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● *Original Contribution*

QUANTIFICATION OF TEMPERATURE RISE WITHIN THE LENS OF THE PORCINE EYE CAUSED BY ULTRASOUND INSONATION

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Abstract—The soft tissue thermal index defined in the Output Display Standard is not applicable to eye exposures because of unique eye properties such as high ultrasound absorption in the lens and orbital fat. To address this potential safety issue, the U.S. Food and Drug Administration has recommended a maximum exposure level for ophthalmic exams of 50 mW/cm^2 (derated spatial-peak temporal-average intensity, $I_{SPTA.3}$) based on a model of ultrasound propagation in the eye. To gain a better understanding of actual temperature rise as a function of $I_{SPTA.3}$, an *ex vivo* experimental study within the porcine lens was performed. Both temperature and acoustic pressure were measured simultaneously in the lens using a fiberoptic probe. At $I_{SPTA.3}$ = 50 mW/cm^2, the maximum and average temperature rises over 133 measurements were 0.23°C and 0.09°C, respectively. A 1.5°C temperature rise was not obtained until $I_{SPTA.3} \approx$ 435 mW/cm^2. The data indicate that operating below the Food and Drug Administration guidance level should result in relatively low heating in ophthalmic exposures. (E-mail: rlkingku@gmail.com or Randy.King@fda.hhs.gov or rlkingku@yahoo.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Ultrasound, Ophthalmic, Safety, Porcine, Temperature rise, Eye, Lens.**

INTRODUCTION

Diagnostic ultrasound is a well-established technology in which benefits generally far outweigh any potential risks. However, there are several ultrasound imaging modes and applications for which safety analyses are still important, and for which current safety models and criteria contained in available safety standards and Food and Drug Administration (FDA) guidance are not applicable, one of which is ophthalmic imaging. With regard to diagnostic ultrasound, current guidance recommends output levels based on average tissue properties and steady-state temperature rise (FDA 2008; British Medical Ultrasound Society 2010). These are not appropriate for ophthalmic and new higher intensity diagnostic applications such as acoustic radiation force imaging. The eye, having unique tissue characteristics such as no blood supply in the lens, cornea and vitreous body; very poor perfusion in the sclera; and high acoustic attenuation in the lens, can have a temperature rise much higher than homogeneous soft tissue when exposed to ultrasound (Herman and Harris 1999). Diagnostic ultrasound devices provide exposure information to users *via* the Output Display Standard (International Electrotechnical Commission [IEC] 2007) which the FDA has incorporated into its regulatory diagnostic ultrasound guidance (FDA 2008).

The Output Display Standard defines acoustic output indices that are available for display so that the operator can monitor and adjust the ultrasound exposure level. One of these indices, called the soft-tissue thermal index (TIS) is related to the potential for temperature rise in most soft tissues in the body. However, because of unique properties of the eye (high absorption of ultrasound in the lens and orbital fat and no cooling blood supply to the lens, vitreous or aqueous humor [British Medical Ultrasound Society 2010; Herman and Harris 1999]) the TIS is inaccurate for eye exposure (Herman and Harris 1999). To address this potential safety issue, the FDA has recommended in its regulatory guidance (FDA 2008) that lower output levels be used for

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ophthalmic exams, which could hinder the clinician's ability to obtain necessary diagnostic information in some cases (Palte et al. 2012). Therefore, more realistic assessments of safety *versus* exposure should be undertaken to ensure safe use while not restricting clinical utility (Cucevic et al. 2005; Silverman et al. 2001).

Diagnostic ultrasound consensus standards and FDA guidance use an estimated average acoustic attenuation of 0.3 dB/cm-MHz for soft tissue. This value is used to calculate the derating factor, a multiplicative factor applied to acoustic output parameters and intended to account for ultrasonic attenuation of tissue between the source and a particular location in the tissue (American Institute of Ultrasound in Medicine/National Electrical Manufacturers Association 2004; IEC 2010). The derated spatial-peak temporal-average intensity is denoted $I_{SPTA.3}$.

The FDA regulatory guidance document contains a recommended maximum level for $I_{SPTA.3}$ of 50 mW/cm^2 for ophthalmic applications. This level was based on theoretical studies and may be too conservative for calculating the temperature rise occurring within the eye (Cucevic et al. 2005). Therefore, an experimental study was undertaken to measure the temperature rises in appropriate tissue over a range of ultrasonic output levels. At each output level, the derated intensity was calculated, the intensity in tissue was derived based on *in situ* pressure measurements and these two intensities were compared.

METHODS

Experimental setup

Fresh, adult, *ex vivo* porcine eyes, obtained from the local abattoir, were used for this study. They were obtained and used as quickly as possible to avoid degradation; all eyes were used within 8 h of harvest. For transport, the eyes were kept in degassed, 0.9% saline solution. Before the experiments, the eyes were cleaned, and superfluous tissue (muscle and fat) was removed.

For the experiments, the eye was mounted to an aluminum plate with sutures placed through the optic nerve and tied to the plate. Figure 1 gives a schematic of the experimental setup. Once secured to the plate, a catheter, used as a cannula, was inserted into the lens of the eye under diagnostic ultrasound guidance (Siemens, Antares, Malvern, PA, USA) (Fig. 2). A Fabry–Perot fiberoptic ultrasonic hydrophone probe (Precision Acoustics, Dorchester, UK) (Morris et al. 2009) was inserted into the lens through the cannula, also under ultrasound guidance (Fig. 2). This fiberoptic probe system was able to record the temperature profile of the tissue caused by the sonication, as well as the acoustic pressure. Once the fiberoptic probe was in the lens, the cannula was removed, and the aluminum plate was attached to a three-axis positioning system and lowered into a small tank of degassed saline that was heated to and maintained at 37°C.

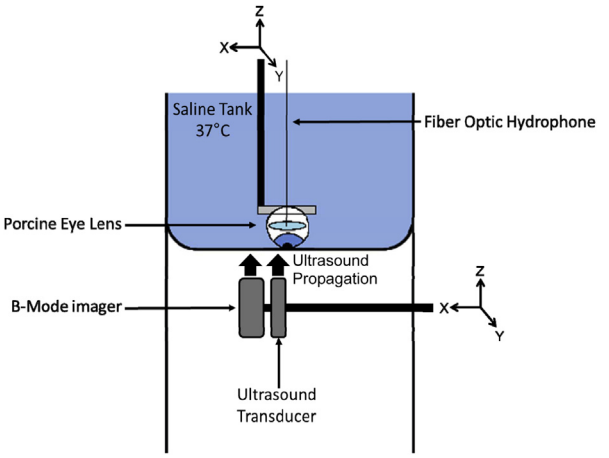

Fig. 1. Schematic of experimental setup. A porcine eye is suspended from a three-axis positioning system in degassed saline heated to 37°C. Two transducers, one for sonication and one for imaging, are on a separate three-axis positioning system below the tank, and access to the eye is through a Mylar window.

The waveform was produced using a Tektronix Model AFG 3021 C (Beaverton, OR, USA) function generator. An ENI (Rochester, NY, USA) radio frequency amplifier, Model 3100 L, was used to drive the sonicating transducer, a custom air-backed transducer with an element with 0.5-in. diameter, 10-MHz center frequency and a 1.0-in. radius of curvature (Olympus NDT, Waltham, MA, USA). The frequency, size and focus are

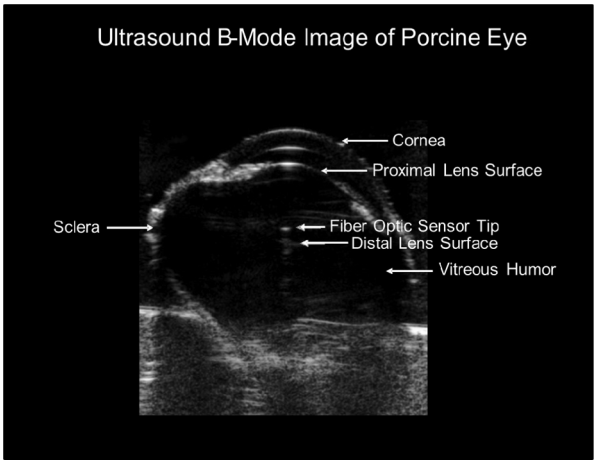

Fig. 2. B-Mode image of the porcine eye in the experimental setup. The cornea, sclera, both edges of the lens and the tip of the fiberoptic probe can be seen in the image. An image such as this was used to guide the placement of the fiberoptic probe to ensure proper placement for every experiment. Refer to Figure 1 for transducer location.