IN-VIVO FETAL ULTRASOUND EXPOSIMETRY

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ABSTRACT

An instrument has been developed to measure the acoustic pressure field during an obstetric ultrasound examination. This permits a more accurate assessment of possible bioeffects since the pressure is sensed at or near the site of the organs under investigation. The ultrasonic field is sampled using a calibrated 7 element linear array hydrophone of poly(vinylidene difluoride) transducers, which is placed as close as possible to the ovary, embryo, or fetus, using a vaginal approach. The RF signals from the hydrophone are digitized at 50 Ms/s, and the maximum amplitude waveform received in the examination is recorded. The output of the clinical B-scanner is calibrated by the hydrophone in a water bath. From the hydrophone measurements, the in-vivo I_{SPTA}, I_{SPTP} and I_{SPPA} can be computed. Further analysis allows the frequency dependent tissue attenuation to be assessed.

I. INTRODUCTION

Diagnostic ultrasound is a widespread technique in all disciplines of medicine, and particularly in the reproductive sciences. Prior to conception, it is used to monitor follicular growth and development, and subsequent ovulation. Once pregnancy is confirmed, in a vast majority of patients, the early human embryo is exposed to ultrasound for confirmation of viability and numerous other indications for exposure during the second and third trimesters [1].

It is assumed that ultrasound levels currently employed in diagnostic instruments are not associated with any biohazard to the embryo and growing human fetus. This assumption is maintained despite an almost complete lack of knowledge concerning the actual energy imparted to the ovary, early embryo, and fetus during diagnostic imaging. There is, therefore, concern about long-term fetal effects [2,3]. The in-vivo and in-vitro investigations of bioeffects in the literature are difficult to apply to the human fetus for several reasons. Often high energy levels are used to produce bioeffects in non-clinical models; the effects of absorption and attenuation from the abdominal wall are not taken into account and the effect of beam focusing is not considered. A cooperative study between the University of Illinois and the University of Cincinnati has been developed to address these issues. The purpose of this paper is to describe the system we have developed to quantify, in-vivo, the amount of ultrasound delivered during obstetrical examinations.

II. INSTRUMENTATION

A block diagram of the experiment is shown in Figure 1.

(a) Hydrophone

Six side-looking hydrophones (Figure 2) were constructed for the project. A seven element array of poly(vinylidene difluoride) (PVDF) transducers is positioned near one end of a curved stainless steel tube. A multi-element array is needed because of the difficulty in aligning the ultrasonic field from the clinical transducer with the hydrophone in-vivo. The continuous outer electrode on the 28 μm PVDF film provides a ground connection. Seven circular back electrodes (0.5 mm diameter, 1.5 mm spacing), fabricated on the other side of the polymer, define the elements of the hydrophone. The transducer array fits in a window in the tube, and is held in place with epoxy. A thin layer of epoxy over the array protects the transducers; this is machined flush with the tube walls before the whole assembly is polished. The device is sufficiently rugged to withstand gas sterilization with ethylene oxide.

In order to present a low input capacitance to the array elements and provide some current gain to drive the hydrophone cable, a surface mount JFET is connected in source follower configuration close to each transducer. The hydrophone assembly also incorporates a temperature sensor - a thermistor which is mounted at the far end of the tube. The various signals and power supply lines are brought out to a Lemo connector on the handle of the hydrophone.

The array was calibrated using a substitution technique. A 3 MHz Panametrics transducer was placed in a degassed, distilled water bath and impulse excited. The

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maximum pressure was found with a calibrated PVDF membrane hydrophone (Marconi, Chelmsford, England). Sensitivities for each of the elements were measured by positioning an element at the (known) pressure maximum and measuring the end-of-cable voltage.

(b) Analog Electronics

The distance from the hydrophone to the A/D converter makes further buffering necessary. To accommodate this, a small enclosure containing a multiplexer for the RF signals, a preamplifier and a buffer amplifier is interposed in the signal path, four feet from the hydrophone. This also houses an oscillator to convert resistance changes in the probe's thermistor to variations in frequency to quantify temperature in vivo. Its 1 MHz square wave is digitized in the same manner as the ultrasonic signals. Selection of transducer element and temperature signal is achieved by three lines from the controlling PC.

The RF signal passes through an anti-aliasing filter and a "gain-riding" programmable attenuator before being digitized. The attenuator is changed before each data acquisition to compensate for variations in sensitivity between transducer elements. This ensures that the full dynamic range of the A/D converter (45 dB) is used at all times.

(c) Digital Electronics

The digitizer used was a TDC1025 (TRW, La Jolla, CA) which provides 8 bits of resolution at 50 Ms/s. This chip is clocked continuously, and feeds a bus expander which produces 32 bit data at 12.5 MHz. The 32 kbyte data memory can then be conservatively designed with 55 ns components. Memory addresses are generated by the address counter in Figure 1, which is enabled by an acquire data signal from the PC. The run length counter is loaded at the start of the cycle with the number of samples to acquire after the trigger. It begins counting down after the PC's "acquire data" line is asserted and an RF trigger is received. Notice that the data acquisition begins before the ultrasonic signal arrives. The equipment can, therefore, operate in a pretrigger mode, as in a digital oscilloscope. This allows us to acquire data without modifying the clinical B-scanner.

The trigger circuit monitors the output of the A/D converter, which runs continuously. Two ECL comparators generate the trigger signal if the raw A/D signal exceeds a preset value for more than 40 ns. Once the data is stored in the digitizer memory, it is read out through a parallel I/O card to the PC. The trigger signal also feeds a counter which measures the time interval between ultrasound pulses. This is needed to convert temporal peak pressures to averages.

(d) Software

Mouse driven control software was written for ease of use by clinical personnel. The user initially indicates which hydrophone is to be used, in order to recall the correct calibration data. Next, in-vivo data is acquired. In this mode, the PC's screen behaves like an oscilloscope, so the clinician can view the incoming RF data. The largest waveform from each sweep through the 7 transducers in the hydrophone array is displayed. The computer "beeps" each time a new maximum signal is received. Positioning of the B-scanner's transducer continues until no further maxima are indicated by the data acquisition system.

Immediately after the examination, and before any of the B-scanner's controls are altered, a reference acoustic power is measured. The transducer and hydrophone are placed in a water tank. The signal with the peak RF pressure is recorded with the transducer and hydrophone the same distance apart as in the in-vivo case. We can then compute in-vivo and calibration values for I_{SPTP}, I_{SPTA} and I_{SPPA} as defined in the AIUM specification [4]:

$$I_{SPTP} = \frac{V^2_{max}}{K^2} \tag{1}$$

$$I_{SPTA} = \frac{1}{K^2(t_2 - t_1)} \int_{t_1}^{t_2} V^2(t)\, dt \tag{2}$$

$$I_{SPPA} = \frac{I_{SPTA}}{D} \tag{3}$$

where V(t) is the hydrophone voltage, and K is its calibration constant; V_{max} is the peak of the waveform; t_1 and t_2 are the arrival times of two successive pulses; and D is the duty cycle of the ultrasound signal.

The in-vivo and calibration pressure waveforms are stored for every study. Spectral analysis is performed on the signals for further characterization of the tissue.

III. RESULTS

To date, this system has been used to examine 35 non-pregnant women and 7 pregnant women who are undergoing spontaneous abortion. This model has been approved by the University of Cincinnati Institutional Review Board. Informed consent was obtained from all patients. The data was obtained using a standard commercial 3.0 MHz ultrasound system.

Figures 3 and 4 show the in-vivo and calibration pressure waveforms. As expected, the in-vivo pressure is substantially smaller. Also, the pulse is spread

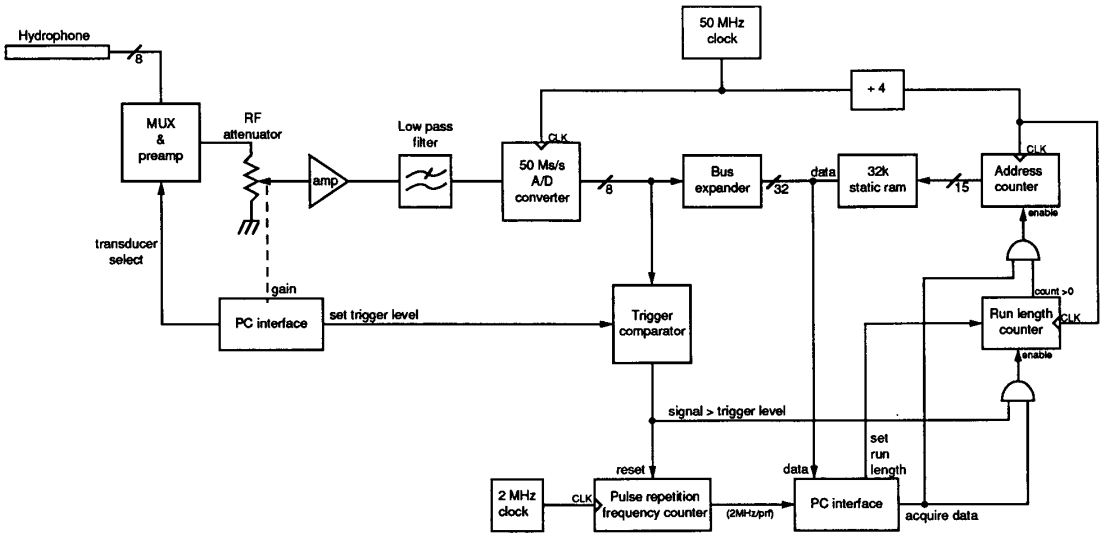


Figure 1: Block diagram of experiment

Figure 2: In-vivo hydrophone

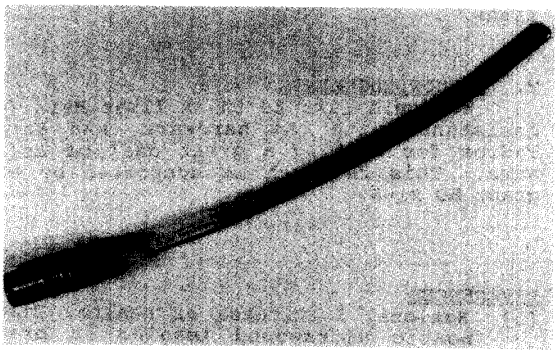


Figure 3: In-vivo pressure waveform

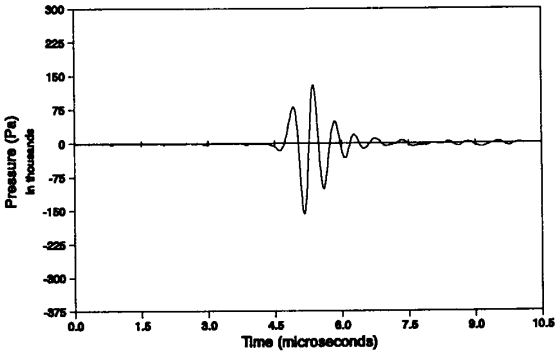


Figure 4: Calibration pressure waveform

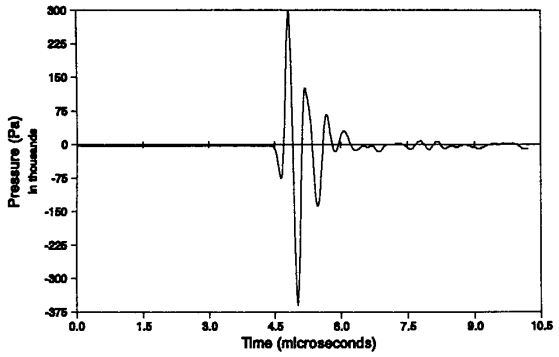
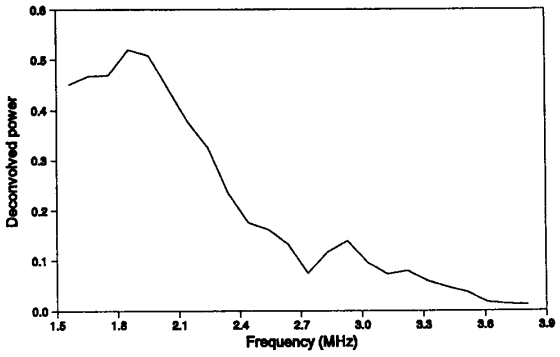


Figure 5: Deconvolution of power spectra



out in time, compared with the calibration signal. Figure 5 shows this quantitatively. The ratio of the power spectra of the in-vivo and calibration signals is plotted. This deconvolved signal is an indication of the rate of increase of attenuation with increasing frequency in the tissue. We plan to calculate this parameter once a statistically significant number of patients have been scanned; correlations with physiological state should also be interesting.

From the data of Figures 3 and 4, the following parameters in W cm^{-2} were computed.

	IN-VIVO	CALIBRATION
I_{SPTA}	1.8×10^{-3}	6.7×10^{-3}
I_{SPPA}	0.24	1.3
I_{SPTP}	1.7	8.8

Of particular interest is the tissue attenuation in dB cm^{-1}. This patient was measured to have a 9.5 cm total path length from transducer to hydrophone. Of this, 6.2 cm was bladder, which is assumed to negligibly attenuate the ultrasound. By considering the differences in I_{SPPA}, the attenuation becomes

$$\frac{10 \log_{10} \frac{1.3}{0.24}}{9.5 - 6.2} = (2.2 \pm 0.4) \text{ dB cm}^{-1}$$

The nature of the experiments make some sources of error difficult to quantify. The inability of maintaining the transducer and receiving hydrophone in the same plane for more than a few seconds was anticipated. Recording the sound field at seven positions, and performing all data analysis on the strongest signal received during the study will minimize this problem. The calibration of the hydrophones has an uncertainty of ±20%. Since the above measurement is of a ratio, this error cancels out.

In the ovarian studies, it is impossible to place the hydrophone within the ovarian substance, or even in immediate contact. Therefore, the actual energy received by the ovary is expected to be slightly higher than our data. In the embryo and fetal studies, the hydrophone will be in physical contact with the products of conception at the mid-uterine cavity level.

IV. CONCLUSIONS

We have demonstrated a method for in-vivo pressure measurements during obstetric ultrasound examinations. The instrument provides absolute pressure readings for the RF signal at or near the site of possible bioeffects. Our preliminary patient data look very reproducible and reliable. We anticipate enrolling 75 patients in the ovarian and embryonic studies, and 20 patients for the fetal study, who will provide a statistically significant database. From these data, means, medians, standard deviations, and ranges will be calculated. We will then be in a position to correlate the measurements with published bioeffects. In the ovarian study, the data will be used to determine whether the ultrasonic exposure could lead to ovarian follicular disruption, chromosomal damage, or increased wastage of ova. The embryonic and fetal data will be compared with, e.g., animal data to determine whether the in-vivo dose produces long-term effects.

The data will also be interesting from the point of view of tissue characterization. In-vivo measurements of tissue attenuation (and its frequency dependence) have been the focus of a good deal of research (e.g., Lizzi et al. [5]). Our method is very simple, since the attenuation is measured in transmission rather than reflection. It will be instructive to observe variations in the shape of the deconvolved spectrum for patients in different conditions.

V. ACKNOWLEDGEMENTS

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