Intraoperative Ultrasound and Tissue Elastography Measurements Do Not Predict the Size of Hepatic Microwave Ablations

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Rationale and Objectives: Image-guided thermal ablation is used to treat primary and secondary liver cancers. Evaluating completeness of ablation is difficult with standard intraoperative B-mode ultrasound. This study evaluates the ability of B-mode ultrasound (US) and tissue elastography to adequately measure the extent of ablation compared to pathologic assessment.

Materials and Methods: An in vivo porcine model was used to compare B-mode ultrasonography and elastography to pathologic assessment of the microwave ablation zone area. In parallel, intraoperative ablations in patients were used to assess the ability of B-mode US and elastographic measures of tissue strain immediately after ablation to predict ablation size, compared to postprocedural computed tomography (CT).

Results: In the animal model, ablation zones appeared to decrease in size when monitored with ultrasound over a 10-minute span with both B-mode US and elastography. Both techniques estimated smaller zones than gross pathology, however, the differences did not reach statistical significance. Biopsies from the edges of the ablation zone, as assessed by US, contained viable tissue in 75% of the cases. In the human model, B-mode US and elastography estimated similar ablation sizes; however, they underestimate the final size of the ablation defect as measured on postprocedure CT scan (median area [interquartile range]: CT, 7.3 cm^2 [5.2–9.5] vs. US 3.6 cm^2 [1.7–6.3] and elastography 4.1 cm^2 [1.4–5.1]; $P = .005$).

Conclusions: Ultrasound and elastography provide an accurate gross estimation of ablation zone size but are unable to predict the degree of cellular injury and significantly underestimate the ultimate size of the ablation

Key Words: Elastography; liver ultrasound; microwave ablation.

Thermal ablation is an accepted therapeutic alternative in selected patients with primary or metastatic liver neoplasms. This approach is used primarily for tumors that are considered inappropriate for resection because of tumor- (multiplicity, location within the liver) or patient-related factors (comorbidities or small, predicted, future liver remnant) (1–3). Local recurrence, however, is common and has been associated with tumor size and tumor location (3,4).

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The ideal image guidance modality would assist in preoperative planning, lesion targeting, real-time ablation monitoring, and ablation zone assessment (5). Intraoperative ultrasound (ioUS) is the most widely used image guidance modality, given its availability, relative ease of use, and ability to provide feedback for ablation probe placement (lesion targeting) (6). However, heat-induced artifact and the underlying characteristics of the liver parenchyma (i.e., steatosis, cirrhosis, and chemotherapy-associated changes) significantly impact ablation zone monitoring and assessment during and immediately after the ablation has taken place. As a result, complete destruction of tumor tissue is impossible to confirm (7,8). In addition, it is unclear how this technical limitation influences local recurrence rates (3,9).

Advanced ultrasound techniques that included color flow Doppler and tissue elastography have recently been introduced and have shown potential value as adjuncts to B-mode ultrasound (6,9–11). Quantitative and qualitative measures of the mechanical properties of tissue (i.e., deformability, elasticity, and stiffness) are now obtainable, and real-time correlation with conventional sonographic imaging is possible (8).

Elastograms are graphical representations of the differences in elasticity among tissues. They allow a qualitative, visual assessment of the interface between different tissues or between live and ablated tissue. Strain analysis is a quantitative measure of tissue stiffness in a given region of interest that provides an objective measure of its mechanical characteristics. It is defined as the change in size or shape in response to a given stress. It is expressed as a ratio (e.g., the change in length per unit length), making this a dimensionless data point (12).

The present study evaluates the correspondence between the ioUS assessment of the ablation zone (thermocoagulation zone [TCZ]) and gross pathologic and histologic extent of necrosis in an animal model of microwave ablations (MWAs). Furthermore, we analyzed the performance of tissue elastography and strain analysis as an adjunct to B-mode ultrasound in the assessment of MWA zone sizes in patients after ablation of metastatic liver tumors.

METHODS

Two models were used to evaluate the performance of ultrasound in the assessment of ablation zone areas.

Porcine in vivo model

Approval to perform a laparotomy and six liver MWAs to generate measurable lesions on a Yorkshire pig under general anesthesia was obtained from the Institutional Animal Care and Use Committee at Memorial Sloan-Kettering Cancer Center.

Lesions were created with MWAs as detailed under "Microwave ablation" section. Maximal ablation zone length and width were measured with B-mode ioUS and on elastograms obtained by direct surface ultrasound immediately after ablation (time: 0 minute), 5 minutes after finishing the ablation, and 10 minutes after ablation. Elastograms were obtained by a computer-generated algorithm that summarized the measured tissue displacement (strain) over a variable number of compression–decompression cycles, which was manually generated by a hepatobiliary surgeon experienced in intraoperative liver ultrasound. Ablated tissue strain was measured and compared to surrounding normal parenchyma. Additionally, using a 14-gauge Tru-Cut biopsy needle (Cardinal Health, Dublin, OH), the same US operator (who has experience in ultrasound-guided procedures), obtained core biopsies at two sonographically visualized edges of each ablation zone (total, 12 cores), 10 minutes after finishing the ablation.

The pig was immediately euthanized and the liver was harvested for pathologic assessment. Each lesion was sectioned longitudinally to obtain 5-mm slices. The TCZ was recognized as an area of pale discoloration of the hepatic parenchyma. The slice that contained the largest section of the lesion was selected and used to obtain lesion measurements. This slice was then stained for 30 minutes in 1% 2,3,5-triphenyltetrazolium chloride (TTC) (Sigma, St. Louis, MO) dissolved in phosphate buffer solution (pH 8.5), which stains viable tissue red and fails to stain nonviable tissue. The area that failed to stain was measured. The six TTC stained sections were then fixed in 10% neutral buffered formalin for 24 hours, processed and embedded in paraffin, and sectioned to include the probe tract and two edges of the lesion. The lesions and the core biopsies then underwent hematoxylin and eosin (H&E) staining to evaluate the extent of cell death.

Human model

The Memorial Sloan-Kettering Cancer Center's Institutional Review Board granted a waiver to perform a human pilot study to assess ioUS and elastography in patients undergoing liver ablations. Between October 2011 and May 2012, 24 MWAs of metastatic liver lesions were performed on 20 patients and evaluated for this study. Their diagnoses were colorectal cancer (19 tumors), breast cancer (two tumors), gastrointestinal stromal tumor (one tumor), solid pseudopapillary tumor of the pancreas (one tumor), and germ line tumor (one tumor); none of these patients had underlying liver disease. Probe placement was guided by US as it is done routinely at our institution. Maximal lesion size (area = maximal length × maximal width) and strain were obtained before and after ablation. The normal liver strain was estimated on 20 additional patients who underwent laparotomy during the same period for disease not involving the liver and who were considered to have normal liver parenchyma. While performing ioUS, images representing the largest dimensions of the lesions were frozen and measured on-screen. All measurements were repeated three times, and the average of these was used for correlation to decrease the possibility of measurement error.

Postoperatively, the ablated area was evaluated visually as a geographic area of uniform low attenuation on computed tomography (CT) by a radiologist who measured the largest diameter and perpendicular diameter of the ablation zone. This evaluation was determined on portal venous phase CT following administration of intravenous contrast (Omnipaque 300, General Electric, Fairfield, CT).

Microwave ablation

Ablations in the animal model were performed with an Evident Microwave System (Covidien, Mansfield, MA) including a Valleylab microwave generator with a frequency of 915 MHz and 45 W. An Evident microwave surgical antenna (17–3 cm active Teflon-coated 3cm tip) was used to deliver energy to the liver tissue. The duration of ablation was set to 10 minutes to achieve mean target dimensions of 3.1 × 3.6 as indicated by the company's guidelines. The same microwave generator, antennas, and energy settings were used in the human model. In the human model, the duration of the ablation was determined by the surgeon at