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● *Original Contribution*

NON-INVASIVE MEASUREMENT OF THERMAL DIFFUSIVITY USING HIGH-INTENSITY FOCUSED ULTRASOUND AND THROUGH-TRANSMISSION ULTRASONIC IMAGING

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Abstract—Thermal diffusivity at the site ablated by high-intensity focused ultrasound (HIFU) plays an important role in the final therapeutic outcome, as it influences the temperature's spatial and temporal distribution. Moreover, as tissue thermal diffusivity is different in tumors as compared with normal tissue, it could also potentially be used as a new source of imaging contrast. The aim of this study was to examine the feasibility of combining through-transmission ultrasonic imaging and HIFU to estimate thermal diffusivity non-invasively. The concept was initially evaluated using a computer simulation. Then it was experimentally tested on phantoms made of agar and *ex vivo* porcine fat. A computerized imaging system combined with a HIFU system was used to heat the phantoms to temperatures below 42°C to avoid irreversible damage. Through-transmission scanning provided the time-of-flight values in a region of interest during its cooling process. The time-of-flight values were consequently converted into mean values of speed of sound. Using the speed-of-sound profiles along with the developed model, we estimated the changes in temperature profiles over time. These changes in temperature profiles were then used to calculate the corresponding thermal diffusivity of the studied specimen. Thermal diffusivity for porcine fat was found to be lower by one order of magnitude than that obtained for agar (0.313×10^{-7}m^2/s vs. 4.83×10^{-7}m^2/s, respectively, $p < 0.041$). The fact that there is a substantial difference between agar and fat implies that non-invasive all-ultrasound thermal diffusivity mapping is feasible. The suggested method may particularly be suitable for breast scanning. (E-mail: haim@bm.technion.ac.il) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **High-intensity focused ultrasound, Ultrasound, Thermal diffusivity, Through-transmission imaging.**

INTRODUCTION

Medical imaging plays a major role in the clinic. Currently, several established technologies are available for imaging. However, there is an ever-increasing need to broaden the spectrum of imaging capabilities. This may be achieved by seeking new technologies using new physical phenomena suitable for imaging, or by creating hybrid systems from existing modalities or by mapping new tissue properties that have not previously been imaged. Current imaging modalities map attenuation coefficients (X-rays and computed tomography [CT]), magnetic relaxation properties (magnetic resonance imaging [MRI]), acoustic scattering (ultrasound), metabolic rate (positron emission tomography), perfusion (single-photon emission CT) and more. Nevertheless, to the best of our judgment, very little attention has been paid to the thermal properties of the tissue (*e.g.*, thermal conductivity, k, and thermal diffusivity constant, K) as a contrast source.

Another motivation related to this study is non-invasive surgery using high-intensity focused ultrasound (HIFU). With the HIFU technique, a special ultrasound transducer is used to generate a virtual acoustic "knife" to ablate non-invasively a small volume of tissue within the body. HIFU non-invasive surgery has become very popular in the past few years. Image-guided HIFU surgery has recently been offered as a non-invasive alternative to conventional lumpectomy in several organs, and it may be considered the surgical knife of the future (Kennedy et al. 2003).

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The major mechanism in HIFU non-invasive surgery is currently thermal ablation. Consequently, much attention has been focused on temperature mapping for the purpose of image-guided surgery, particularly by MRI (*e.g.*, Gianfelice et al. 2003; Huber et al. 2001; Hynynen et al. 2001; McDannold et al. 2010; Madersbacher et al. 2000; Tempany et al. 2003; Wu et al. 2002). However, temperature mapping is not the only important feature in monitoring thermal ablation. Thermal diffusivity and perfusion at the ablation site also play an important role in the final therapeutic outcome. Hence, mapping the thermal diffusivity at and around the target site, before and during treatment, may potentially optimize the procedure.

Thermal diffusivity is a property that combines the thermal conductivity and heat capacity of the medium to express the rate at which heat dissipates. Thus, it directly influences the temporal dependence of the temperature distribution in the tissue at and around the heated zone. In practice, thermal diffusivity is highly variable between tissue types and also between different sources of the same tissue. Therefore, development of non-invasive methods for measuring it at the treatment location may reduce the uncertainty in therapeutic dose planning and delivery.

Moreover, as reported by Lagendijk et al. (1988), for example, tissue thermal diffusivity is different in tumors as compared with normal tissue. Tumors generally have higher and more variable perfusion (Song 1983), and their vasculature has a poorer response mechanism to stress than that of a normal tissue (Emami and Song 1984). This may be the reason for the differences in thermal properties. On the basis of these differences, it may also be possible to differentiate tumors from normal tissues and perhaps to differentiate between malignant and benign tumors. Thus, the development of a non-invasive method for measuring tissue thermal diffusivity could be valuable in the diagnosis of tumors as well. This may be beneficial in the diagnosis of breast cancer, for example.

Imaging techniques for thermal diffusivity and perfusion measurements using MRI have been reported (Cheng and Plewes 2002). However, very few studies have attempted to measure these parameters by ultrasound (Anand and Kaczkowski 2008). An “all-ultrasound” thermal estimation technique is a more attractive option to use with therapy and diagnostic systems, because the cost and operating expenses of the MRI scanning system are very high, and it has a lower temporal resolution compared with ultrasound imaging. Additionally, access to the patient within the MRI scanner is quite limited, and the sensitivity of the scanner to radiofrequency energy imposes severe restrictions on the use of additional medical equipment, when needed.

Previous attempts to measure thermal diffusivity by ultrasound were based on the pulse-echo (B-scan) technique, in which data are collected from the backscattered waves. The use of pulse-echo ultrasound is very popular in the clinic, but the recorded signals are characterized by relatively poor signal-to-noise ratio (SNR); geometric measurements are based on the inaccurate assumption that the speed of sound is constant; and quantitative measurements of the tissue acoustic properties are very difficult to obtain. In contrast, through-transmission (TT) ultrasound provides much superior SNR and allows quantitative measurements of the acoustic properties of tissues.

In this study, using the concept of an ultrasonic CT-guided HIFU system, as suggested in Azhari (2012), we describe a method for evaluating the thermal diffusivity of a tissue directly from speed-of-sound (SOS) profiles. The SOS profiles were obtained by TT ultrasonic imaging during cooling of the tissue after it was heated by HIFU.

THEORY

Through-transmission ultrasonic imaging

With TT imaging, ultrasonic pulses are transmitted across the scanned object from one side to the other. A coupling medium (usually water), enabling efficient conduction of the waves, is needed to fill the space between the transducer and the object. Scans are usually performed in the raster scanning mode, in which the transducers move synchronously along parallel lines. The signal in TT is in fact an acoustic projection and contains integrative information about the scanned object.

Time of flight (TOF) is equal to the integration of the reciprocal distribution of the SOS in the examined object and may be expressed as

$$\mathrm{TOF}(x,z) = \int \frac{1}{C(x,y,z)} dy \tag{1}$$

where y is the transmission's direction, (x,z) constitutes the projection plane and $C(x,y,z)$ is the SOS at each point in space.

If the distance between the two transducers, L, the width of the scanned object, $D_y(x,z)$, the SOS in water, C_{water}, and the TOF through water only,