ELASTOGRAPHIC IMAGING OF THERMAL LESIONS IN THE LIVER
IN VIVO FOLLOWING RADIOFREQUENCY ABLATION:
PRELIMINARY RESULTS

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Abstract—Radiofrequency (RF) ablation is an interstitial focal ablative therapy that can be used in a percutaneous fashion. This modality provides in situ destruction of hepatic tumors. However, local recurrence rates after RF ablative therapy are as high as 34% to 55%, believed to be due in part to the inability to visualize accurately the zone of necrosis (thermal lesion). This can lead to the incomplete ablation of the tumor, generally in areas near the tumor edges. In this paper, we show that ultrasound (US)-based in vivo elastography can accurately depict thermal lesions after thermal therapy. However, elastography of the liver and other abdominal organs is challenging due to the difficulty in providing controlled and reproducible compression. The use of the RF ablation probe as the compressor/displacement device reduces lateral slippage or nonaxial motion that may occur with externally applied compressions or imaging during the respiratory cycle. This technique also provides controlled and reproducible compressions of the liver for in vivo elastographic imaging. Comparison of elastograms with histology of ablated tissue demonstrates a close relationship between elastographic image features and histopathology. (E-mail: tvarghese@facstaff.wisc.edu) © 2002 World Federation for Ultrasound in Medicine & Biology.

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INTRODUCTION

Radiofrequency (RF) ablation (RFA) is an interstitial focal ablative therapy, in which an electrode is placed into a lesion to cause tissue heating from ionic agitation. This results in heating and cauterization of the tumor mass and probe track (Goldberg et al 1998, 2000; De-Santis et al 1998; Lee et al 1999a, 1999b; Curley et al 1999; Rhim and Dodd 1999; Livraghi et al 1999; Cha et al 2000). Temperatures greater than 42°C are considered potentially lethal, depending on the duration of application (Rosner et al 1996), and temperatures greater than 60°C are associated with uniform tissue necrosis (Zervas and Kuwayama 1972). RFA has the advantage of tissue coagulation at the probe insertion site, resulting in a low rate of intra- and postprocedural bleeding (Rhim and Dodd 1999; Livraghi et al 1999). The RFA probes are of small diameter (generally 15 to 18 gauge) and can be used in a percutaneous fashion (Curley et al 1997; Solbiati et al 1997a).

Guidance and monitoring RFA for treatment of hepatic tumors has been almost exclusively through the use of transabdominal sonography (Solbiati et al 1997a, 1997b). Advantages of using ultrasound (US) guidance for RFA includes widespread availability, real-time guidance for probe placement, and accurate and convenient puncture guides available for most probe systems. However, local recurrence rates as high as 34% to 55% have been reported for percutaneous RFA guided by conventional sonography (Solbiati et al 1997a, 1997b; Rossi et al 1996). This is a much higher rate than the 12% local recurrence rate reported for cryosurgical patients followed over the last 5 years (Kane et al 1997) or the 16.7% local recurrence rate reported for surgical resection (Hughes et al 1989).

One of the critical factors contributing to the success of cryoablation of liver tumors has been the excellent imaging of liver tumors and the ensuing iceball with intraoperative sonography. Reflection of the US beam at the interface between frozen and unfrozen tissue pro-
vides visualization of the treated region. In contrast, the zone of necrosis during RFA is not easily visualized by transabdominal sonography, as a result of low intrinsic contrast between normal and ablated liver and artifacts from gas bubble formation and the RFA generator. These conditions result in uncertainty in determining the extent of ablation during an RFA procedure monitored using US, and they may be a contributing factor to the high positive recurrence rates seen in clinical series.

Grey-scale US imaging during thermal ablation generally is not sufficiently accurate in predicting the extent of coagulation (Solbiati et al 1997a; Goldberg et al 1998). The progressively increasing hyperechogenic region due to formation of gas bubbles in heated tissue does not represent the region of tissue coagulation (Malone et al 1994), and generally resolves within 1 h of ablation (Goldberg et al 2000). In addition, this region varies in size, and its contours are quite irregular in shape, often obscuring the visualization of the ablation probe and treated region. This increases the difficulty in probe repositioning for further treatment. Color flow and power Doppler sonography also are unable to assess the extent of induced coagulation (Solbiati et al 1997a). Magnetic resonance (MR) images of ablated regions reveal altered signals on both T1- and T2-weighted images (Goldberg et al 1998; Hydohh et al 1998; Steiner et al 1997), with the treated areas devoid of gadolinium enhancement. Radiologic and pathologic correlations in both experimental and clinical studies have shown that computerized tomography (CT) and MR imaging predict the region of coagulation to within 2 to 3 mm (Goldberg et al 2000). MR imaging has the ability to help determine the extent of coagulation, allowing tailoring of energy deposition using heat-sensitive sequences (Steiner et al 1997).

Imaging tissue elastic properties (Wilson and Robinson 1982; Krouskop et al 1987; Yamakoshi et al 1990; Parker et al 1990; Ophir et al 1991, 1997, 1999; O’Donnell et al 1991, 1994; Céspedes 1993; Plewes et al 1995; Fowlkes et al 1995; Muthupillai et al 1995; Varghese et al 1997a; Goldberg et al 1998; Varghese et al 2000) is another technique that has been proposed to monitor thermal lesions. Elastographic techniques have been used previously for imaging thermal lesions generated using high-intensity focused ultrasound (HIFU) in ex vivo liver tissue (Stafford et al 1998; Righetti et al 1999) and ex vivo thermal lesions formed using RFA (Varghese et al 2002b). MR elastography also has been used to visualize focused US lesions in ex vivo porcine tissue (Wu et al 2001).

In elastography (Ophir et al 1991, 1997, 1999), we typically estimate the axial strain (along the direction of insonification/compression) by analyzing ultrasonic signals obtained from standard medical US diagnostic equipment. Frames of RF echo signals acquired before and after a small amount (about 1%) of compression are compared. Differential displacements in small regions are detected using classical time-delay estimation techniques (Weinstein and Weiss 1984; Quazi 1981; Knapp and Carter 1976). Finally, the strain is computed from the gradient of the time-delays or tissue displacements.

A problem that must be overcome for elastography to be used successfully for monitoring liver tumor ablations is that of introducing controlled compressions of liver tissue. This paper reports on a novel technique for doing this effectively and presents in vivo US-based elastographic imaging of thermal lesions created in the liver of a porcine animal model. The in vivo elastograms of RFA lesions were obtained using the ablation probe to induce small, controlled displacements, along with synchronized acquisition of the RF echo signals (Varghese et al 2002b, 2002c). The use of the ablation probe eliminates lateral slippage or nonaxial motion that could easily occur with externally applied compressions. This concept is discussed in the next section. Other techniques for in vivo elastography of the liver relate to the use of a conventional, fixed-geometry elastography system (Ophir et al 1991) on an open pig model with the liver exposed (Merritt et al 2002), diaphragmatic motion due to respiration to induce compression in the liver (Varghese et al 2002a, 2002b) and the use of cardiovascular motion (Kolen et al 2002). However, diaphragmatic motion may not generate reproducible and controlled compressions in the liver and may also induce slippage of the liver with respect to other abdominal organs.

In this paper, we first present the elastographic depiction of thermal lesions in vitro as a proof of feasibility of the method for visualizing RFA lesions. We then describe our in vivo method to determine the extent of tissue coagulation and necrosis of RFA lesions in the liver. Elastography in conjunction with transabdominal sonography may provide the interventionalist the tools for both probe guidance and visualization of the treated region (i.e., the zone of thermal necrosis).

MATERIALS AND METHODS

Initially, RFA was performed on lobes of freshly excised porcine liver tissue with approximate dimensions of 40 mm by 40 mm and 20 mm thickness. The samples were encased in a gelatin cube with dimensions of 80 mm. Tissues were encased in the gelatin phantom so that it would provide a regular surface for compression. US imaging to guide the RFA probe placement and for elastographic imaging of the thermal lesion was performed using an Acuson 128XP real-time scanner (Acuson Inc., Mountain View, CA, USA). The scanner operates with dynamic receive focusing using a 5-MHz lin-
ear-array transducer (40 mm) with a 30% bandwidth. The US RF signals were digitized using a 12-bit data-acquisition board (Gage Applied Inc., Lachine, QC, Canada) at a sampling rate of 50 MHz. The system includes a stepper motor-controlled motion/compression system, and a compression/displacement device. A personal computer controlled the operation of the entire system. A schematic diagram of the system used is illustrated in Fig. 1.

A RITA model 30 electrosurgical device was used for in vitro RFA, and a model 1500 electrosurgical device was used for subsequent in vivo procedures (RITA Medical Systems Inc., Mountain View, CA, USA). The RF probe consists of a 15-gauge shaft through which four sharp prongs, each 0.021 inches (0.53 mm) in diameter (25 gauge) can be deployed. Fully extended, the prongs are in an “umbrella” configuration with prongs at 90° intervals. The last 1-cm of the probe tip and each prong constitute the electrically active surface. The probe is inserted into the lobe of the liver, and the prongs are deployed, taking care to keep them within the liver parenchyma. The RFA probe was inserted into the liver tissue through the gelatin phantom at a depth of 3 cm. Imaging was performed in a direction perpendicular to the scan plane of the US transducer.

In vivo elastographic imaging of the thermal lesions was performed immediately after RFA, using the RFA probe itself as the “displacement device.” The RFA probe was displaced in 0.5-mm increments to provide the effect of compression. Having the ablation probe mounted in a stepper motor-controlled slide, as illustrated in Fig. 2 facilitated its use for in vivo elastography. Elastographic imaging, done by tracking the tissue motion/displacement induced by the RFA probe, significantly eliminates nonaxial tissue motion that may be a factor with an externally applied compression, as illustrated in Fig. 3b. The schematic diagram illustrates the method of external compression elastography in Fig. 3a, where the compression is applied using the transducer. As illustrated schematically, the resultant motion of the liver and the thermal lesion may be complex and may include lateral slippage. In contrast, when the compression is applied using the RFA probe as in Fig. 3b, the motion or displacement of the thermal lesion is along the axis of the ablation probe. If the transducer is aligned along the axis of the displacement, then the displacement
of the tissue before and after RFA probe displacement will be along the axial direction of the transducer.

The use of the RFA probe as the displacement device allows control of the degree and amount of motion of the thermal lesion, as illustrated in Fig. 3b. This technique eliminates lateral slippage altogether. Under this situation, we track the motion of the ablated tissue induced solely by the probe motion. Elastography was performed during time increments when there was minimal motion caused by physiological sources (respiration). The stepper motor-controlled compressor system was mounted on a ring stand, with the transducer held stationary to acquire the RF echo signal data. RF acquisitions were synchronized to the stepper motor-induced displacement of the RFA probe.

**RESULTS**

In this section, we present both *in vitro* and *in vivo* elastograms obtained from porcine liver tissue. Cross-correlation analysis of RF echo signals from pre- and postcompression data sets was done using a window length of 3 mm with a 50% overlap between data segments. This yielded local tissue displacements with the gradient of the displacement providing strain estimates (Ophir et al 1991, 1997, 1999). The strain images shown in this section depict an imaging depth of 6 cm and a width of 4 cm (transducer footprint).

Examples of *in vitro* elastograms of the thermal lesions created in excised liver tissue along with the US B-mode images of the same regions are illustrated in Figs. 4 and 5. B-mode images acquired before and after an ablation duration of 7 min are illustrated in Fig. 4a and b. Note that, other than the presence of a region above the liver tissue sample where some of the gelatin had melted and created a slight reduction in the echogenicity, sonography alone does not provide information about the size and position of the thermal lesion. However, observe that the thermal lesion appears to be clearly visualized in the elastogram in Fig. 4c, where darker shades indicate areas that incurred smaller compressions (stiffer regions) under the applied strain. Observe also that the thermal

![Fig. 3. Schematic diagram illustrating (a) the nonaxial motion and lateral slippage produced using external compression elastography, and (b) where displacement of the tissue is produced using the RFA probe with all the motion generated along the axis of the probe.](image)

![Fig. 4. B-mode grey-scale images and elastograms obtained from a lobe of liver tissue encased in a gelatin phantom; (a) a B-mode image before RFA, (b) a B-mode image after RFA. The melting of the gelatin above the liver sample, and a slight reduction in echogenicity in (b) are the only visible changes evident from RFA, and (c) illustrates the axial strain elastogram obtained on the ablated liver tissue using a 1% applied compression. Note the delineation of the ablated region (thermal lesion) from the surrounding tissue, due to the increased stiffness (low strain) in the ablated region.](image)

![Fig. 5. B-mode grey-scale images and elastograms obtained from a lobe of liver tissue encased in a gelatin phantom; (a) a B-mode image before RFA, (b) a B-mode image after RFA. In this case, we observe increased echogenicity at the site of the ablation and the presence of the shadowing below the thermal lesion. Note that it is difficult to accurately ascertain the size and position of the thermal lesion from the B-mode images. Axial strain elastograms obtained (c) before and (d) after RFA on liver tissue using a 1% applied compression. Note the accurate delineation of the ablated region (thermal lesion) from the surrounding tissue. The top 1 cm and 0.5 cm at the bottom of the elastogram is the gelatin region, which is slightly stiffer (low strain regions appear darker) than the normal liver tissue.](image)
lesion appears to be clearly demarcated from the regions of liver tissue that are not ablated.

In a similar manner, grey-scale B-mode images and elastograms obtained before and after ablation using a heating duration of 3 min are illustrated in Fig. 5. Note that, in this case, we observe increased echogenicity near the ablation site and some shadowing below the region of high echogenicity in the B-mode image in Fig. 5b. Nevertheless, it is still difficult to ascertain the thermal lesion size and position from conventional US images. On the other hand, the thermal lesion is clearly visualized in the axial strain elastogram shown in Fig. 5d. Note that, before ablation, liver tissue exhibits uniform stiffness throughout the sample, as observed in Fig. 5c. However, after the ablation procedure, the size and position of the thermal lesion can be clearly identified as a stiffer region on the elastogram. Although information provided by the elastograms still must be verified by pathology, it appears that elastography would significantly help the physician identify if the ablation procedure was successful and if the entire tumor region had been treated. The in vitro elastograms in Figs. 4 and 5 illustrate the potentially significant information regarding the size and position of the thermal lesion that is provided using elastography.

As previously mentioned in the Methods section, the RFA probe itself was used as the displacement device to obtain in vivo elastograms. Figure 6 presents US B-mode images, in vivo elastograms, and pathology photographs obtained for four different thermal lesions (Fig. 6a–d) created in intact liver tissue. Note the presence of several large blood vessels close to the ablated region. The thermal lesions appear as stiffer regions in the liver parenchyma surrounded by softer tissue; soft, untreated tissue gives rise to the “bright halo” around each thermal lesion. Sections through the RFA lesion obtained using light microscopy demonstrate two distinct zones surrounded by normal liver tissue. The white zone corresponds to regions of completely ablated tissue, where 100% of the cells have been destroyed. Surrounding the white zone is an area of partial necrosis and hemorrhage. The outermost zone around the thermal lesion is the edematous zone. The edematous zone is softer, and is probably responsible for the formation of the “bright halo” around the stiffer thermal lesion. Because the displacement in the liver was induced by the RFA probe (very localized displacement), most of the liver tissue regions distal to the lesion also appear stiffer because tissue motion/displacement is minimal in these regions. The other darker regions correspond to the areas inside blood vessels, with lower signal-to-noise ratio (SNR) in the US signals. The in vivo liver elastograms in Fig. 6 clearly illustrate the potential of this technique in depicting and characterizing the zone of necrosis generated by RFA.

**DISCUSSION AND CONCLUSIONS**

A very important use of advanced US methods will be to improve visualization of treated margins during RFA therapy. In this paper, we apply a promising technique (i.e., elastography) for this task. Elastography is a method of visualizing the zone of necrosis by imaging the stiffness of treated tissue. Although the lesion boundaries are barely perceptible with conventional US, elastography provides distinct visualization of the zone of thermal necrosis. Protein denaturation due to ablation induces elevation of the elastic modulus of soft tissue. These changes appear as regions that incur less strain upon displacement than the surrounding untreated tissue.
Thus far, elastography of the liver and other abdominal organs has seen limited success, likely because of the difficulty in providing controlled compressions. The use of externally applied compressions may induce non-axial motions due to lateral slippage accompanying the axial compression. We illustrate in this paper that, in fact, it is possible to obtain elastographic images of thermal lesions using the RFA probe itself as the compressor. This paper presents one of the first in vivo elastographic images of thermal lesions created in liver tissue. The use of the RFA probe eliminates lateral slippage or nonaxial motion because the perturbation is localized to the thermal lesion site.

The motion of the RFA probe is controlled using a stepper motor to induce incremental displacements around the lesion. This approach, along with synchronized acquisition of the RF echo signal frames before and after displacement, generates high-quality elastographic images. Acquiring RF data for elastography during the exhalation time, where the respiratory motion is minimal, can easily reduce additional sources of motion in the liver due to respiration. Elastograms can be obtained while the ablation is being performed or after ablation is completed.

A comparison of the elastograms depicted in Fig. 6 with those in Figs. 4 and 5 also indicates that the in vivo elastographic depiction of the thermal lesions is similar to that observed in the in vitro cases using a bench mounted (fixed geometry) elastography system. These in vivo elastograms clearly illustrate the feasibility of performing in vivo imaging of the stiffness properties of thermal lesions generated in abdominal organs. This information is not currently available to the interventionist performing RFA. We believe that the clear visualization of the lesion size generated using elastography will significantly help in determining if the entire tumor region has been treated.

Elastography shows promise for delineating treated from surrounding normal tissue. Comparison of elastograms with tissue specimens demonstrates a correlation between elastographic image features and ablated tissue, especially along the edges of the thermal lesion, as observed in Fig. 6. Close correspondence was observed between the pathology images and the corresponding elastograms. The elastograms provide additional information about the thermal lesion that is not obtained from US B-mode images.

Because the stiffness of thermal necrotic tissue may increase with temperature and heating duration, elastography may provide a means for characterizing areas in the thermal lesion that undergo different levels of thermal dose deposition. A case in point will be the evaluation of lesions formed near large blood vessels, to ascertain if elastography can be used to identify any softer regions (regions of partial necrosis) around the blood vessel that may not have been treated by RFA. This is an important area of research because areas around a blood vessel undergo only partial necrosis due to reduction in the thermal dose due to blood flow (Livraghi et al 2000). These regions of partial necrosis may contain viable cancer cells that could grow aggressively if undetected and lead to recurrences of the cancer.

Because US is routinely used to guide the RFA procedure, the same system can be adapted for elastographic imaging. Elastographic visualization of thermal lesions may, therefore, provide clinicians valuable feedback that would ultimately reduce the recurrence rates with RFA. In addition, multimodality imaging that includes thermal images of the temperature distribution during RFA can also be generated (Varghese et al 2002a).

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