal metastasis after its resection from a human liver. The excised tissue sample was imaged within 12 h of resection, was not fixed in formalin and was imaged at room temperature, surrounded by saline-saturated gauze. Manual palpation of the excised liver revealed the tumor to be stiff and rigid relative to the surrounding nontumorous liver parenchyma at specimen margins. The malignancy is apparent in the B-mode image (Fig. 1a) as an hypoechoic region extending to roughly 16 mm in depth. However, tumor boundaries are ambiguous despite the use of a transmit frequency (7.2 MHz) that is generally considered to be too high to be efficient for transcutaneous abdominal imaging in adults. The ARFI displacement map (Fig. 1b) obtained 0.9 ms after the removal of radiation force shows improved tumor visualization, as the stiffer tumor (darker area) is displaced less than the surrounding nontumorous tissue (brighter regions). Lateral lesion boundaries are apparent, but the distal tumor boundary is still vague because of the reduced radiation force applied beyond the image’s focal depth (15 mm). Time-gain control (TGC) processing compensates for focal-gain effects in ARFI images by applying a laterally-uniform axially-varying gain to the image. The applied gain is equal to the inverse of the normalized displacement-depth curve shown Fig. 1d. The tumor is best visualized in the TGC-processed ARFI image (Fig. 1c). No “gold standard” evidence was available for comparison of actual tumor boundaries with boundaries shown in ARFI images.

Figure 2 shows B-mode and ARFI images of an excised portion of a human liver containing a melanoma.
metastasis. The excised tissue sample was imaged within 12 h of resection, was not fixed in formalin and was imaged at room temperature, surrounded by saline-saturated gauze. The tumor is visualized in the B-mode image (Fig. 2a) as an hyperechoic region extending from 12 to 25 mm axially and −6 to 2 mm laterally (solid arrows). The linear hyperechoic structure in Fig. 2a at 26–27 mm depth (dashed arrow) is the plastic membrane used to support the tissue sample. The linear structure observed as a bright region in the right-hand side of Fig. 2b and c from 19 to 22 mm (indicated by arrows) is likely the track of an old needle biopsy of this tumor. Although the TGC-ARFI displacement map Fig. 2b depicts the tissue response at a specific time (0.9 ms) following the removal of radiation force, the time-to-peak image (Fig. 2c) illustrates the tissue’s dynamic response to the applied force.

Figure 2b shows the TGC-ARFI displacement image, where logarithmic compression has been performed on the data to visualize smaller displacements induced at the bottom of the tumor without saturating larger tissue displacements located elsewhere. The figure shows that the tumor has a stiffness that resembles that of the healthy tissue directly above it and, in this case, the proximal boundary is not well visualized. Visualization of this malignancy is improved by examining its dynamic response to the applied radiation force, because contrast between the tumor and healthy tissue is significantly improved in the time-to-peak image (Fig. 2c) relative to the displacement map shown in Fig. 2b. The metastasis reaches its peak displacement in approximately 1.25 ms, and nontumorous hepatic tissue in the same axial region reaches its peak in 2.5–3 ms. Again, no “gold standard” evidence was available for comparison of actual tumor boundaries with boundaries shown in ARFI images.

In vivo images

Figure 3 shows matched longitudinal B-mode and ARFI displacement images of the liver of a healthy 30-y-old male volunteer. The ARFI image has been centered in the B-mode image for anatomical reference.

Fig. 2. (a) Matched B-mode, (b) TGC ARFI and (c) Time-to-peak ARFI images of an ex vivo melanoma metastasis in the liver after resection. Solid arrows in (a) = tumor location; dashed arrow in (a) = plastic membrane used to support the tissue sample. TGC image is formed with an axially-varying gain and, thus, has a scale of relative displacement. Scale of (c) is time in ms. Arrows in (b) and (c) indicate the track of a previous needle biopsy of this tumor.

Fig. 3. (a) B-mode and (b) ARFI images of the liver and hepatic and portal veins of a healthy 30-y-old male. The ARFI image in (b) has been centered in the corresponding B-mode image for anatomical reference. Solid arrows in (a) point to hepatic veins; dashed arrows in (a) point to portal veins. Scale of ARFI image (b) is displacement in μm.
The solid arrows in Fig. 3a refer to hepatic veins, and the dashed arrows refer to the volunteer’s portal veins. Liver tissue surrounds the vessels and is seen throughout the majority of the image.

The ARFI displacement image is shown in Fig. 3b. The beam sequence used to create the ARFI image included 30 280-μs pushing pulses and used a line density (0.84 degrees/beam) equal to one third of that used in the B-mode image. The ARFI image had a focal depth of 8 cm and was acquired using an F 2.5 transducer configuration. The liver tissue in the ARFI image exhibits roughly uniform stiffness from depths ranging from 2–7 cm, being displaced 2.5–4 μm by the applied radiation force. The vessels in the B-mode image (Fig. 3a) are visualized as noisy regions in the ARFI image (Fig. 3b), because of highly-decorrelated echoes returning from mobile scatterers in the blood. The presence of the vessels also disturbs the uniformity of the applied force field in axially-deeper regions, as indicated by the varying displacements induced in the regions of liver tissue located at depths of 7–8 cm.

Figure 4 shows matched transverse B-mode and ARFI displacement images, magnified for clarity, of the liver and kidney of the same male volunteer. The solid black arrows in Fig. 4a indicate the liver/kidney interface. Liver tissue is more proximal to this boundary in the image and the volunteer’s kidney lies below it. The dashed arrow indicates a fat pad that begins at the bottom of the gallbladder (white arrow) and extends downward to the right of the kidney.

The ARFI image shown in Fig. 4b was created using the same beam sequence as for the image shown in Fig. 3b. Again, we see a roughly uniform displacement (4.5–6 μm) induced in the volunteer’s liver by the applied radiation force. There are several possible causes of the difference in displacement magnitude between the liver section imaged in Fig. 3b and that imaged in Fig. 4b and this issue will be revisited in the Discussion section of this paper. The layer of fat at the liver/kidney interface and the fat pad to the right of the kidney are displaced the furthest in the image, moving > 6 μm. The parenchyma of the kidney is displaced by a relatively small amount (1–2.5 μm). Near zero displacements are induced in the kidney beyond the axial focus of the image (8 cm), where relatively weaker radiation forces are applied. However, these weaker radiation forces were still able measurably to displace the more compliant fatty tissues located adjacent to the kidney at similar depths.

In order to better investigate the mechanical properties of the kidney, it is desirable to place the organ above the axial focus in the ARFI image, so that measurable displacements can be induced with the applied radiation forces. This is done in Fig. 5, which has been magnified to enlarge regions-of-interest (ROIs). Again, there is good correspondence between structures in the transverse B-mode (Fig. 5a) and ARFI displacement (Fig. 5b) images. The fatty tissue at the liver/kidney interface, indicated by the solid arrows in Fig. 5a, is again displaced more (6+ μm) by applied radiation force than is liver tissue (3.5–5 μm) in the near field. The renal sinus fat and hilar structures (dashed arrow in Fig. 5a) are also displaced significantly (5+ μm). The parenchyma of the kidney has also experienced roughly uniform displacements (1–2.5 μm) over much of the organ. The beam sequence used to create the ARFI image in Fig. 5b included 40 320-μs pushing pulses spaced at a line density of 0.84°/beam. The axial focus of the ARFI pushing beams was 6.5 cm, so reduced displacement values for tissues lying deeper than this radius likely arise from a reduction in applied radiation force and not necessarily from an increase in tissue stiffness. An F 3.5 focal configuration was used.

In addition to liver and kidney imaging, ARFI imaging also may potentially have use in visualizing other abdominal anatomy. Figure 6 shows B-mode and ARFI images of a healthy 30-y-old male volunteer that have...
been magnified to focus on the gallbladder (dashed arrow in Fig. 6a). The largest displacements (8 μm) in the ARFI image are seen in the adventitia of the gallbladder. The lower right section of gallbladder adventitia in the ARFI image (white arrow in Fig. 6b) experienced smaller displacements relative to other portions of the adventitia. This difference in mechanical properties is possibly due to the cross-section of the gallbladder captured in the imaging plane or to different boundary conditions associated with the spatial location of the fluid-filled bladder relative to the orientation of the beams of radiation force. There appear to be negligible (<1 μm) displacements induced inside the majority of the gallbladder. The apparent larger displacements that appear in some regions within the gallbladder are image noise resulting from significant echo decorrelation. The slightly hyperechoic structure adjacent to the gallbladder in the B-mode image (outlined with solid arrows) is visualized in the ARFI image as a relatively soft region of tissue. Again, structural boundaries in the ARFI image (Fig. 6b) correspond well with their appearance in companion B-mode image (Fig. 6a). The ARFI image was acquired using 280-μs pushing beams in 34 interrogation locations. The transducer was focused at 6.5 cm and used an F 3.5 focal configuration.

**Thermal simulation results**

Figure 7 shows results from FEM simulations of the temperature rise induced in hepatic tissue by an aggressive ARFI imaging beam sequence. The beam sequence modeled is nearly identical to that used to create Figs. 3b and 4b, with the exception being that the pushing pulse in the model sequence has a longer duration (320 μs) and will, thus, induce larger temperature increases in target tissues. Figure 7a shows the heating pattern associated with a single pushing pulse, assuming a tissue attenuation of 0.3 dB/cm/MHz. The peak heating occurs at the axial focus of the pushing beam (8 cm). The heating induced by the center and outer pushing beams that

---

**Fig. 5.** (a) B-mode and (b) ARFI images of liver and kidney of a healthy 30-y-old male. ARFI image in (b) has been centered in the corresponding B-mode image for anatomical reference. Solid arrows in (a) = liver/kidney interface; dashed arrow in (a) = renal sinus fat and hilar structures. Scale of ARFI image (b) is displacement in μm.

**Fig. 6.** (a) B-mode and (b) ARFI images of liver and gallbladder of a healthy 30-y-old male. ARFI image in (b) has been centered in the corresponding B-mode image for anatomical reference. Dashed arrow in (a) = gallbladder; solid arrows in (a) = boundaries of the mildly hyperechoic structure adjacent to the gallbladder; solid arrow in (b) = portion of gallbladder adventitia with decreased displacements. Scale of ARFI image (b) is displacement in μm.
would be used to create a 2-D ARFI image is shown in Fig. 7b. It should be noted that the model takes into account the tissue cooling that occurs in the time period between when the first (left) and last (right) pushing beams are fired. However, because the time constant for tissue cooling is significantly longer than the insonification time (Palmeri and Nightingale 2004), the figure shows minimal temperature differences between tissue regions associated with the first and last beams. The figure shows that, although the maximum heating associated with each individual beam is still located at a radial depth of 8 cm, the three beams do not have overlapping pressure fields at this depth. However, beam overlap does occur at shallower depths (< 3 cm in this case) and, thus, near field heating can be significant in 2-D ARFI imaging.

Figure 7c shows the heating induced by the complete 2-D ARFI imaging beam sequence. Peak temperature rises are induced in the center of the image, in the region where overlap from the emitted pressure fields of the various pushing beams is most significant. The maximum temperature rise associated with this beam sequence is shown to be on the order of 0.35 °C.

Although modeling tissue attenuation as 0.3 dB/cm/MHz perhaps results in the most intuitive spatial heating patterns, this attenuation is not a realistic value for hepatic tissue. Actual attenuation values for human hepatic tissues range from 0.5–0.8 dB/cm/MHz (Garra et al. 1987; Fujii et al. 2002). Figure 8a shows the heating pattern associated with the same ARFI imaging beam sequence as Fig. 7c, when tissue attenuation is modeled as 0.7 dB/cm/MHz. Induced temperature rises have climbed to a peak value of 0.56 °C and the location of maximum temperature increase has now moved much further into the near field (1.5 cm from the transducer face).
When using ARFI imaging to interrogate the abdomen, adipose tissue may lie in the propagation path of the emitted pushing beams. This is a concern, because adipose tissue has a lower thermal conductivity and a lower specific heat than does hepatic tissue and will, thus, generally be subjected to larger temperature increases during ARFI imaging. Figure 8b shows simulation results for heating in adipose tissue for the same beam sequence and tissue attenuation as depicted in Fig. 8a. The spatial heating pattern that results is identical to that found in hepatic tissue, but temperature rises have increased to a peak temperature of 0.89 °C.

The “worst-case” tissue heating condition in abdominal ARFI imaging would be to have a minimally-attenuating tissue in the near field and a more attenuating tissue with thermal properties resembling those of fat at the beam focus. Figure 8c models the temperature increase induced under these circumstances. Field pressure amplitudes were derated at 0.3 dB/cm/MHz, but initial temperatures, eqn (4), were computed with \(\alpha = 0.7\) dB/cm/MHz. Thermal properties of adipose tissue were used in the simulation. As shown, in this “worst-case” scenario, induced temperature rises can be as high as 1.35 °C.

All of the thermal simulations exhibited in this manuscript were run for a focal depth of 8 cm. However, in ARFI imaging, focal depths are typically chosen on a session-by-session basis to best correspond with the anatomical features to be imaged. Figure 9 shows how the maximum value of the heat source function, eqn (3), from a single pushing pulse varies with focal depth for four different values of tissue attenuation. The transducer apertures have been modeled as clinically-implemented in ARFI imaging, with focal depths of 8 cm and beyond.

Fig. 8. FEM simulation of heating patterns associated with an aggressive ARFI imaging beam sequence. Sequence includes 30 320 µs pushing pulses arranged with a line density of 0.84°/beam. All pushing beams were transmitted with an F 2.5 focal configuration. (a) Models heating in hepatic tissue with an attenuation of 0.7 dB/cm/MHz; (b) Models heating in adipose tissue with attenuation of 0.7 dB/cm/MHz; (c) Models “worst-case” tissue heating, with a low attenuating (0.3 dB/cm/MHz) tissue in the near field and a more attenuating (0.7 dB/cm/MHz) tissue with thermal properties of adipose tissue at the focus. Scale of images is induced temperature rise in °C.
utilizing an F 2.5 aperture and shallower focal depths utilizing an F 3.5 aperture. The resulting values have been normalized for visualization purposes. In the plot, the maximum value of 1 corresponds to $q_w = 1113.6 \text{ J/cm}^3/\text{s}$.

As shown in Fig. 9, for $\alpha = 0.3 \text{ dB/cm/MHz}$, the greatest heating would occur when focusing at 7 cm (the elevation focus of the transducer). For more attenuating tissues, shallower transmit foci will lead to significantly greater maximum heat-source function values than the thermal models provided in this paper demonstrate. Figure 9 also shows that, although higher attenuation tissues experience greater temperature increases during 2-D ARFI imaging (due to more energy deposition in the near field, where beam overlap is most prevalent), the temperature increase associated with a single pushing pulse becomes lower as tissue attenuation increases.

**DISCUSSION AND CONCLUSIONS**

We have demonstrated the feasibility of utilizing ARFI imaging to investigate the mechanical properties of abdominal tissues. To our knowledge, this is the first application of ARFI imaging at depths that are clinically realistic for transcutaneous abdominal imaging in adults. Quality images have been created of anatomical structures such as the liver, kidney, gallbladder and hepatic vessels. Generally speaking, there exists good correspondence between anatomical structures in the B-mode and ARFI displacement images shown in this paper.

ARFI imaging also appears to be a promising complement to conventional sonography in visualizing abdominal malignancies. Soft tissue contrast in the ARFI images of ex vivo metastases presented in this paper is comparable with that achieved in their B-mode image companions. Similarly, preliminary results from imaging in vivo malignant breast masses (Sharma et al. 2004) indicate a contrast improvement in ARFI images relative to conventional B-mode imaging. Although this contrast improvement may not be present in images of all cancers, ARFI images can serve as an additional source of information to physicians assessing potential malignancies. Initial results from studies assessing the diagnostic utility of viewing combined B-mode and ARFI images of breast masses are encouraging (Sharma et al. 2004) and current data suggest that, with further development, the diagnostic utility of ARFI imaging will apply to abdominal masses as well. Future efforts will focus on attempting to visualize abdominal malignancies in humans in vivo with ARFI imaging.

Abdominal ARFI imaging may also find use in guiding certain interventional and surgical procedures. For example, radio-frequency ablation (RFA) has become a popular treatment option for patients with liver or kidney tumors who are not candidates for surgical resection. RFA uses local ionic agitation to produce a volume of thermal necrosis in and around the target tumor (Dodd et al. 2000). For an RFA procedure to be successful, the induced thermal lesion must be of adequate volume to destroy the target tumor in its entirety, plus a rim of nontumorous parenchyma. Because the preset algorithms used by ablation systems may induce thermal lesions of markedly different volumes in different patients (Montgomery et al. 2004), a modality capable of visualizing the size of growing thermal lesions in real-time is desired to optimize the success rate of RFA procedures, particularly when multiple overlapping ablations are applied to larger malignancies. Preliminary studies have demonstrated that ARFI images can provide more information concerning the size of a growing RFA lesion than conventional sonography in healthy liver tissue (Fahey et al. 2004). Even when target tumors appear to be stiffer than surrounding nontumorous tissues in ARFI images prior to RFA treatment, we expect to see a further increase in stiffness and image contrast associated with the creation of a thermal lesion within the tumor. We, thus, believe that ARFI imaging is a promising modality for real-time RFA guidance.

The quality of ARFI images is influenced considerably by tissue motion in regions of interest. Linear motion filters can be employed to minimize artefact stemming from transducer or physiological motion, but are only marginally effective if significant tissue acceleration is present during data acquisition. ECG-triggered beam sequences used simultaneously with patient breath-hold minimizes the degree of cardiac and respiratory motion encountered during data acquisition. Our experi-
ence indicates that using these two techniques in conjunction with one another minimizes the prevalence of motion-related artefacts in ARFI images. Because acquisition times in ARFI imaging are short (typically < 400 ms), patient breath-hold during imaging is generally a feasible option.

The displacements induced by applied radiation forces in vivo can vary for a given tissue, even when identical beam sequences are used. The properties of tissues overlying and adjacent to target tissues can impact the strength of the push field reaching the target and the dynamic response of tissues to the applied force. System factors, such as transducer focal configuration, ARFI pushing pulse intensity and location of the target tissue relative to the axial focal position of the pushing beams, can also affect induced displacements. Physiological factors, such as the state of contraction in muscle tissues (Fahey et al. 2005; Nightingale et al. 2002b), also play a role in tissue displacement magnitude. TGCP processing algorithms can help to account for differences in applied radiation force magnitudes at different depths, but are typically not implemented in abdominal ARFI imaging, because beam sequences are designed to optimize pushing beam depth of field (Fahey and Trahey 2004). ARFI imaging is, thus, currently more reliable for use as a qualitative modality, discerning potential malignancies as softer or stiffer structures embedded in relatively homogeneous background tissues. Current efforts are underway to improve the quantitative information that can be extracted from ARFI displacement and parametric images.

Results from FEM simulations predict that tissue temperature increases induced by the ARFI imaging beam sequences used in this study are within the limits imposed by the US Food and Drug Administration for short duration diagnostic imaging in soft tissue (Herman and Harris 2002; NCRP 1992). However, tissue heating will be a limiting factor when determining maximum achievable frame rates in real-time ARFI imaging applications. Factors that impact the heating associated with an ARFI imaging beam sequence include the number of pushing locations and the spatial separation between adjacent pushing locations. The size of the active transducer aperture used in transmit also impacts the degree of temperature rise. Smaller apertures reduce overlap between adjacent pushing beams and, thus, lower induced temperature increases. Ultimately, trade-offs must be made between desired frame rate, field-of-view, line density and aperture size to avoid heating tissues to potentially damaging temperatures.

Figure 9 indicates that, for tissues with attenuations of at least 0.5 dB/cm/MHz, focusing at depths of 5–6 cm will lead to significantly greater tissue heating than is demonstrated by the models in this paper if identical beam sequences are used. However, at these shallower foci, pushing beams undergo less attenuation prior to reaching their focal depth relative to deeper foci and, thus, in general, identical tissue displacements can be induced with shorter-length pushing pulses at these depths. Therefore, although the heat source function, eqn (3), has an increased magnitude for a focus of 5 cm relative to a focus of 8 cm, this heat source is applied to tissues for shorter time periods in the 5-cm focus case. Consequently, tissue heating at shallower focal depths is not expected to be significantly greater than the heating values at a focal depth of 8 cm shown in this paper.

The temperature rises shown in Figs. 7 and 8 are approximately 4 times larger than values previously reported for a similar ARFI imaging beam sequence (Fahey and Trahey 2004). This increase in temperature reflects an increase in available scanner output power and, thus, a corresponding increase in ARFI pushing beam intensities. Current abdominal ARFI imaging applications use the pushing beam intensities described in this paper.

Theoretically, changes in sound speed due to the temperature rises associated with ARFI imaging beam sequences may affect the accuracy of the correlation-based algorithms used to track induced tissue displacements by a few micrometers. However, both ex vivo and in vivo data collected to date do not appear to contain significant heating artefacts. This possibly stems from an overestimation of ARFI pushing beam in situ intensities determined using linear extrapolation of small-signal derated fields. Because tissue cooling times are on the order of several seconds, it is also possible that heating artefacts are eliminated by linear motion filters implemented during data processing. A more thorough discussion concerning the effects of tissue temperature increases on ARFI imaging displacement tracking is provided by Palmeri and Nightingale (2004).

There are several limitations to the thermal model used in this study. For example, the cumulative effects of transducer heating on tissue temperatures near the surface have been neglected. In addition, nonlinear wave propagation effects have not been taken into account. Future investigations that use nonlinear simulation packages to model tissue intensity fields are, thus, necessary more accurately to predict the maximum temperature increases induced in tissues by ARFI beam sequences. Until these future studies have been performed, conservative safety factors must be implemented when determining acceptable imaging frame rates.

ARFI imaging offers several potential advantages for abdominal imaging. Because the radiation force is localized and can be applied in selected remote locations, considerably smaller forces are required than in techniques utilizing global compression, where large strains...
near the transducer are required to generate small strains at depth. Thus, deep-lying lesions can be detected without exposing the tissue to large strain fields. In addition, ARFI imaging is implemented using a single transducer on a modified diagnostic scanner, which allows for coregistered B-mode, color Doppler and ARFI images without the introduction of any additional equipment. Further, ARFI imaging is safe, inexpensive, portable and allows for real-time visualization of acquired data. These advantages indicate that ARFI imaging may be a convenient complement to conventional sonography for assessing abdominal pathology.

Acknowledgements—The authors thank Siemens Medical Solutions, USA, Ultrasound Division for their system support. They thank Dr. Rex Bentley for his help with pathology. This work was supported by the US NIH (grants 1R01-HL-075485-01 and 1R01-EB-002132-04).

REFERENCES


