Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–10, 2016

0301-5629/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.ultrasmedbio.2016.07.015

● *Original Contribution*

POST-PROCEDURE EVALUATION OF MICROWAVE ABLATIONS OF HEPATOCELLULAR CARCINOMAS USING ELECTRODE DISPLACEMENT ELASTOGRAPHY

WENJUN YANG,* TIMOTHY J. ZIEMLEWICZ,† TOMY VARGHESE,*‡ MARCI L. ALEXANDER,† NICHOLAS RUBERT,* ATUL N. INGLE,‡ MEGHAN G. LUBNER,† JAMES L. HINSHAW,† SHANE A. WELLS,† FRED T. LEE, JR.,† and JAMES A. ZAGZEBSKI*

*Department of Medical Physics, University of Wisconsin School of Medicine and Public Health, University of Wisconsin–Madison, Madison, Wisconsin, USA; †Department of Radiology, University of Wisconsin School of Medicine and Public Health, University of Wisconsin–Madison, Madison, Wisconsin, USA; and ‡Department of Electrical and Computer Engineering, University of Wisconsin–Madison, Madison, Wisconsin, USA

(*Received* 21 *December* 2015; *revised* 2 *May* 2016; *in final form* 13 *July* 2016)

Abstract—Microwave ablation has been used clinically as an alternative to surgical resection. However, lack of real-time imaging to assess treated regions may compromise treatment outcomes. We previously introduced electrode displacement elastography (EDE) for strain imaging and verified its feasibility *in vivo* on porcine animal models. In this study, we evaluated EDE on 44 patients diagnosed with hepatocellular carcinoma, treated using microwave ablation. The ablated region was identified on EDE images for 40 of the 44 patients. Ablation areas averaged 13.38 ± 4.99 cm^2 on EDE, compared with 7.61 ± 3.21 cm^2 on B-mode imaging. Contrast and contrast-to-noise ratios obtained with EDE were 232% and 98%, respectively, significantly higher than values measured on B-mode images ($p < 0.001$). This study indicates that EDE is feasible in patients and provides improved visualization of the ablation zone compared with B-mode ultrasound. (E-mail: tvarghese@wisc.edu) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Ablation, Elastography, Elasticity imaging, Microwave ablation, Hepatocellular carcinoma, Strain imaging.**

INTRODUCTION

Hepatocellular carcinoma (HCC) is the sixth most common cancer and third leading cause of cancer-related mortality worldwide (Lencioni and Crocetti 2012). Surgical resection of liver tissue was the standard procedure for the cure of HCC, although there are critical constraints for its widespread use. Specific criteria have to be met for successful surgical resection: (i) The cancer is limited to a single liver lobe; (ii) liver function is well preserved; and (iii) the patient has neither abnormal bilirubin nor portal hypertension (Lencioni and Crocetti 2007). However, cirrhosis commonly occurs with HCC, and only up to 5% of cirrhotic patients with HCC fit the constraints described above for liver resection (Lencioni and Crocetti 2007). Therefore, only 9% of patients with HCC are suitable candidates for surgical resection (Liang and Wang 2007). With the development of minimally invasive treatments such as percutaneous radiofrequency ablation (RFA) and microwave ablation (MWA), thermal ablation has been adopted as the primary treatment option for HCC, especially for early-stage interventions (tumor size <3 cm) (Lencioni and Crocetti 2012; Shiina et al. 2012). Existing clinical studies have indicated that treatment outcomes with ablation procedures are superior or at least equivalent to surgical resection or ethanol injection for these early-stage HCC tumors (Lencioni and Crocetti 2007, 2012; Liang and Wang 2007; Lu et al. 2005; Maluccio and Covey 2012; Shiina et al. 2012).

Microwave ablation, introduced as an ablation technique initially in Japan (Murakami et al. 1995), has now been increasingly applied worldwide (Liang and Wang 2007; Lu et al. 2005; Maluccio and Covey 2012; Qian et al. 2012; Shibata et al. 2002; Swan et al. 2013).

Address correspondence to: Tomy Varghese, Department of Medical Physics, University of Wisconsin School of Medicine and Public Health, University of Wisconsin–Madison, Madison, WI 53706, USA. E-mail: tvarghese@wisc.edu

Instead of generating the thermal dose by incorporating the patient as part of a closed-loop circuit as in RFA, MWA emits microwave energy to agitate water molecules, causing coagulation necrosis with a local impact. Thus, MWA delivers consistently higher intra-tumor temperatures, with reduced impact from blood flow in large vessels, enables faster ablation times and provides an improved convection profile (Lencioni and Crocetti 2012; Liang and Wang 2007; Qian et al. 2012). Multiple probes can be applied simultaneously to create larger tumor ablation volumes (Harari et al. 2015). MWA therefore has several advantages over RFA including increased power, increased volume of direct heating, ablation consistency in different tissue types and no requirement for ground pads (Lubner et al. 2013; Wells et al. 2015; Ziemlewicz et al. 2016). With these technological advantages, MWA has been increasingly cited as the more commonly used percutaneous ablation method (Wells et al. 2015; Ziemlewicz et al. 2015). Some investigators have reported that MWA does not result in an obvious improvement over RFA in treatment outcomes (Lu et al. 2005; Qian et al. 2012; Shibata et al. 2002); however, these studies used previous-generation microwave technology. In evaluations of current-generation technology, MWA has resulted in a significantly lower rate of local tumor progression than RFA (Potretzke et al. 2016). The modality limitation might also be compensated by other treatment methods such as trans-arterial chemoembolization (TACE) to limit the blood supply from the hepatic artery to reduce the heat sink effect of large vessels (Liang and Wang 2007; Maluccio and Covey 2012). One recent study reported that MWA could lead to satisfactory outcomes even for tumors larger than 3 cm, which was previously considered to be the maximum suitable size for thermal ablation procedures (Ziemlewicz et al. 2015).

Ultrasound elastography has been considered as an alternative for ablation monitoring because the stiffness contrast between an ablated region and surrounding tissue is high (Bharat et al. 2005, 2008b; Fahey et al. 2008; Kolokythas et al. 2008; Mariani et al. 2014; Righetti et al. 1999; Rubert et al. 2010; Varghese et al. 2002, 2003a; Zhang et al. 2008; Zhou et al. 2014) and is not significantly affected by the presence of gas bubbles (Varghese et al. 2004). Conventional, quasi-static ultrasound elastography is dependent on either externally applied compression (Ophir et al. 1991) or internal physiologic deformations (Shi and Varghese 2007; Varghese and Shi 2004; Varghese et al. 2003b) to produce displacements for estimating local tissue strain. The need for an external compressor would restrict the use of ultrasound elastography because it is cumbersome and generally cannot produce tissue displacements at sufficient depth. Acoustic radiation force impulse (ARFI) (Bing et al. 2011; Fahey et al. 2008; Hoyt et al. 2008; Mariani et al. 2014; Nightingale et al. 2001; Sarvazyan et al. 1998) may be more suited for this task, but ARFI is limited by the small tissue displacements that can be generated (around 0.01 mm) and a relatively shallow imaging depth of around 8 cm. Beyond this depth, the acoustic radiation force generated is too small to deform tissue because of attenuation of the signal (Deng et al. 2015; Zhao et al. 2011). The resulting data are also very sensitive to physiologic motion such as cardiac pulsation and respiratory artifacts.

We previously introduced a novel, quasi-static ultrasound elastography technique, referred to as *electrode displacement elastography* (EDE) (Bharat et al. 2008b; Rubert et al. 2010; Varghese et al. 2002), designed specifically for monitoring percutaneous ablation procedures. Here the local tissue deformation for elastography is induced by manual perturbation of the ablation antenna (Varghese et al. 2002). In this article, we investigated the feasibility of EDE in a pilot study on 44 patients diagnosed with HCC and treated with MWA. The delineation of the ablated region on EDE images was compared with ablated region contours taken from conventional B-mode images. The two modalities were compared with respect to estimated ablation zone area and detectability using contrast and contrast-to-noise ratio (CNR) features.

METHODS

Patients and MWA system

Forty-four patients who underwent MWA for their HCC tumors were involved in this study. Informed consent to participate in this study was obtained before the ablation procedure under a protocol approved by the institutional review board at the University of Wisconsin–Madison. Patients received MWA treatments under general anesthesia. Ultrasound radiofrequency data for EDE were acquired after antenna insertion, before onset of ablation and immediately after the ablation procedure before the ablation antenna was removed from the insertion site. EDE images that exhibited clearly distinguishable ablation regions were obtained for 40 of the 44 patients. Four patients were excluded from analysis because the ablation zone could not be clearly delineated because of insufficient compression or excessive signal decorrelation artifacts.

Microwave ablation was performed with a Neuwave Medical Certus 140 (Madison, WI, USA) operating at 2.45 GHz. Ablation duration and power were adjusted for each patient depending on tumor size and location, with typical values of 5 min and 65 W, respectively. The MWA antenna was inserted under conventional ultrasound B-mode imaging guidance in a computed