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ULTRASONICALLY INDUCED TEMPERATURE ELEVATION IN MOUSE OVARY.

This communication was first received as a manuscript on August 22nd 1983 and in the form of a Letter to the Editor on 23rd March 1984.

Sir:

ABSTRACT

Temperature increases, resulting from exposure to 1 MHz ultrasound, were measured in in situ and in exteriorized mouse ovaries. It is concluded that temperature increases from exposure to 10 W/cm^2 and less are probably not significant for producing ovarian tissue damage, but that 25 W/cm^2 exposures, and greater, are of such magnitude that damaging thermal levels ensue. The significance of blood flow in removing ultrasonically generated heat has been observed quantitatively.

A. INTRODUCTION

An earlier study (O'Brien et al., 1979) showed that morphological changes were produced in mouse testicular tissue exposed *in vivo* to a CW ultrasonic intensity of 25 W/cm^2 for 30 sec at 1 MHz. Based on these results, and the fact that human ovarian tissue has the opportunity for receiving ultrasonic radiation from a multitude of clinical exposure procedures and as it occupies a central role relative to fertility and maintenance of pregnancy, an investigation of the effects of ultrasound on the mouse ovary was undertaken. This study (Bailey et al., 1983) showed that relatively short exposures of 15 to 60 sec to 1 MHz CW ultrasound at intensities of 25 W/cm^2 and greater can be highly destructive to the ovary and to surrounding structures, while longer exposures at lesser intensities, e.g., 5 W/cm^2 at 300 sec, produce more subtle effects.

While such morphological effects are now being characterized at the light microscopy level, the responsible physical mechanism(s) remain unidentified and must be uncovered before a full understanding of all events which occur during ultrasound-ovarian interaction can be achieved. It is well known that the acoustic absorption coefficient of biological media is relatively large in the ultrasonic frequency range and leads to significant temperature increases upon exposure to ultrasound of appreciable intensities. Therefore, an investigation of thermal events extant during this ovary-exposure study was conducted and this note is a reporting of the early findings.

B. METHODS

Hap (ICR):BR female mice of age 5 months were anesthetized with methoxyflurane, shaved on the back and sides, depilated, and bathed in a mild detergent to effect wetting by the aqueous coupling medium. The animals were then mounted in a holder especially designed in this

laboratory (Fry et. al., 1978) with the muzzle protruding above the surface of the coupling medium when the assembly was placed in the irradiation tank. Since the ovaries in the mouse lie below the rib cage and approximately 1 to 3 mm below the skin surface, irradiation from the specimen's back allows unimpeded access by the ultrasonic beam.

An incision was made over the right ovary, followed by location and exteriorization of the ovary but without severing it from the oviduct. A copper-constantan needle thermocouple, employed with a Bailey monitor (Bailey Instruments), was inserted through the center of the ovary and the ovary was replaced at the edge of the incision. The physiological saline solution used as the coupling medium was maintained at $37^{o}C$. The transducer was energized and temperature recordings were made at time 0, 15 sec, 30 sec, 1 minute, and at each minute thereafter until temperature stabilization occurred, at 5 to 6 minutes. Spatial peak intensities employed were 5, 10, 25, and 50 W/cm^2.

Following exposure of the right ovary, the entire assembly was removed from the tank and the left ovary was prepared for treatment in situ, i.e., it was left in place in the body cavity with the needle thermocouple inserted through its center. The assembly was replaced in the tank, the transducer was energized, and temperature recordings were made as previously described.

A single animal was used at each intensity and, except for the vascular flow cessation observation, each animal was sacrificed by cervical dislocation following exposure.

C. RESULTS

The exteriorized ovaries (right) developed equilibrated temperature rises of $0.7^{o}C$, $1.8^{o}C$, and $4.9^{o}C$, at, respectively, exposure intensities of 5, 10, and 25 W/cm^2 (see Fig. 1). For these three intensities the temperature stabilized at approximately 1 min of exposure and remained

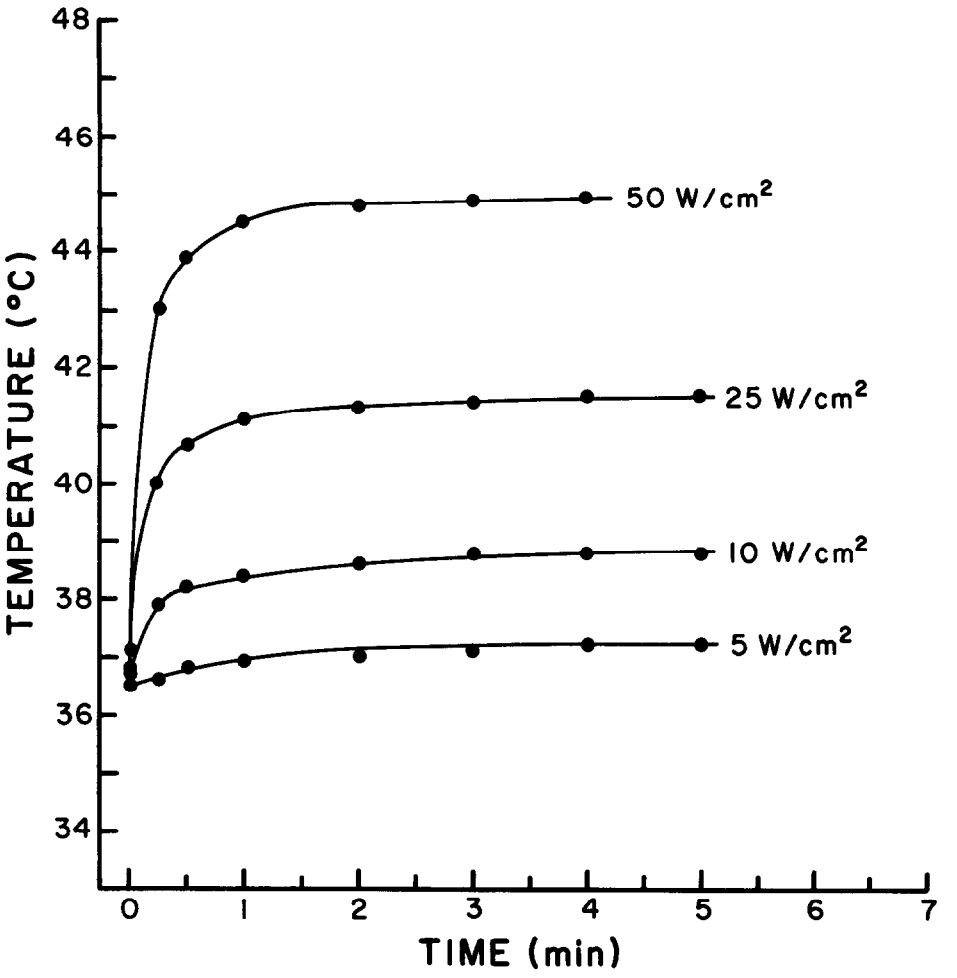

Figure 1: Temperature rise produced in exteriorized mouse ovary by 1 MHz ultrasound.

until placed in the tank, so that the zero time temperature was 34.2°C and the temperature reached equilibrium after 5 minutes, having increased 3.5°C. The remaining three animals were maintained alive during the exposure procedure. The temperature rise for the 10 W/cm^2 exposure was 2.2°C, with equilibrium established at 3 minutes. For the 25 W/cm^2

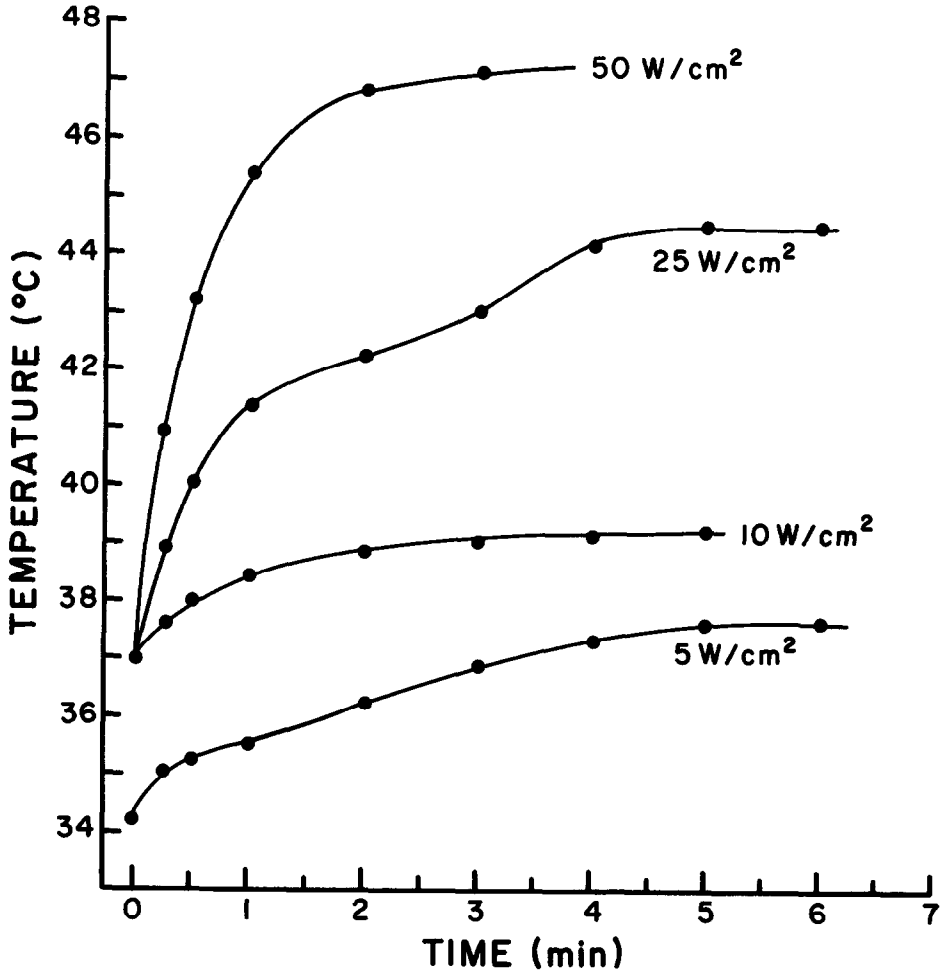

Figure 2: Temperature rise produced in mouse ovary *in situ* by 1 MHz ultrasound. (Note that the animal exposed to 5 W/cm^2 ultrasound had its blood flow terminated prior to exposure and did not have a functioning vascular system.)

essentially constant thereafter. For the 50 W/cm^2 exposure, a 7.8°C temperature increase occurred and equilibrium was reached within 2 to 3 min of exposure.

The temperature profile differed for the *in situ* ovary (left) with regard to both the temperature increase and the length of time required for temperature equilibrium to take place (see Fig. 2).

The animal exposed to 5 W/cm^2 had its blood flow terminated prior to exposure. It was at room temperature exposure the temperature rise was 7.5°C, with temperature equilibrium occurring at 5 minutes. The 50 W/cm^2 exposure established temperature equilibrium at approximately 3 minutes; the temperature increase at that time being 10.2°C.

D. DISCUSSION

Results of the preliminary temperature study yield two points of major interest.

First, the temperature increases at the lower intensities, viz., 10 W/cm^2 and below, are probably not a significant factor in causing thermal damage to ovarian tissue. However, the temperature increases at 25 W/cm^2 and above are of such magnitude that significant heat and damaging thermal effects may ensue.

Second, the significance of blood flow and the presence of other fluids (depending upon ovarian physiological state) in removing the heat generated by ultrasound has been observed quantitatively. It is to be noted that the ovaries are exceptionally well perfused, having a relative blood flow rate of between two and seven times that of the brain, depending on species and method of measurement (Bindon, 1969; Ellenwood, et al., 1978). The exteriorized ovaries, which were bathed in a constant temperature 37°C fluid, exhibited lesser temperature increases and faster temperature stabilization than those ovaries exposed within the body cavity at normal placement, where heat could only be removed by the intact vascular system. Further, the 5 W/cm^2 *in situ* exposed animal, which had its blood flow terminated prior to

exposure and which thus had no perfusion available for removing heat, experienced an increase in temperature approximately 1.6 that of the 10 W/cm^2 exposed animal. The curves of Fig. 2 suggest that vascular flow has the effect of reducing the effective ultrasonic absorption coefficient to approximately one-third to one-half that observed for the *in vitro* cases.

E. ACKNOWLEDGEMENT

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Yours etc.,

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ULTRASONIC STYLETS FOR NEEDLES AND CATHETERS

Sir:

Ultrasonic techniques are well-suited to the guidance of needles and catheters since the procedure can be observed in real-time. Since ultrasonic imaging is often the best way of visualising a needle being inserted into the body, it would appear worthwhile to develop the technology further to make identification of the needle tip easy. At present, difficulties can be experienced in visualising needle tips with certainty. These difficulties may be due to the technique employed, the types of tissues surrounding the needle, tissue movement or the limited time available for the procedure. If there are problems concerning sterility or if flexibility is required in placing the needle and the scanner separately on the patient a technique is often employed in which the needle is not physically linked to the ultrasonic scanner. This technique increases the difficulties of identifying the needle tip.