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OBSERVATIONS OF FINITE-AMPLITUDE DISTORTION IN TISSUE

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INTRODUCTION

The severe finite-amplitude distortion which occurs in ultrasonic pulses generated by medical pulse-echo imaging systems following transmission through water is now well recognised (Bacon, 1984; Duck and Starritt, 1984). The extent to which similar ultrasonic pulses may be distorted during clinical scanning procedures following transmission through a variety of tissue layers is more complex, and less well investigated. This paper draws together results of recent experiments in which we have investigated finite-amplitude transmission through tissue, both in-vivo and in-vitro.

The importance of tissue non-linearity in the transmission of ultrasound has been recognised by a number of authors. Goss and Fry (1981) reported measurements showing the dependence of absorption on intensity, particularly at temporal average intensities above 100 W cm^{-2}, at 1.11 MHz in a variety of mouse tissues. This was attributed to the generation of harmonics within the tissue or coupling medium, harmonics which suffered greater absorption because of the frequency dependent absorption coefficient of the tissues. Swindell (1985) has predicted theoretically that in focused fields such increased absorption will result in excess tissue heating with enhancement ratios of up to 2 at 1 MHz. Haran and Cook (1983), in another theoretical paper, take account of the frequency-dependent attenuation of tissue and predict that in unfocused fields using pressure levels encountered clinically, acoustic shocks may occur in body fluids, but not in liver tissue. We have demonstrated using clinical pulse- echo equipment, that there is measurable harmonic generation following transmission of a pulse (nominal frequency 2.5 MHz) through human calf muscle in-vivo (Starritt et. al., 1985) and more recently, using the same pulsed field, that second and third harmonics reaching 10.5 dB and 19 dB below the fundamental may be observed in the focal region following transmission through ox liver in vitro (Starritt et. al., 1986).

Some results from these experiments will be collated below, together with further data from measurements made at a nominal transducer frequency of 3.5 MHz through ox liver.

EXPERIMENTAL DETAILS

Broadly the experimental details for both human calf, and ox-liver experiments were the same. Ultrasonic pulses were generated by a standard pulse echo transducer, immersed in a water bath. The 2.5 MHz transducer was 20 mm in diameter, focused in water at 58 mm. For the results given here the peak positive pressure at the transducer, P_0, was 580 kPa. The measured zero crossing frequency was 2.2 MHz. The 3.5 MHz transducer was 13 mm in diameter, focused in water at 53 mm, and had a zero crossing frequency of

3.3 MHz. It was driven at two powers giving maximum pressures at the transducer of 1.1 MPa and 350 kPa. In this paper, transducers and fields are referred to by nominal frequency rather than zero- crossing frequency. The transmitted pulse was received on a calibrated PVdF bilaminar membrane hydrophone 2 x 25 μm thick, 1.0 mm sensitive area, positioned using a micro-manipulator. The signal was fed through a broad-band head amplifier to an oscilloscope, and RF spectrum analyser. The ox-liver samples were contained in plastic bags and covered with a small volume of saline. All liver measurements were made at 21 ± 1 °C. The sample bag (or leg) was placed in contact with the transducer and the hydrophone advanced axially to be in contact with the sample. Amplitudes were read directly from the oscilloscope and spectrum analyser screens. Some pulses were recorded on film for subsequent digitisation and analysis.

RESULTS

The pulse waveforms observed through tissue thicknesses greater than about 2 cm in general exhibited some finite-amplitude distortion. One example is shown in Figure 1 where the measurement was in the high-amplitude 3.5 MHz field at 5.0 cm depth. The assymetry which is observed in pulses transmitted through water appears less obvious here but the tendency to form a triangular shaped wave is clear. Here, as with all observations, it was noted that both the zero crossing frequency and peak spectral frequency had reduced following passage through tissue. The variation of peak positive pressure with distance for the 2.5 MHz field is shown in Figure 2 where all measurements through ox-liver are compared with the axial variation in water under identical conditions. It is seen that pressures up to 2 MPa were observed in the focal region in comparison with peak positive and negative pressures in water of 6.8 and 2.1 MPa respectively. Furthermore the peak pressures were reached in liver closer to the transducer than in water.

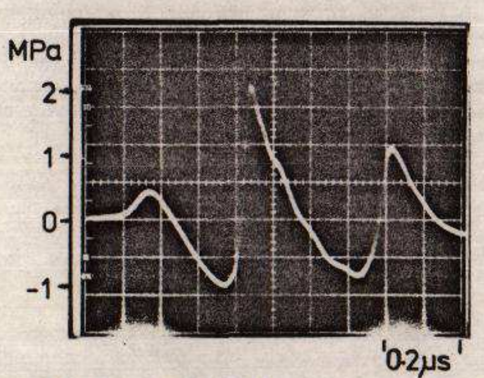

Figure 1 Pulse waveform following transmission through 5.0 cm ox-liver in-vitro. Nominal transducer frequency 3.5 MHz focused, pressure at transducer 1.1 MPa.

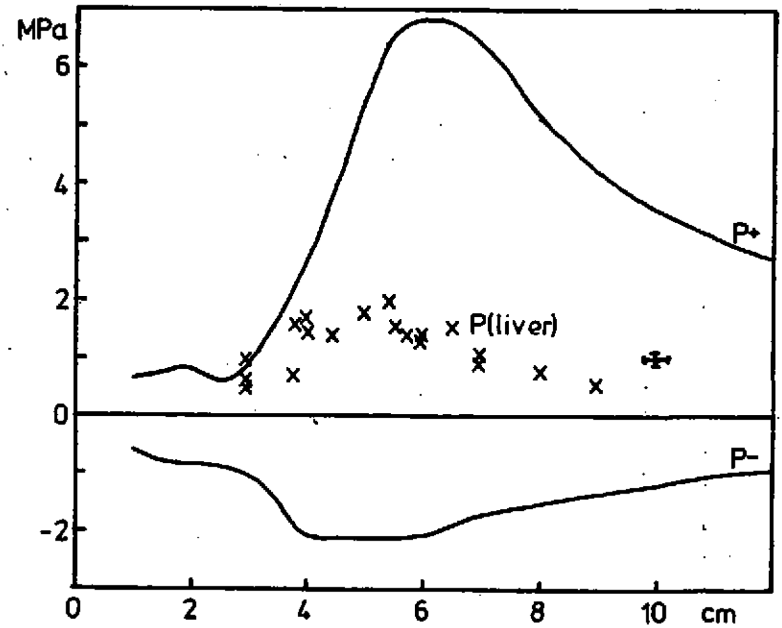

Figure 2 Axial pressure variation in water for the 2.5 MHz focused transducer; positive (p+) and negative (p-) peak values. Superimposed are measured peak pressures for transmission through ox-liver. Pressure at transducer, 0.58 MPa

Figure 3 shows the magnitude of the second harmonic peak with respect to the fundamental peak as measured from the pulse spectrum, for all measurements at 2.5 MHz. This includes all measurements from ox-liver together with all those from the leg muscle. There was no overlap in tissue thickness in these two groups. It can be seen that the relative second harmonic content, f_2/f_1, increased to a maximum detected of -10.5 dB at about 6 cm following which it decreased. There was no measurable difference in the amount of second harmonic content in the region of overlap between liver and muscle measurements. It would appear that differences in B/A and attenuation may not result in substantial differences in the non-linear response of tissue. (The values plotted for leg muscle are from Starritt et. al. (1985) corrected for the spectrum analyser response which had resulted in a systematic error of about -1.5 dB).

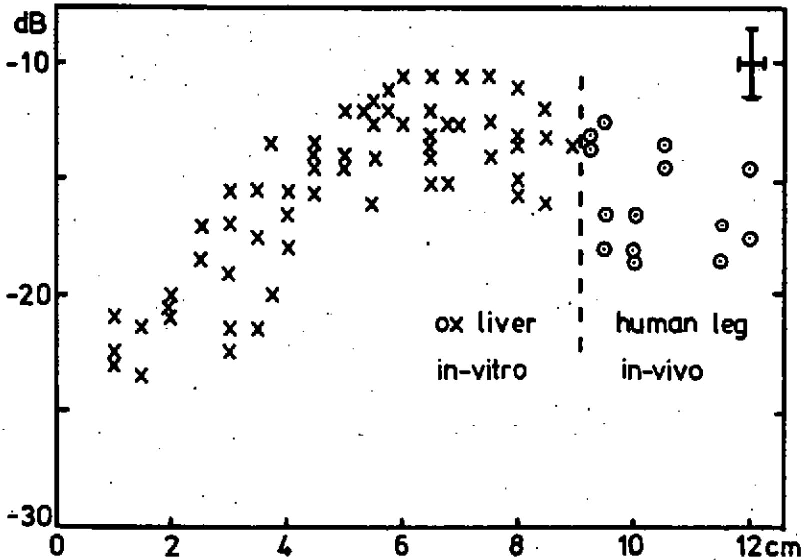

Figure 3 Variation with distance of peak second harmonic referred to the fundamental (f_2/f_1) for all 2.5 MHz measurements in both ox-liver (in-vitro) and human leg muscle. P_o = 0.58 MPa

The measurements at 3.5 MHz were carried out at two different input pressures, 1.1 MPa and 0.35 MPa, and the transmission through ox-liver only was investigated. The relative magnitude of the second harmonic peak is shown in figure 4 for all measurements, at each of the two input pressures. For the higher power, f_2/f_1 reached a maximum of -8.5 dB and for P_o = 0.35 MPa, maximum f_2/f_1 = -14 dB. Again, as with the results at 2.5 MHz there is a considerable spread in the measurements. However they suggest that there are circumstances where the second harmonic amplitude may reach 37% of that of the fundamental. A recent survey of the pressures generated by commercial ultrasonic imaging equipment (Duck et. al., 1985) has shown that pressures at the transducer in excess of 1 MPa occur at the upper end of the range of powers used. The value of P_o = 0.35 MPa is lower than the mean value for all equipment in the survey (0.53 MPa).

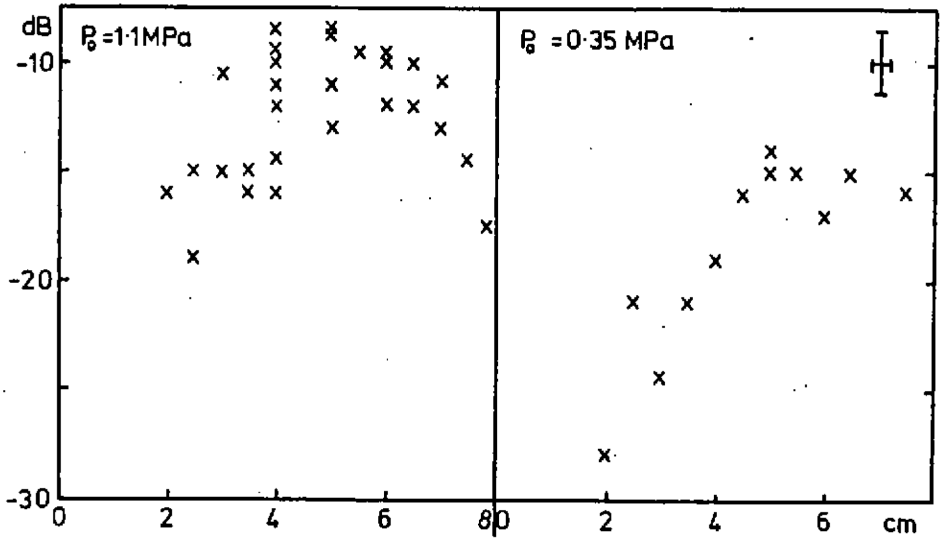

Figure 4 Variation with distance of peak second harmonic referred to the fundamental (f_2/f_1) for the 3.5 MHz pulse in ox-liver; P_o = 1.1 MPa and P_o = 0.35 MPa

A restricted series of measured 3.5 MHz pulses were digitised by hand and the magnitude and relative phase of the harmonic content in the largest full cycle calculated. These values for the second and third harmonics are given in table 1. The second harmonic content is seen to have a maximum value of -6.6 dB with respect to the fundamental at 5 cm, and that of the third harmonic -11.1 dB. The relative phase over the range of measurement shows a phase lag for both harmonic components.

CONCLUSION

It has been demonstrated that finite-amplitude distortion of pulses can occur in tissue at the levels of pressure used in medical imaging applications. Measurements have shown second harmonic content in a focused 3.5 MHz pulse 8.5 dB below the fundamental, following transmission through ox-liver in vitro. The analysis of the single cycle of greatest magnitude showed second harmonic content of 6.6 dB below the fundamental. Even at pressure levels lower than the average of those found in a recent survey of imaging equipment, second harmonic levels of -14 dB were observed. There

Thickness of Liver ±0.1 cm	f_2/f_1 dB	ϕ_2 $\pm 1^\circ$	f_3/f_1 dB	ϕ_3 $\pm 2^\circ$
3.0	-8.0	-11°	-14.1	-33°
4.0	-7.3	-21°	-12.2	-41°
5.0	-6.6	-27°	-11.1	-57°
5.5	-7.9	-25°	-13.6	-60°
6.0	-7.8	-28°	-14.8	-58°
7.0	-8.1	-21°	-15.6	-44°

Table 1 Magnitudes and phases of second and third harmonic components from the largest full cycle of a 3.5 MHz pulse following transmission through various thicknesses of freshly excised ox-liver at 22°C. Focused field P_o = 1.1 MPa, focal length in water 5.3 cm.

was no substantial difference between the measurements made in muscle in-vivo, compared with liver in-vitro for given ultrasonic field parameters. It is concluded that finite-amplitude distortion of pulses may commonly occur in clinical imaging procedures.

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