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● *Original Contribution*

A COMPARISON OF ACOUSTIC CAVITATION DETECTION THRESHOLDS MEASURED WITH PIEZO-ELECTRIC AND FIBER-OPTIC HYDROPHONE SENSORS

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Abstract—A Fabry-Perot interferometer fiber-optic hydrophone (FOH) was investigated for use as an acoustic cavitation detector and compared with a piezo-ceramic passive cavitation detector (PCD). Both detectors were used to measure negative pressure thresholds for broadband emissions in 3% agar and *ex vivo* bovine liver simultaneously. FOH-detected half- and fourth-harmonic emissions were also studied. Three thresholds were defined and investigated: (i) onset of cavitation; (ii) 100% probability of cavitation; and (iii) a time-integrated threshold where broadband signals integrated over a 3-s exposure duration, averaged over 5–10 repeat exposures, become statistically significantly greater than noise. The statistical sensitiviy of FOH broadband detection was low compared with that of the PCD (0.43/0.31 in agar/liver). FOH-detected fourth-harmonic data agreed best with PCD broadband (sensitivity: 0.95/0.94, specificity: 0.89/0.76 in agar/liver). The FOH has potential as a cavitation detector, particularly in applications where space is limited or during magnetic resonance-guided studies. (E-mail: victoriabull1@googlemail.com) © 2013 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Passive cavitation detection, High-intensity focused ultrasound, Focused ultrasound surgery, Fiber-optic hydrophone, Cavitation thresholds.**

INTRODUCTION

The use of high-intensity focused ultrasound (HIFU), also known as focused ultrasound surgery, for the treatment of soft tissue tumors is increasing. It is a non-invasive, conformal, non-ionizing alternative to surgical procedures, chemotherapy and/or radiotherapy (Ahmed et al. 2009; Kim et al. 2011; Murat et al. 2009) and to thermal techniques such as cryotherapy, radiofrequency, laser and microwave ablation, all of which require the implantation of an applicator (Carrafiello et al. 2008; Izawa et al. 2001; Ng and Poon 2005; Omata et al. 2004; Rempp et al. 2013). The high pressures reached within the HIFU focal region can lead to acoustic and/or thermally induced cavitation, both of which have been shown to cause unpredictable tissue damage as a result of their effect on energy deposition, and thus heat distribution, within target tissues (Bailey et al. 2001; Chavrier et al. 2000; Watkin et al. 1996). Acoustic cavitation bubbles may oscillate stably or undergo rapid growth, followed by inertial collapse. These processes are known as stable (or non-inertial), and inertial cavitation, respectively. Stable oscillations of cavitation bubbles close to cell membranes have been reported to increase cellular permeability, which may aid in the delivery of therapeutic agents (Collis et al. 2010; Coussios and Roy 2008), but may also cause mechanical damage directly or through the formation of streaming currents (Bull and ter Haar 2013; Collis et al. 2010; Wu 2001, 2002). These oscillations lead to the emission of acoustic signals at harmonics and sub-harmonics, in particular the half harmonic, of the HIFU drive frequency (Eller and Flynn 1969). Inertial cavitation activity results in direct mechanical damage and the emission of shock waves, which can be strongly absorbed in the immediate vicinity, causing extremely high local temperature rises (Holt and Roy 2001). Acoustic emissions from these bubbles at harmonics of the drive frequency can be detected, as can broadband noise arising from inertial collapse (Neppiras 1968a). Indicators of stable and inertial

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cavitation are commonly accepted to be emissions at the half harmonic of the drive frequency and broadband noise, respectively.

There are a number of ways in which acoustic emissions from cavitation activity, both stable and inertial, can be detected. Passive cavitation detectors (PCDs) are commonly single-element, focused transducers that sit some distance from the exposed medium, are co-aligned with the HIFU transducer and are used in receive mode as hydrophones to listen for acoustic emissions (Canney et al. 2010; Coleman et al. 1996; Hynynen 1991; Zhang et al. 2009). Additionally, unfocused hydrophones (Hallow et al. 2006) and ultrasound imaging transducer arrays (Farny et al. 2009; Jensen et al. 2012; Salgaonkar et al. 2009) have been used as PCDs. Active detection involves the introduction, into the focal region, of additional ultrasound pulses, which are then reflected by acoustic cavitation bubbles (Bailey et al. 2005; Madanshetty et al. 1991; McLaughlan et al. 2010; Rabkin et al. 2005; Roy et al. 1990).

There are several potential advantages of fiber-optic hydrophones (FOHs) for passive cavitation detection. First, the fibers are inherently magnetically compatible, making them ideal for magnetic resonance (MR)-guided studies. Although MR-compatible focused PCD transducers are commercially available, they are costly and do not exhibit the versatility of a FOH, which can be used as both a hydrophone and a thermocouple (Morris et al. 2009). Second, FOH sensors may be implanted into soft tissues and phantoms (Bull et al. 2011; Huber et al. 1994; Morris et al. 2009), allowing precise and rapid localization of the HIFU focus and resulting in minimal acoustic emission amplitude loss from attenuation in the path from the region of bubble activity to the sensor. Finally, the small fiber tip diameter (150 μm) is advantageous when working with animal models or in complex or spatially restrictive experimental arrangements (Tokarczyk et al. 2013). Two potential disadvantages are also evident. First, the use of unfocused sensors does not allow precise localization of the cavitation signal source. Second, the fragility of the FOH fibers used in this study (Precision Acoustics, Dorchester, UK) is a significant disadvantage, as it is not possible for the user to repair a damaged fiber because of the complexity of the interferometer tip.

Fiber-optic hydrophones have previously been investigated for cavitation detection. Huber et al. (1994) constructed a hydrophone based on the system designed by Staudenraus and Eisenmenger (1993) that detected changes in refractive index in the surrounding medium arising from pressure changes. Fibers 50 and 120 μm in diameter were used, and although the system as a whole had lower pressure sensitivity (1.1 mV/MPa) than their needle and membrane hydrophones (6.7 and 8.3 mV/MPa, respectively), it was able to detect cavitation activity in subcutaneous tumors in the thighs of rats exposed to lithotripter pulses. This device was compared with membrane and needle hydrophones in terms of its pressure sensitivity, but no attempt was made to quantify the cavitation being detected. The study related to lithotripter pulses, which are designed to work at pressures far above the threshold for inertial cavitation. The ability to detect cavitation at pressures close to the threshold has not been studied. Furthermore, no discussion was provided relating to the effect of using this device *in vivo*, where the changes in index of refraction of blood may differ from those of water.

Koch and Jenderka (2008) used a FOH system based on a heterodyne interferometer to measure bubble activity in a de-ionized, de-gassed water-filled ultrasonic cleaning bath. Fiber tips 125 μm in diameter, coated in a single layer of titanium, allowed measurement of the changing optical index of the fiber caused by compression and decompression of its tip. One advantage of this device was the ability to easily cleave and re-coat the fiber if it was damaged by cavitation activity. To make continuous measurements within regions of cavitation activity over many days, the fiber tips had to be either embedded in polyurethane rubber or surrounded by stainless steel tubing. The minimum pressure the system could detect was 1 kPa, over a bandwidth of 20 MHz. It was used to measure both the incident acoustic pressure and half-harmonic and broadband bubble emission signals simultaneously. The pressure sensitivity of this device was not quoted. The measured fundamental, half-harmonic and broadband "cavitation noise power" from 1 to 1.25 MHz were compared with those measured using a piezo-electric hydrophone. The authors concluded that although the FOH exhibited a lower signal-to-noise ratio than the piezo-electric device, the small dimensions of the fibers and their ability to withstand cavitation over long periods provided significant advantages. These studies have provided useful information in environments where cavitation is expected to occur, but have not addressed the lower limit of detection of cavitation signals at pressures close to the cavitation onset threshold, which is important for HIFU applications.

A number of definitions of cavitation thresholds exist in the literature. Studies have used visual detection to determine a threshold pressure for either the appearance of cavitation bubbles coming out of solution in water (Connolly and Fox 1954) or the onset of oscillation and/or collapse of pre-existing microbubbles (Emmer et al. 2007). Sono-luminescence resulting from cavitation inception in water has also been detected (Fowlkes and Crum 1988; Roy et al. 1985), and in both studies, subtraction or exclusion of background noise was carried out before a "true" signal could be defined.