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1pBAb9. Real-time three-dimensional passive cavitation detection for clinical high intensity focussed ultrasound systems  
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Bubble activity during High Intensity Focused Ultrasound (HIFU) surgery has been linked with desirable effects, such as an enhanced heat deposition caused by inertial cavitation, and undesirable effects, such as lesion migration caused by boiling bubbles. There is presently no reliable way of achieving spatiotemporal monitoring of cavitation activity during clinical HIFU treatments. In the present work, a near-acoustically-transparent two-dimensional 32-element PVDF array was designed and mounted on the therapy transducer of a clinical HIFU device (Model JC200, Chongqing Haifu) to enable detection of acoustic emissions arising from cavitation during therapy. The signal detected by each of the elements was digitized and processed in real time on a Graphical Processing Unit (GPU), and beamformed using our previously described Passive Acoustic Mapping (PAM) algorithm to produce real-time three-dimensional (3D) maps of cavitation activity with a frame rate in excess of 5 Hz. The system was initially validated in agar-based tissue-mimicking materials, demonstrating that the displayed volume of cavitation activity agreed with predictions based on in situ pressure calibrations. The system was further validated during clinical HIFU treatments of kidney tumour, liver tumour and uterine fibroid ablation, and was found to enable accurate localization of the HIFU focus at sub-lesioning intensities.

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INTRODUCTION

The idea of a threshold beyond which the behaviour of a bubble in a sound field changes dramatically is something that has been the subject of much speculation and many different measures have been proposed to describe this threshold. Apfel and Holland [1] use numerical models of adiabatic collapse to give a threshold in terms of the maximum temperature of the gas within the bubble during collapse in pure water. This estimate of the pressure threshold for violent acoustic cavitation became the basis for the Mechanical Index (MI), a scale used to judge the likelihood of violent cavitation, often referred to as inertial cavitation [2], occurring during a single cycle of excitation [3]. The high acceleration of the bubble wall as it rebounds after such a collapse leads to a correspondingly large acoustic emission from the bubble.

Observations of acoustic emissions during a continuous wave excitation can be summarized in terms of the amplitude of the excitation [4]. At low amplitudes the emissions are only at the driving frequency. As the driving amplitude is increased the integer harmonics of the driving signal can also be detected. At higher amplitudes still, fractional-harmonic emissions appear and broadband noise is present. The power radiated as broadband noise from the bubble increases as the inertial cavitation threshold is approached. This broadband noise is taken to be due to the very short time-scale of the collapse producing a very short emission in the time domain which corresponds to a broad response in the frequency domain.

The emergence of these higher harmonics and broadband noise when the inertial cavitation threshold is approached has a dramatic implication for the heating due to the sound emissions: the non-linear oscillation of an inertially cavitating bubble takes energy from an incident sound wave and re-radiates it at a higher frequency. Due to the frequency dependent attenuation coefficient observed in both tissue and tissue mimicking materials, acoustic energy converted to these higher frequencies is more readily absorbed than energy at the incident frequency, increasing the rate of heat deposition. If the additional heating due to inertial cavitation is dominant then the relationship between the increased rate of heat deposition and the acoustic emissions can be used as a means of monitoring the heating. The use of an array of passive detectors has been shown to enable localisation of cavitation events, using a beamforming technique called time exposure acoustics [5]. Maps of cavitation activity produced by such techniques have been shown in ex vivo tissue to correlate more closely with lesion formation than conventional B-mode imagery [6].

In this paper we describe an array that is suitable for use as a 3-d cavitation mapping sensor that can be retrofitted to existing HIFU transducers. Use of this sensor for real-time feedback is evaluated both in vitro and in vivo.

METHODS

The new detecting array that is used in this work consists of eight dart shaped sub-arrays that each contain four elements. These are formed from a layer of polyvinylidine flouride (PVDF), a peizo-polymer, that is between a sputter coated gold electrode and a flexible printed circuit board that defines the individual elements. As shown in figure 1, these flexible sub-arrays can be attached to the surface of a HIFU transducer, ensuring that the detecting elements remain at a constant location with respect to the driving transducer. Signals from these elements are conditioned using custom filters and pre-amplifiers (DNV, Portland, UK). The signals are then digitized (NI5752, National Instruments, Newbury, UK) and processed using a graphical processing unit (GPU) (GTX260, Nvidia) and optionally stored to disk for later post-processing.

Array Transducer Characterisation

Characterization of the sensor falls into two categories: characterization of the device's detection ability and characterization of its effect upon the performance of the HIFU transducer to which it is mounted. For the first of these a measurement of the sensitivity of the elements was performed through a substitution method. The elements were mounted on a flat aluminium plate. This gives the elements the same backing impedance as experienced when mounted on the surface of the JC200 HIFU transducer since it uses an aluminium lens for focussing. The elements were then aligned on the axis of two different insonating transducers (V306, V320, Olympus) with centre frequencies at 2.25 MHz and 7.5 MHz respectively. By
**FIGURE 1:** Eight cavitation detection sub-arrays each with four elements mounted on the surface of the clinical transducer (JC200, Chongqing HAIFU systems) retained in position by a mounting ring.

**FIGURE 2:** Schematic of the experimental setup showing the detecting array mounted on the HIFU transducer and the associated receiving electronics.
setting a fixed tone burst length of 50\(\mu\)m interference from reflections was avoided and the frequency swept over the range of 0.5-10 MHz and the output recorded using a digital oscilloscope (WaveRunner, LeCroy). The elements were then removed and replaced with a calibrated 0.5 mm needle hydrophone (HPM05, Precision Acoustics) and the frequency sweep repeated.

To characterize the extent to which the mounting of the array affects the output of the HIFU transducer to which it is mounted hydrophone scans were performed using a three axis positioning system along the axis of the transducer and in the focal plane. This was done for three different configurations: with nothing mounted on the transducer, with a mounting ring used for alignment and to fix the sensors in position, and with both the sensors and the mounting ring in place.

**Cavitation detection assessment**

In to demonstrate the mapping ability of the sensor in vitro HIFU exposures were performed. The sensor was mounted on a clinical HIFU transducer (JC200, Chongqing HAIFU) that had been removed from its machine and was instead driven using a signal generator (33250A, Agilent Technologies) and power amplifier (A300, ENI). A cavitation promoting agar-talc tissue phantom (3% agar, 2% talc, 95% water) was placed at the focus. Exposures at a range of amplitudes were performed and the received signals both stored and processed in real time.

Passive cavitation data was collected during exposures using the full clinical HIFU system both in agar gels and as part of a kidney tumour trial.

**RESULTS**

**Array Characterisation**

In figure 3 the sensitivity of a representative element is shown over the frequency range of 0.5-10 MHz. This calibration was performed with the custom pre-amplifier and filter in place. Of particular interest is the sharp notch in sensitivity at the 0.97 MHz driving frequency of the HIFU transducer. This is designed so that when the sensor is mounted on the surface of the HIFU transducer the signal due to transmission from the therapy transducer is rejected while still allowing the higher frequency signals to be received that are likely to be due to cavitation events.

The effect of mounting the sensor onto the JC200 HIFU transducer is shown in figure 4. Here the three different scenarios are compared: the transducer alone, the transducer with only the mounting ring, and the transducer with the mounting ring and the sensor attached. The amplitude is seen to drop by around 10% when both the mounting ring and the elements are attached, as shown in axial scans the top part of the...
**Cavitation detection assessment**

The ability of the system to map cavitation events is demonstrated in figure 5 where time exposure acoustics is performed on an axial slice and on a transverse slice through the focus of the driving transducer. The signals are digitally filtered and are plotted for the components at the harmonics of the 0.97 MHz driving signal and for the non-harmonic components, showing some grating lobes both transverse to and along the axis of the HIFU transducer. The software controlling the acquisition and the processing (LabView, National Instruments) returned timing information for the display of the maps. Data acquisition on 32 channels for 80μs at a rate of 50 MS/s and 3-d volumetric processing consisting of 18081 (21x21x41) voxels can performed approximately every 200 ms, giving a near real-time frame rate of five frames per second.

The performance of the passive cavitation detection array combined with the full clinical HIFU system was first assessed using an agar target, as shown in figure 6. Passive acoustic maps for an axial slice from an exposure well above the cavitation threshold are shown for non-harmonic and harmonic components in columns one and four respectively. For the maps formed from the non-harmonic components, extensive electromagnetic pickup of broadband noise from the JC200 driving electronics overwhelms any signal from activity at the focus of the driving transducer (column one); the harmonic images (column four) are still affected by this, but the focus can nonetheless be clearly localized. The effect of broadband noise on maps formed from the harmonic and from the non-harmonic components can be seen on simulated data, as shown in columns two and three for the non-harmonic components and five and six for the harmonic components. Similar effects are seen to those observed during experiments using the full clinical system.

Since the broadband passive mapping was found to be overwhelmed by noise in agar gel experiments, the plots on the left of figure 7 show only the amplitude of the harmonic components for ramps of the driving...
**FIGURE 5:** Cavitation maps produced during a 0.97 MHz HIFU exposure at 2.5 MPa in an agar-talc phantom. The time taken to process this is approximately 200 ms per frame.

**FIGURE 6:** Cavitation maps averaged over 20 frames of a HIFU exposure in agar. This uses the full clinical HIFU system, and significant electrical broadband noise was experienced. The maps are formed from digitally filtered broadband and harmonic components and are compared against simulated results.

**FIGURE 7:** Ramped exposures in kidney and agar showing detection of scattering
signal both in agar gel (top) and in two kidney tumour patients (bottom). In agar, the amplitude of the received signal jumps in amplitude above 160W nominal acoustic power, accompanied by audible boiling. In contrast measurements in tissue are approximately linear, suggesting that scattering of the harmonics of drive signal by tissue is being detected. No significant change in B-mode hyper-echo was seen during the ramps in patients. The ability of the array to detect the scattered signal at sub-lesioning intensities raises the possibility of using such an array to spatially localize the focus within the body before a treatment takes place.

**CONCLUSIONS**

A 32 element acoustically transparent array has been developed. This has been demonstrated to be capable of localizing cavitation events when mounted on the surface of a clinical HIFU transducer. When so mounted it has also been shown to reduce the output of the therapy transducer by only 10%, and to not significantly change the beam shape of the therapy field. This allows it to be used without impacting on patient care as the targeting of the treatment is unchanged.

Localization of cavitation in *vitro* has been demonstrated for both harmonic and broadband elements of the spectrum. Detection in *vivo* as part of a kidney tumour trial was hampered by broadband electrical noise, but detection at the harmonics was shown to enable mapping both of cavitation and also of scattered signals from the focus of the driving signal. This second effect could be used to enable localization of the focus of the HIFU beam at sub-lesioning intensities. Parallelization of the processing on a graphics card enabled full 3-d volumes of the cavitation activity to be calculated with a frame rate of 5 Hz, allowing near real-time feedback.

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**REFERENCES**


