THE FEASIBILITY OF ELASTOGRAPHIC VISUALIZATION OF HIFU-INDUCED THERMAL LESIONS IN SOFT TISSUES

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Abstract—The potential for visualizing high-intensity focused ultrasound (HIFU)-induced thermal lesions in
biological soft tissues in vitro using elastography was investigated. Thermal lesions were created in rabbit
paraspinal skeletal muscle in vivo. The rabbits were sacrificed 60 h following the treatment and lesioned tissues
were excised. The tissues were cast in a block of clear gel and elastographic images of the lesions were acquired.
Gross pathology of the tissue samples confirmed the characteristics of the lesions. © 1999 World Federation for
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Key Words: Ultrasound, Elastography, Strain, Tissue ablation, HIFU, Minimally invasive surgery.

INTRODUCTION

Various minimally invasive surgical procedures are becoming possible with the use of image-guided high-
intensity focused ultrasound (HIFU). Several major benefits derive from minimally invasive surgery. First, the
risk of complication is reduced. Second, the procedure may require only local anesthesia. Third, the recovery
time is significantly reduced. Finally, as a consequence of the previous benefits, the surgery cost is reduced.
Although the principles of noninvasive surgery using HIFU had been proposed more than 50 years ago by
Lynn et al. (1942) and were extended by Fry et al. (1955), it remained a research field that was not considered
a viable clinical reality until recently. The main reasons for the delay were the difficulty in accurately
positioning the ultrasound (US) beam in a complex, heterogeneous target in vivo and also in monitoring the
induced tissue damage for treatment-delivery verification. After substantial progress had been made in the
field of medical imaging, several clinical trials for the treatment of benign and malignant tumors of the prostate
(Foster et al. 1993; Gelet et al. 1993), bladder and kidney (Vallancien et al. 1993) and eye (Coleman et al. 1985)
were conducted. These first procedures were based on the combination of a focused ultrasound surgery system
with a diagnostic ultrasound imaging scanner. The scanner provided a method to target the treated tissue and the
lesion is depicted as a bright (hyperechoic) area on the sonogram. However, this brightness change was not possible
unless gas microbubbles had been generated during the treatment. These bubbles resulted from tissue boiling
or cavitation (Hill and Ter Haar 1995). It has been reported that the hyperechoic areas fade with time due to the
diffusion of the bubbles (Watkin et al. 1995). Yang et al. (1993) have shown that, immediately after the treat-
ment, HIFU-induced damage in the rabbit liver in vivo was depicted as hypechoic lesions. They related the
decreased echogenicity in the lesion to increased water content due to tissue edema. They also reported that, as
a result of calcium deposition and condensation of nuclear debris from the infiltrating leukocytes around the
lesion periphery, a hyperechoic rim was seen around the margin of the lesion 4 days after treatment. Bush et al.
(1993) carefully studied, in vitro, how heating affects the acoustic properties of tissue (attenuation, speed of sound
and backscattering coefficient) and demonstrated significant increases in the speed of sound and attenuation,
whereas backscatter was shown not to change in any significant manner. They concluded that tissue attenuation was the most sensitive acoustic parameter for the visualization of HIFU-induced lesions.

Recently, magnetic resonance (MR) imaging was proposed for improving the localization of the lesion and for monitoring the temperature during HIFU surgery (Cline et al. 1993). Although MR imaging has been proven to be quite adept at imaging thermal lesions and temperature monitoring (Cline et al. 1993, 1996), it has also shown several drawbacks and limitations. MR imaging is expensive, not portable, and is not suitable for some patient populations (those with pacemakers, pregnant women, children or very large patients). To conduct HIFU treatments in an MR system also requires specialized electronic and positioning equipment that is compatible with the system.

We have recently demonstrated that tissue thermal damage created by a surgical laser resulted in a localized change of the tissue elastic modulus (Stafford et al. 1998). We have also shown that elastography accurately assessed the extent of the lesions that were created. In this study, we demonstrated that HIFU-induced lesions can be visualized by elastography. We demonstrated that, with elastography, it is possible to evaluate the treated volume. Moreover, because elastography is sensitive to small changes in the elastic modulus (Kallel et al. 1998), a variety of tissue damage mechanisms, such as coagulated necrosis, tissue vaporization and tissue inflammation, may be evaluated from the elastogram.

MATERIAL AND METHODS

Thermal lesions were induced in rabbit paraspinal muscles using a prototype MR-compatible high-intensity focused ultrasound surgery system (GE Medical Systems, Milwaukee, WI) (Cline et al. 1995; Hynynen et al. 1996; Hynynen 1996). The system uses a single, spherical, air-backed transducer operating at a center frequency of approximately 1.5 MHz, with an 80-mm radius of curvature and 100-mm diameter (h = 17.55 mm is the depth of the spherical shell) to generate the focused ultrasound field. The resulting 6-dB ultrasound beam dimension is 2 mm. The transducer was placed in a tank of degassed water (Degas Model B2L2P, Intec Research, Sunnyvale, CA) to provide coupling between the transducer and the rabbit. A thin plastic film (0.1-mm thick polyvinylchlorhide) enclosed the water tank and an 11-cm diameter magnetic radiofrequency surface coil was placed on top of the PVC window. A gel phantom (3M, Minneapolis, MN) that mimics the ultrasonic properties of tissue was placed in the center of the coil above the transducer. The center of the transducer was aligned with the axial center of a 1.5-T MR scanner (GE Medical Systems). A low-power sonication pulse was delivered to the phantom (20 W RF power) while a thermally sensitive fast spin-echo sequence was acquired. A phase change in the phantom at 57°C allows the position of the focal spot to be accurately determined in the MR coordinate system (Cline et al. 1993). This allows the HIFU beam positioning and MR coordinate systems to be registered. After the coordinate systems are registered, the phantom is removed and a bag of degassed water is placed in the center of the coil. The rabbits were anesthetized with a ketamine “cocktail,” shaved, depilate and placed over the surface coil with the bag of degassed water serving as the acoustic coupler to the water bath (Fig. 1).

T1-weighted images of the appropriate anatomic structures of the rabbit were acquired and loaded onto a workstation (Sparc 5; Sun Microsystems, Mountain View, CA) for treatment planning and US control during therapy delivery. The location, number, power setting and duration of all sonication were controlled from this workstation. Online monitoring of the treatment was accomplished using a temperature-sensitive, fast, 2-D gradient-recalled acquisition in the steady state (GRASS) pulse sequence with a 16 cm² field of view (TE/TR/flip = 7.9 ms/16.9 ms/25°) in the prescribed plane parallel to the transducer surface. An unspoiled fast GRASS sequence was chosen over a spoiled sequence (SPGR) for the rabbits because of a reported increased temperature-sensitivity in the muscle (Cline et al. 1996). This pulse sequence allowed the changes in the proton reso-
nance frequency of the tissue to be monitored during heating by taking the complex phase difference between an initial reference image and subsequent images acquired during therapy (Chung et al. 1996). The temporal resolution of this imaging sequence was about 3 s. This, in turn, allowed placement of the focus in the sample to be monitored during treatment and estimations of the temperature rise in this region.

Two rabbits were treated in this study. The rabbits were used in compliance with animal welfare committee approval. In the first rabbit, the lesion was produced with a single focused sonication using RF power of 75 W and pulse duration of 10 s. In the second rabbit, a treatment area was created by sonicating a total of 9 separately focused adjacent areas at an RF power of 75 W for 10 s each. Due to the conversion from electrical to mechanical energy, the acoustic power is around 60% of the RF power (Cline et al. 1993). The lesions were induced in the right paraspinal muscle in both animals. Both rabbits were sacrificed 60 h after treatment.

Immediately after the rabbit was sacrificed, the lesioned muscles were carefully removed and cast in blocks of clear gel prepared as previously described by Kallel et al. (1998). The gelatin block containing the rabbit muscle was placed in the compression apparatus. The data acquisition was performed at room temperature. The square compression plate used was larger than the size of the gelatin block sample to maintain a uniform applied axial stress distribution. The linear array transducer was acoustically coupled to the gelatin block via an opening in the metal plate. The experiment was conducted with a real-time linear array scanner (Diasonics Spectra II, Santa Clara, CA) that operates with dynamic receive focusing and a single transmit focal zone centered at 30 mm and a center frequency of 5 MHz. The region of interest (ROI) for most elastography images was 40 \times 50 \text{ mm}^2 along the longitudinal beam axis. Different parallel planes from the sample were imaged until the lesion was no longer seen on the elastogram. The spacing between two consecutive planes was 0.5 mm and the thickness of each slice was about 2 mm corresponding to the beamwidth in the elevational direction. For all elastograms, 100 A-lines (40 mm) along the transverse axis were used.

Precompression of each sample was about 0.5%. A maximum of 8 compression steps for each scan with a compression step size of 0.5 mm (compressor/transducer axial motion) were acquired. This step size in applied displacement resulted in a 0.5% average applied strain. The RF signals for each step were digitized using an 8-bit digitizer (Lecroy Corp., Chestnut Ridge, NY) operating at a sampling frequency of 48 MHz, and saved to a desktop computer for off-line processing.

**Fig. 2.** Proton density weighted MR image of the in vitro rabbit muscle cast in gel. The lesion is pointed to by the arrow.

**Processing of elastographic data**

For each compression step, the displacement was estimated using a cross-correlation technique applied to the pre- and postcompression RF signals, using 1.8 mm correlation windows with 60% overlap. The elastogram was estimated using a least squares strain estimator (LSQSE) (Kallel and Ophir 1997). For the LSQSE, a kernel size of 4 mm was used. Qualitatively, it was found that this kernel size resulted in a good compromise between spatial resolution and elastographic contrast-to-noise ratio (CNRs). All the elastograms were displayed on the same strain dynamic range of 0–2%. Some noisy strain estimates, resulting from using RF data where the sonographic signal-to-noise ratio (SNRs) was very low, were artificially assigned to an arbitrary strain value of 0.5%. The SNRs was low in the clear gelatin due to the lack of acoustic scatterers.

**RESULTS**

A proton density MR image (Fig. 2) of the muscle sample cast in the gel shows a lesion created using a single sonication of 75 W RF power and a pulse duration of 10 s (arrow). The three top dark circular areas are trapped air bubbles. As shown below, these bubbles caused acoustic shadows when elastographic data were acquired. The rectangular box outlines the region of interest from which ultrasonic data were acquired. Figure 3 shows a series of sonograms and matching elastograms obtained from parallel planes 1 mm apart in the elevational direction. The 75-W,10-s lesion is clearly depicted by the elastogram in every plane. In this case, the extension of the lesion in the elevational direction is evaluated to be about 4 mm. Observe that this lesion is not clearly depicted in the corresponding sonograms. In the sonogram, at the corresponding location of the lesion ob-
tained from the elastogram, we notice a hypoechoic rim surrounding a relatively echogenic central zone (arrows). The hypoechoic rim is probably due to an increased water content caused by edema surrounding the lesion, which was confirmed histopathologically. In the first and second sonograms, we clearly notice the acoustic shadow caused by the bubble. As shown by the two first elastograms, this acoustic shadow (distal to the air bubble) resulted in a noisy strain estimation.

Figure 4 compares the elastographic depiction of the lesion to its corresponding gross pathology photograph. Grossly and histopathologically, the lesion is characterized by two different regions: a central dull white area of coagulative necrosis surrounded by a brown zone of tissue disruption, edema and hemorrhage. The elastogram appears to depict these two different regions with the area of tissue necrosis being harder than the zone of tissue disruption. For a better visualization of
these regions, the inverse of the strain image magnified around the lesion is shown in Fig. 5a. From this figure, we notice a different level of hardness inside the lesion. For a better illustration of this hardness variation across the lesion, a profile from the inverse of the strain image at the level shown by the arrow (Fig. 5a) is shown in Fig. 5b. This variation may be related to a difference in the mechanism of tissue damage. At present, this can only be hypothesized; this point will be investigated further in a future work. The size of the lesion as depicted from the elastogram correlates well with the size of the lesion in the gross pathology photograph (Fig. 4).

A gross pathology photograph of multiple slices of the second lesion, induced in the second rabbit, sliced in a plane parallel to the axis of the imaging ultrasound beam is shown in Fig. 6. Like the single sonication lesion, the lesion is characterized by multiple central dull white areas of coagulonecrotic tissue surrounded by brown zones of tissue disruption, edema and hemorrhage. Figure 7 shows a series of 4 elastograms and the
CONCLUSION

We have obtained preliminary in vitro data for the elastographic visualization of HIFU-induced thermal lesions. It was shown that elastography allows the visualization of a treated volume and may also reveal different types of tissue damage, including coagulonecrotic tissue and tissue disruption and/or acute tissue inflammatory response. Although the results are preliminary, they demonstrate that elastography may offer a relatively effective, low-cost alternative for monitoring tissue thermal treatment. To further ascertain the preliminary imaging and pathological characteristics reported in this paper, a larger study is being conducted to characterize a large number of lesions of various sizes.

As shown by Figs. 4a and 6a, and also as known from the literature (Bush et al. 1993), the sonograms do not clearly depict thermal damage. This major disadvantage restricts the use of ultrasound for guiding thermal surgery. Recently, new ultrasonic techniques for beam guidance by means of temperature-change mapping were proposed (Ueno et al. 1990; Straube and Arthur 1994; Seip and Ebbini 1995; Moreno et al. 1995; Simon et al. 1998). Some of these techniques are based on the analysis of the frequency-dependent attenuation (Ueno et al. 1990), backscattered power (Straube and Arthur 1994), mean scatterer spacing (Seip and Ebbini 1995) and speckle tracking (Seip and Ebbini 1995; Moreno et al. 1995; Simon et al. 1998). The combination of one of these techniques with elastography may lead to a fully ultrasound-based surgery system.

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REFERENCES


