The Design And Implementation Of A Passive Cavitation Detection System For Use With Ex Vivo Tissue

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Abstract. A passive cavitation detection (PCD) system has been constructed around a National Physical Laboratory (NPL) cavitation sensor. This system, which has been used to detect the acoustic emissions when ex vivo tissue is exposed to a number of different HIFU intensities, can monitor acoustic emissions throughout an exposure. It has been observed that for the higher harmonics, specifically the 4th (6.77 MHz), the emissions undergo a sharp transition from a low magnitude slowly varying signal, to rapidly varying and high magnitude signal. A sonochemical reaction (in a potassium iodide solution) was simultaneously monitored with the passive cavitation detection and a correlation with free radical production (caused by inertial cavitation) and high frequency broadband emission (7-8 MHz) was observed.

Keywords: Cavitation, Passive Cavitation Detection, Acoustic Emissions, Sonochemistry, HIFU.
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INTRODUCTION

High intensity focused ultrasound (HIFU) or focused ultrasound surgery (FUS) is a technique in which tissue is ablated using highly focused ultrasound beams. This technique can be used as a non-invasive treatment for tumours within the body.

HIFU-induced thermal damage results from raising the tissue temperature to about 56°C for 1s. Acoustic cavitation (see below) in which bubbles can act as scatterers and locally redistribute the ultrasound energy may also occur during HIFU. The mechanical motion of bubbles may cause damage directly. In order to investigate whether acoustic cavitation can be used to advantage in clinical HIFU treatments, a cavitation detection system has been constructed.

There are many detection methods currently in use. However a passive cavitation detection (PCD) system is the most appropriate for this application. A passive system detects the acoustic emissions from oscillating bubbles. A bubble may oscillate stably or collapse. For a stable cavity perturbed by an acoustic field, the internal gas pressure is able to balance the external acoustic pressure and the tension applied by the liquid,

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allowing it to expand and contract for many acoustic cycles. This is non-inertial cavitation. Inertial cavitation occurs when there is significant growth of the cavity in the rarefaction portion of the acoustic cycle, and the cavity collapses during a compression phase. The main emissions from cavitating bubbles are subharmonics, broadband ‘noise’ and super-harmonics of the drive frequency. The occurrence of a particular type of emission may correspond to a particular type of cavitation, as summarised by Neppiras[1].

METHODS

The PCD system was designed to enable monitoring of acoustic emissions in the range 0-10 MHz and their variation in time.

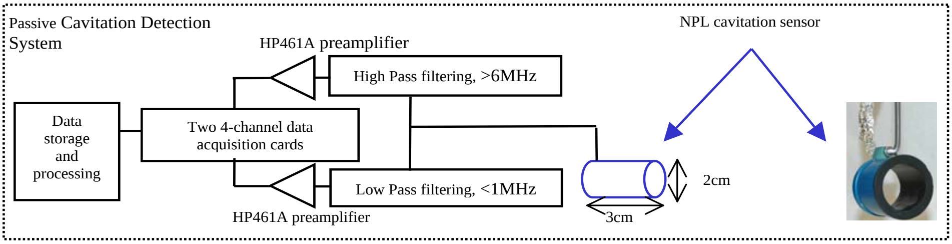

FIGURE 1. The passive cavitation detection system, which includes a broadband cavitation sensor.

The PCD system shown in fig. 1 incorporates an NPL cavitation sensor[2]. The sensor comprises a cylinder of PVDF film mounted inside a 4mm thick acoustic absorber. Due to the geometry of the sensor, it is not possible to use it *in vivo*. The broadband response (0-10 MHz) of the sensor allows monitoring of a wide range of acoustic emissions. The drive frequency of the HIFU transducer is 1.693 MHz (15cm focal length, f-number 1.79). The detection system uses low and high pass radio frequency (RF) filters (input impedance $50\ \Omega$) to attenuate the 1.693 MHz signal from the HIFU source. The low pass filter (Allen Avionics, F5099, frequency cut off 850 kHz at –77 dB per octave) and the high pass filter (Allen Avionics, F5100, frequency cut off 6 MHz at –25 dB per octave) are connected to two different HP461A preamplifiers (Agilent, 0.1-150 MHz bandwidth, 40 dB amplification). Low frequency (max 50MHz sample rate) and high frequency (max 200 MHz sample rate) 4 channel data acquisition cards (Spectrum Inc.) are installed in a dual PCI bus computer (Supermicro, USA). This data acquisition system allows the voltage signal from the sensor to be recorded throughout the duration of the HIFU exposure. The *ex vivo* tissue sample (fresh bovine liver) is cut so as to completely fill the sensor, and the HIFU focus is placed inside the sensor (15 mm from its front face). All tissue was exposed for 2s over the spatial peak intensity[3] (I_{sp}) range 500-5250 W/cm^2.

Frequency data is obtained using a fast fourier transform (FFT) routine in MatLab^{TM} from the raw voltage information recorded by the data acquisition system. An FFT calculation is performed for every time step. From this, each specific frequency or area under the frequency spectrum is recorded at a rate governed by the sampling frequency and the number of points used in the FFT.

In an attempt to interpret the emissions detected by the PCD system, a secondary indication of (inertial) cavitation was used in conjunction with this system. This used the Weissler reaction[4], where free radicals generated from bubble collapse result in iodine production in an exposed potassium iodide solution. 1.9 ml of solution was placed in a perspex (2 mm thick) container and exposed for 5s, and the relative absorbance of this exposed solution at 350 nm was then measured in a spectrometer (Lambda EZ 201). The sample volume was located within the NPL sensor volume, with the focal zone of the HIFU transducer inside the sample holder.

RESULTS AND DISCUSSION

Figure 2 shows results from 2s HIFU exposures in *ex vivo* liver using the PCD system.

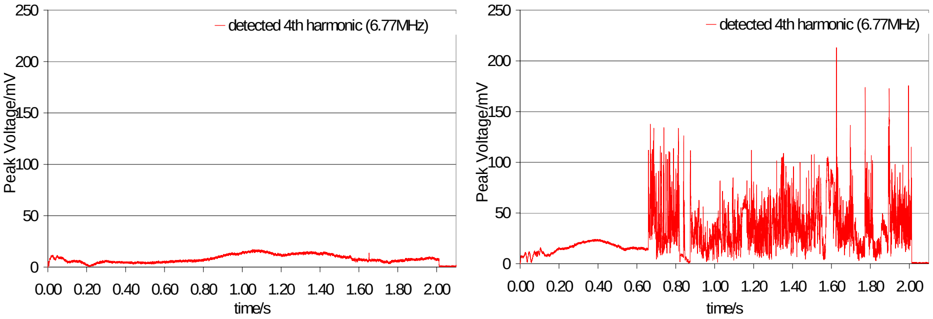

FIGURE 2. The 4th harmonic emission detected during two separate 2s HIFU exposures of *ex vivo* liver. Left -3.25 MPa (I_{sp} = 1250 W/cm^2), right -3.50 MPa (I_{sp} = 1500 W/cm^2).

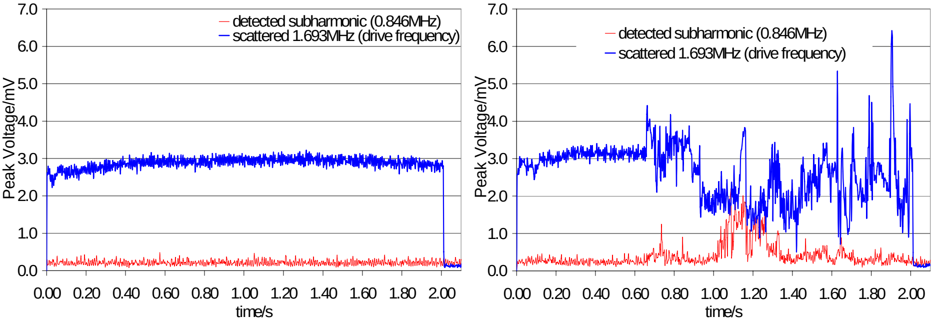

FIGURE 3. The subharmonic harmonic emission and scattered drive signal detected during two separate 2s HIFU exposures of *ex vivo* liver. Left -3.25 MPa (I_{sp} = 1250 W/cm^2), right -3.50 MPa (I_{sp} = 1500 W/cm^2).

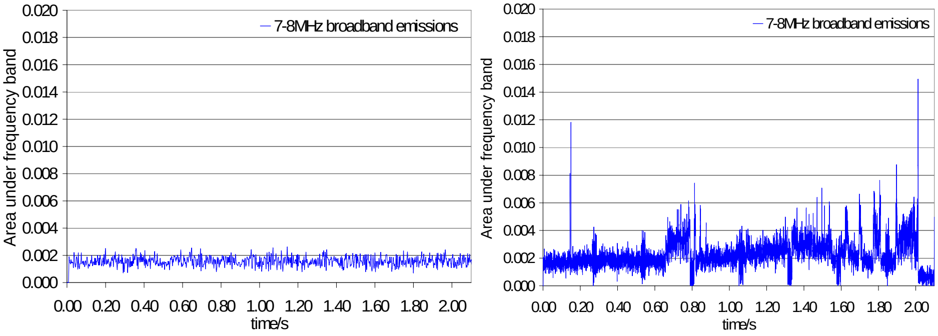

FIGURE 4. The high frequency broadband emissions detected during two separate 2s HIFU exposures of *ex vivo* liver. Left -3.25 MPa (I_{sp} = 1250 W/cm^2), right -3.50 MPa (I_{sp} = 1500 W/cm^2).

Figures 2-4 show typical examples of the detected emissions at two different peak negative pressure levels at the focus. At the lower level (-3.25 MPa / 1250 W/cm^2) no emissions are detected, however at the higher level (-3.50 MPa / 1500 W/cm^2), there are emissions. The high frequency broadband emissions (fig. 4) occur earliest (0.15s), but are intermittent. Figure 2 shows that at a specific time (0.7s) the nature of the emissions change from those probably due to non-linear effects in the HIFU field to an increased signal and a chaotic appearance. This is most likely to be the onset of cavitation activity. The scattered drive signal (fig. 3) appears to scale fluctuate during the same time interval as the chaotic variation in the 4th harmonic, most probably due to the presence of multiple scatterers within the focal region. The half harmonic seems to be anti-correlated with the scattered drive (fig. 3), however this was not a typical result.

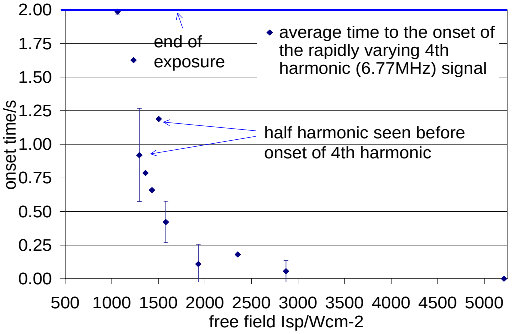

FIGURE 5. Onset times for the chaotic behaviour from the 4th harmonic, (as seen at 0.7s in figure 2, left) as a function of HIFU intensity.

The onset of the chaotic 4th harmonic signal behaviour was repeatable, except when half harmonic signal had been detected earlier in the exposure. In an attempt to determine a direct relationship between acoustic emissions and cavitation activity, a sonochemical reaction was used. Figure 6 shows correlations between the increase in iodine production and high frequency broadband emissions measured in the KI solution with HIFU intensity. No correlation was found for other emissions. As the sonochemical reaction cannot be monitored as a function of time, the broadband noise has been displayed as the maximum value detected over the entire exposure time. This result would agree with previous assumptions[5] that high frequency broadband emissions are an indicator of inertial cavitation.

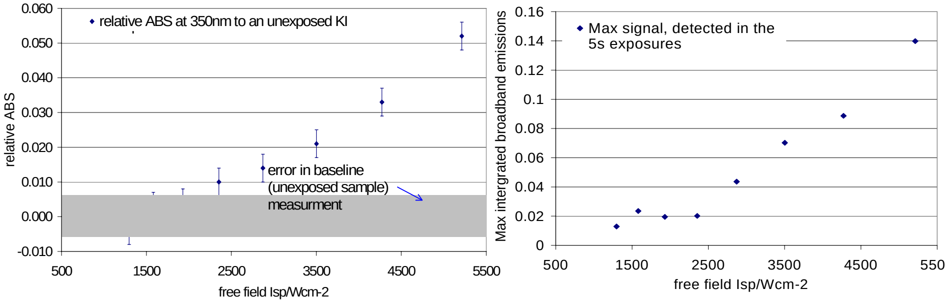

FIGURE 6. Left, a plot of the relative UV absorbance at 350 nm for KI samples exposed at increasing intensity levels. Right, a comparison with the maximum high frequency broadband (7-8 MHz) emissions detected during these exposures.

CONCLUSION

A broadband passive cavitation detection system for use with HIFU has been constructed, and tested with *ex vivo* tissue. It has been shown that the 4th harmonic emission has significance when attempting to detect cavitation in tissue. In an attempt to obtain further evidence about they way in which acoustic emissions relate to cavitation activity, it was shown that high frequency broadband emissions were related to free radical generation from inertial cavitation.

The current system can be modified such that a passive sensor of appropriate geometry could replace the NPL sensor, thus allowing the system to be used for *in vivo* studies.

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