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● *Original Contribution*

NONINVASIVE MEASUREMENT OF LOCAL THERMAL DIFFUSIVITY USING BACKSCATTERED ULTRASOUND AND FOCUSED ULTRASOUND HEATING

AJAY ANAND* and PETER J. KACZKOWSKI

Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA, USA.

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Abstract—Previously, noninvasive methods of estimating local tissue thermal and acoustic properties using backscattered ultrasound have been proposed in the literature. In this article, a noninvasive method of estimating local thermal diffusivity *in situ* during focused ultrasound heating using beamformed acoustic backscatter data and applying novel signal processing techniques is developed. A high intensity focused ultrasound (HIFU) transducer operating at subablative intensities is employed to create a brief local temperature rise of no more than 10°C. Beamformed radio-frequency (RF) data are collected during heating and cooling using a clinical ultrasound scanner. Measurements of the time-varying "acoustic strain", that is, spatiotemporal variations in the RF echo shifts induced by the temperature related sound speed changes, are related to a solution of the heat transfer equation to estimate the thermal diffusivity in the heated zone. Numerical simulations and experiments performed *in vitro* in tissue mimicking phantoms and excised turkey breast muscle tissue demonstrate agreement between the ultrasound derived thermal diffusivity estimates and independent estimates made by a traditional hot-wire technique. The new noninvasive ultrasonic method has potential applications in thermal therapy planning and monitoring, physiological monitoring and as a means of noninvasive tissue characterization. (E-mail: ajay.anand@philips.com)   © 2008 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Thermal ablation, Ultrasound treatment monitoring, Tissue characterization, Ultrasonic signal processing, Ultrasound thermometry.**

INTRODUCTION

The delivery of an accurate thermal dose is essential for the success of ablative thermal therapies such as high intensity focused ultrasound (HIFU) (Vaezy et al. 1997; Sanghvi et al. 1999; ter Haar 2001; Wu et al. 2002) and radio-frequency ablation (Mahnken et al. 2004; Frericks et al. 2005; Nour and Lewin 2005) in the clinic. The thermal parameters at the ablation site, namely, thermal diffusivity and perfusion loss, play important roles in the final therapeutic outcome as they influence the evolution of temperature distributions in space and time achieved in the tissue. The thermal diffusivity is an intrinsic tissue thermal property that combines the thermal conductivity and the heat capacity to express the rate at which heat dissipates and, thus, directly influences the time dependence of the temperature distribution in tissue. Perfusion acts as a local sink for excess heat energy by convective transport and depends on the degree of vascularity at the ablation site and proximity to larger blood vessels. In reality, these tissue specific thermal parameters are highly variable between tissue types and also across individuals. Hence, noninvasive methods of measuring these thermal parameters at the treatment location can reduce the uncertainty in therapeutic dose planning and delivery. Development of such technologies could also provide a means of tissue characterization to monitor physiological response to stimulus, or to detect abnormal tissue pathologies, for example (Lagendijk et al. 1988; Cheng and Plewes 2002).

Recently, the use of numerical simulation tools to predict the temperature distribution and thermal dose for therapy dosimetry planning applications has been widely reported in the literature (Meaney et al. 1998; Kolios et al. 1999; Curra 2001). The Pennes bio-heat transfer equation (BHTE) (Pennes 1948) is used to compute the temperature distribution and the thermal dose is computed using the formalism proposed by Sapareto and

* Present address: Philips Research North America, Briarcliff Manor, NY, USA.

Address correspondence to: Ajay Anand, PhD, Philips Research North America, 345 Scarborough Road, Briarcliff Manor, NY 10510 USA. E-mail: ajay.anand@philips.com

Dewey (1984). These simulation tools typically use *a priori* knowledge or assume standard values for tissue thermal parameters, namely, thermal diffusivity and perfusion loss. Uncertainties in the knowledge of these parameters can result in significant errors in the temperature distribution computed using the BHTE and consequently the thermal dose, which is a clinically important indicator of the endpoint of thermal therapy. Providing *in situ* estimates of the thermal parameters in the treatment region as inputs to the simulation tools would reduce errors in the predicted temperature distributions during planning phases and improve the ability of these tools to effectively adapt to varying local conditions for planning or during treatment.

Imaging techniques based on magnetic resonance imaging (MRI) (Cheng and Plewes 2002) and infrared (IR) imaging (Telenkov et al. 2001) to noninvasively estimate tissue thermal diffusivity and/or perfusion have been previously reported. However, no ultrasound based noninvasive method to estimate these parameters has been developed to the best of the knowledge of the authors. An ultrasound-based estimation technique is a more attractive option for use with therapy delivery systems because MRI requires specialized therapy equipment compatible with high magnetic fields and has lower temporal resolution (frame rate) compared with ultrasound imaging. IR imaging methods are limited to estimation of surface thermal measurements and may not be suitable for deeper ablation sites due to poor penetration.

Ultrasonic methods of estimating tissue thermal and acoustic properties have been recently proposed. Yao and Ebbini (Hui et al. 2004) demonstrated the feasibility of reliably estimating the initial heating rate at a localized heating spot by inducing a temperature change on the order of 1°C and proposed that the ultrasonically estimated initial heating rate can be used to compute the local tissue absorption. They also demonstrated that the ultrasonically determined initial temperature decay rate after turning off the heating demonstrates excellent agreement with the decay rate obtained from invasive thermocouple readings and conclude that the local perfusion can be estimated from these decay rate measurements. However, no quantitative estimate of the local tissue properties, absorption and perfusion, is obtained in that study. Recently, Sumi and Yanagimura (2005, 2007) proposed a technique for reconstructing the thermal properties such as thermal conductivity and diffusivity provided that quantitative spatial and temporal temperature information of the region-of-interest and reference values of the thermal properties are independently measured *a priori*. The temperature rise in the sample was induced using a heated waterbath. Simulations and experimental results obtained in a tissue mimicking phantom were presented. Practical application of the methods in noninvasive therapy modalities such as HIFU was not presented in that study.

In this article, a noninvasive ultrasound-based technique for estimating the local thermal diffusivity *in situ* using focused ultrasound or HIFU heating and application of novel backscattered radio-frequency (RF) signal processing techniques is presented. The technique is designed such that the thermal diffusivity estimation can be performed in the treatment region as part of a therapy planning calibration procedure conducted prior to the therapy delivery session. The theoretical framework underlying the estimation procedure is developed for the *in vivo* situation using the Green's function solution for the BHTE including the effect of bulk perfusion as a heat sink. It is shown from the theoretical analysis that the thermal diffusivity can be obtained by tracking the rate of change of the size of the heated region without knowledge of the absolute temperature. The estimated thermal diffusivity can then used as a known quantity to estimate the unknown perfusion term if information about the heat source is available. The effects of heat transport in the presence of a large blood vessel are not considered in this theoretical formulation. Since the current experimental work is limited to *in vitro* scenarios, the estimation of perfusion is not included in the parameter estimation step. Discussions on extending the parameter estimation step to the *in vivo* case for measuring perfusion are provided. The parameter estimation technique is based on visualizing the spatiotemporal variation of *temperature induced strain* (Miller et al. 2002, 2004) estimated from the raw ultrasound backscatter data after a short focused ultrasound heating pulse is applied at subablative intensities. The *temperature induced strain* is caused by changes in the local sound speed of the medium and thermal expansion (Maass-Moreno et al. 1996; Simon et al. 1998; Varghese et al. 2002). The maximum induced temperature rise is less than 10°C to avoid any permanent changes in tissue. A mathematical analysis of the solution to the heat transfer equation illustrates that the spatiotemporal rate of change of the temperature induced strain profile transverse to the HIFU beam axis of propagation is directly related to the thermal diffusivity. The technique is applied to ultrasound backscatter data collected during *in vitro* experiments performed in a tissue mimicking phantom and excised turkey breast muscle tissue.

THEORY

The technique adopted in this work for the estimation of the thermal diffusivity is based on determining unknown thermal parameters from the BHTE. For the *in vitro* case, in the absence of perfusion, the BHTE reduces