Temperature Changes Produced in Tissue during Ultrasonic Irradiation*†

WILLIAM J. FRY AND RUTH BAUMANN FRY
Department of Electrical Engineering, University of Illinois, Urbana, Illinois
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This paper is concerned with the technique of temperature measurement in living tissue during irradiation by high intensity ultrasound. The interpretation of data obtained by the use of thermocouples is presented. The specific biological object used in this study is the spinal cord of rat exposed by laminectomy. This particular preparation serves to illustrate the relative importance of the heat conduction process in contributing to the temperature change as a function of the proximity of the imbedded thermocouple to bone and the time elapsed after initiation of the exposure.

The ultrasonic frequency used in these studies was 980 kc. The sound intensities incident on the cord were between 60 and 80 watts/cm^2.

The experimental results presented in the paper are used to obtain values for the acoustic absorption coefficient of the tissue of the spinal cord. The range of values obtained for the intensity absorption coefficient per centimeter from measurements made on six adult rats at various positions in the spinal cord is 0.19 to 0.23 if the heat capacity of the tissue at constant pressure is 1.00 calorie/cm^3.

1. INTRODUCTION

IN an investigation concerned with the mechanism of action of intense ultrasound on tissue, the possible role of temperature changes caused by the ultrasound must be considered. In our previously reported work on the physical factors involved in the action of ultrasound on nerve tissue the temperature factor has been examined in a number of different ways[1,2] and has been shown not to enter into the mechanism. This analysis is reviewed in an accompanying paper.[3]

This paper is concerned with the technique of temperature measurement in living tissue under acoustic irradiation and with the interpretation of the experimental results.

The determination of temperatures in tissue during ultrasonic irradiation has received the attention of other investigators.[4,5]

The measurement of the temperature changes in the spinal cord of rats by thermocouples during ultrasonic irradiation is considered herein. We will be concerned with the relation between the temperature change indicated by a thermocouple imbedded in the tissue and the temperature rise of the tissue with the thermocouple absent. Experimental measurements on the rat cord will be presented which illustrate the influence of acoustic absorption in the bone on the temperature changes in the tissue in the immediate neighborhood. In particular, the temperature changes which occur in the cord in regions not immediately adjacent to bone are contrasted with changes which occur in the tissue in the immediate neighborhood of the bone. From the experimental determinations of the dependence of the temperature on time under accurately controlled conditions of irradiation, acoustic absorption coefficients for the tissues can be obtained.

In addition, the relation between the temperature of the saline bath which acts as the transmitting medium for the sound passing from the transducer to the tissue and the temperature near the ventral surface of the spinal cord is investigated.

2. EXPERIMENTAL METHODS

Instrumentation

The ultrasonic irradiation experiments were performed with apparatus which permits accurate control of the absolute sound level and precise location of the sound beam with respect to the region to be irradiated.

The transducer consists of an X cut quartz crystal mounted in a housing which supports a lens for focusing of the sound. The ultrasonic beam leaves the housing by passing through a thin polyethelene diaphragm. Boiled water is used as the coupling medium between the crystal, lens, and diaphragm. The transducer was operated at the resonant frequency of the crystal, 980 kc. The beam focuses at a distance of 6.4 cm from the diaphragm face. The sound intensity is down to 0.7 of the peak value at a lateral distance of 1.3 mm from the beam axis. The sound intensity in the direction of the beam axis varies by approximately 2 percent over a length of $\frac{1}{2}$ centimeter centered at the focal spot.

The transducer is driven by an rf amplifier excited by a signal generator. An electronic switch is inserted between the signal generator and the amplifier for controlling the duration of the acoustic pulse. The envelope of the rf, which is applied to the crystal, is a square wave with a rise time of about 0.01 sec. The duration of the acoustic pulse could be varied in steps of 0.1 second.

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[1] Fry, Wulff, Tucker, and Fry, J. Acoust. Soc. Am. 22, 867 (1950).

[2] Fry, Tucker, Fry, and Wulff, J. Acoust. Soc. Am. 23, 364 (1951).

[3] W. J. Fry, J. Acoust. Soc. Am. 25, 1 (1953).

[4] Anderson, Wakim, Herrick, Bennett, and Krusen, Arch. Phys. Med. 32, 71 (1951).

[5] J. F. Herrick, J. Acoust. Soc. Am. 25, 12 (1953).

The transducer is mounted in a supporting device which enables the operator to move it in the directions of three rectangular coordinates. The animal is held in a fixed position for an experiment, and the sound beam is moved about in any desired pattern. The ultrasound is transmitted to the tissue of the animal through boiled physiological salt solution. The beam passes through the polyethelene diaphragm directly to the salt solution which is in contact with the tissue.

The transducer is calibrated by the radiation pressure method described by Fox and Griffing.[6] The steel ball used in calibrating is 0.062 inch in diameter. Correction is made for the nonuniformity of the sound beam over the surface of the ball. Day to day check on the calibration is accomplished with a small, stable thermocouple probe which has been developed recently at this laboratory. A paper describing this probe and its characteristics is currently in preparation.

The copper-constantan thermocouples used to determine the temperature changes in the spinal cords of rats were connected to a galvanometer of a magnetic oscillograph. The galvanometer used in these experiments responds to a step function signal by deflecting to $1-1/e$ of its maximum deflection in about 0.02 of a second. The magnetic oscillograph is designed for both direct visual observation of deflections and for recording.

Experimental Procedure

A rat weighing between 250 and 300 grams is anesthetized by an intraperitoneal injection of dial with urethane. It is then placed in a holder which supports the body by means of a sponge rubber cushion. A fixed position is maintained by ear bars, mouth piece, and pelvic strap. A length, approximately 1.5 cm of the spinal cord in the region of the lumbar enlargement, is exposed by laminectomy. The cross-sectional dimensions of the cord in this region are approximately 3.5 mm laterally and 3 mm in the dorsal-ventral direction. The skin is then fastened with a tourniquet to a cup-shaped funnel for holding degassed saline which acts as a transmitting medium for sound from the transducer. A 0.003 inch diameter copper-constantan thermocouple with a soldered, lapjoint junction between 0.005 and 0.010 inch in length is readily directed into the cord at right angles to its length without removing the dura. The thermocouple is made so that the constantan wire extends a few thousandths of an inch beyond the junction. The end is sharpened before assembly of the thermocouple. The depth of the junction in the spinal cord is predetermined by bending the wires at right angles the distance desired above the junction. The thermocouple position is secured by threading it through the muscle of the back—copper through the muscle on one side, constantan through the muscle on the other. The wires are then supported from the funnel. In order to prevent any electrical contact between the thermocouple wires at any point other than the junction, enameled copper wire is used. The enamel coating can readily be preserved immediately adjacent to the solder.

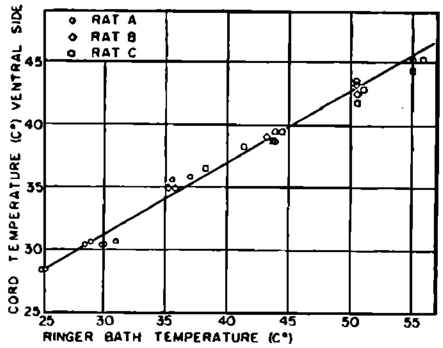

FIG. 1. Relation between temperature of bath in contact with dorsal surface of rat cord and cord temperature near ventral surface.

The procedure just outlined for insertion of the thermocouple was followed on all rats with one exception. On this rat the thermocouple was drawn through the cord transversely. The end of the constantan wire opposite from the junction was sharpened in order to facilitate penetration of the dura. The position of the junction in the cord was determined after the temperature measurements were made. The cord was fixed in the animal, the thermocouple wires were cut near the surface, and a length of cord containing the thermocouple was excised and dehydrated. Position measurements could then be taken under a microscope.

Since the position of the ultrasonic beam is known with respect to the transducer housing, it can be brought into line with the cord and positioned over the thermocouple. From the coordinate positions, longitudinal and transverse, a rectangular array of points one millimeter apart is determined for the irradiation pattern. By irradiating at these positions the exact position of the thermocouple in the cord can be found by recording the deflection of the galvanometer of the magnetic oscillograph at the end of each sound pulse. Sufficient time, of the order of one minute at peak deflection for a one-second pulse, is allowed between irradiation periods for the temperature of the cord, as measured by the thermocouple, to return to its initial value. The temperature of the saline in contact with the cord affects the temperature distribution within the cord. Because of this, a temperature for the saline is chosen and kept relatively constant during the experiment.

3. EXPERIMENTAL MEASUREMENTS AND INTERPRETATION

The temperature of the saline bath which transmits the sound from the transducer to the exposed spinal cord is important in determining the temperature distribution within the cord. Therefore, thermocouple measurements were made of the temperature near the ventral surface of the cord with the dorsal surface

[6] F. E. Fox and V. Griffing, J. Acoust. Soc. Am. 21, 352 (1949).

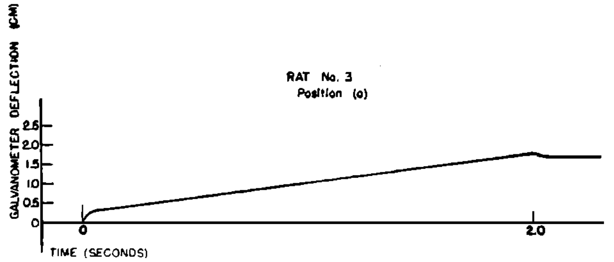

FIG. 2. Rat No. (3) position (a). Trace of a recording of galvanometer deflection as a function of time for a two-second pulse of radiation at an incident intensity of 67 watts/cm². Thermocouple junction is imbedded in the spinal cord of the rat.

exposed to saline baths at various temperatures. Figure 1 shows the relationship between the cord temperature, ventral side at equilibrium, and the temperature of the bath. Data were taken on three rats designated A, B, and C on the graph. As can be seen from the graph, a linear relationship obtains over the range of bath temperatures from 25° to 55°C. That portion of the graph covering the range of bath temperatures less than the normal temperature of the rat can be used in conjunction with data on the temperature changes produced by ultrasonic irradiation of the tissue to obtain an upper limit for the temperature reached in the tissue under exposure to acoustic radiation.

In order to compute acoustic absorption coefficients, as discussed later, from the temperature data presented in this paper, it is necessary to know the acoustic intensity at the thermocouple junction. The intensity of the acoustic disturbance at the junction is reduced from the intensity incident on the cord by absorption in the material interposed between the surface at which the sound enters the cord and the junction. In order to determine the possible importance of reflection at a nerve tissue-saline boundary in reducing the intensity, a piece of rat cortex of average thickness 2.5 mm was inserted in the beam of the focusing irradiator between the transducer and a probe. Relative intensities of the sound at the probe were determined with the piece of

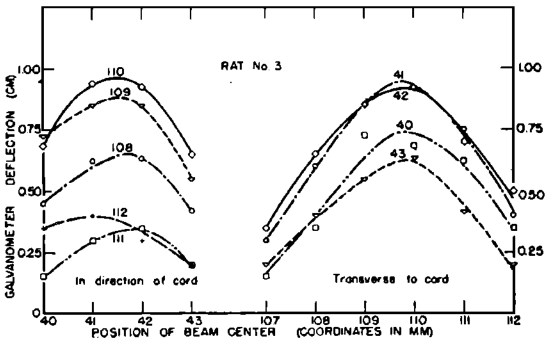

FIG. 3. Rat No. (3) position (a). Deflection of galvanometer at termination of a 1.0-second acoustic pulse as a function of the relative position of thermocouple junction and beam center. The thermocouple is in a fixed position in the cord. The transducer is mounted in a movable support.

cortex absent and with the cortex placed at various angles with respect to the direction of the incident radiation. Within the accuracy of the experimental measurements, the absorption in the tissue accounted for the decreased intensity at the probe. Reflection of the sound at the cord-saline boundary is, therefore, neglected in the computation of absorption coefficients in this paper.

The temperature changes produced in the spinal cord of an adult rat during acoustic irradiation and made manifest by a thermocouple inserted into the cord will now be considered. We present first the situation in which the amount of heat entering by conduction from bone into the region of the cord in which the thermocouple is placed is not significant during the time required for the temperature of the tissue to rise to a maximum when it is subjected to a pulse of acoustic radiation. This condition is satisfied for most positions of the thermocouple in the cord for the pulse durations of interest in this study. Figure 2 illustrates the type of relation observed experimentally between time in seconds and galvanometer deflection in centimeters, when the region of the cord containing the thermocouple is subjected to a 2.0-sec pulse of acoustic radiation at an intensity of about 67 watts/cm² incident on the cord. The galvanometer is in series connection with the thermocouple, whose junction is located at a depth of about 2 mm in the cord which places it near the ventral surface. It is situated extremely laterally to the right of the mid-line.

The curve of Fig. 2 indicates that the temperature change at the thermocouple undergoes at first a relatively rapid change which begins simultaneously with the incidence of the radiation. A second relatively slow phase then ensues, and this exhibits an almost linear characteristic for the duration of the 2.0-sec acoustic pulse. Immediately upon cessation of the radiation, a rapid decrease in temperature occurs. This is followed by a slow monotonic return of the temperature to its initial value. The duration of the fast initial phase and the fast phase at the termination of the period of irradiation is of the order of the time required by the galvanometer of the oscillograph to respond with essentially full deflection to step function excitation. This initial rise and corresponding rapid fall in temperature at the thermocouple are caused by the conversion of acoustic energy into heat by action of the viscous forces between thermocouple and tissue. A detailed analysis of the mechanism will appear in the paper on thermocouple probes which is in preparation. This initial rapid rise in temperature whose magnitude is proportional to the acoustic intensity would, of course, not be present in the tissue if the thermocouple were absent. The second, or linear, phase of the curve in the figure represents the only temperature change which would occur if the thermocouple were absent. If the thermocouple wires are sufficiently small in diameter, the slope of the line $(dT/dt)_0$ is then simply related to the acoustic absorp-

TABLE I.[a] Adult rat cord cross-section dimensions (lumbar). Lateral diameter—approx. 3.5 mm. Dorsal-ventral diameter—approx. 3 mm.

Rat No.	Thermocouple position in cord	I (watts/cm²)	$\left(\frac{dT}{dt}\right)_0$ deg. C/sec	ΔT(1.0 sec) deg. C	ΔT(2.0 sec) deg. C	μ 1/cm
1	Lateral—1 mm Depth—2½ mm	65	3.3	3.2	6.4	0.22
2	Lateral (adjacent to center blood vessel) Depth—2 mm	64	2.8	2.4	3.7	0.19
3(a)	Lateral (close to lateral surface)	67	3.1	3.0	6.3	0.20
3(b)	Lateral (adjacent to center blood vessel) Depth—2 mm	64	3.4	2.9	4.5	0.23
4	Lateral (⅓ length of lateral diameter from surface) Depth (on lateral diameter)	63	3.4	3.3	6.5	0.23
5	Lateral—1 mm Depth—2 mm	61	2.9	2.9	5.5	0.21
6	Lateral (adjacent to center blood vessel) Depth—1½ mm	78	3.4	3.4	6.8	0.19

[a] For all rats the bath temperature in contact with the cord was within the range 28° to 30.5°C.

tion coefficient of the tissue.

$$\left(\frac{dT}{dt}\right)_0=\frac{\mu I}{\rho C_p K}, \tag{1}$$

where μ is the intensity absorption coefficient per unit path length, ρ is the density of the tissue, C_p is its heat capacity per unit mass, I is the acoustic intensity and K is the mechanical equivalent of heat. The initial time rate of change of temperature from the linear portion of the record is 3.0°C/sec. The calculated value of μ using formula (1) is 0.19 per centimeter. In computing this value and all subsequent values of μ in this paper, account was taken of the reduction in intensity from the incident value caused by absorption. It is sufficiently accurate in evaluating this slight correction to the intensity to use a value of μ obtained by inserting the value of the incident intensity in formula (1). The density of the tissue of the central nervous system is two to three percent greater than that of water.[7] In the absence of a value for C_p, the heat capacity per unit mass at constant pressure, we have arbitrarily chosen the numerical value of the product ρ C_p equal to 1.00 calorie/cm³. The temperature rise in the rat cord, attained as the result of a 2.0-sec pulse of radiation at an incident intensity of about 67 watts/cm² with the thermocouple absent, is computed as the product of the galvanometer deflection (1.77−0.25=1.52 cm) and the thermocouple sensitivity (4.14°C per centimeter deflection on the galvanometer). This yields the value 6.3°C. The initial rapid decrease in temperature at cessation of the acoustic pulse is explained in terms of the same mechanism which accounts for the initial rapid rise. This record was obtained on rat (3) position (a), see Table I. The values given in the table are averages based on a number of experimental measurements.

Figure 3 shows the galvanometer deflection, observed visually, as a function of the relative position of the thermocouple junction and the axis of the focused beam. The rat (No. (3) position (a)) is in a fixed position and the transducer is moved about in a rectangular pattern. Along the horizontal axis of the graph the rectangular coordinate positions (scale readings on coordinate system which supports transducer) are designated. Each curve is plotted for a fixed value of one of the coordinates. At each position the cord is subjected to a 1.0-sec pulse of radiation of intensity about 67 watts/cm². The time between pulses is sufficient to permit the temperature distribution to return to its state preceding irradiation. The maximum deflection is obtained when the junction of the thermocouple is on the axis of the focused beam. The temperature rise in the rat cord near the ventral surface, with dorsal surface exposed and in contact with a saline bath, under a 1.0-sec pulse of acoustic radiation at an intensity of 67 watts/cm² is obtained by subtracting the fast response deflection for this intensity (0.25 cm from Fig. 2) from the maximum deflection indicated on the graph of Fig. 3 (0.97 cm) and combining the result with the value for the thermocouple sensitivity. The resulting value for the temperature rise is 3.0°C. The thermocouple used in obtaining the data just discussed was again inserted into the cord at a point on the surface close to the midline and the junction was placed at essentially the same depth. This position is designated (b) in Table I. Data

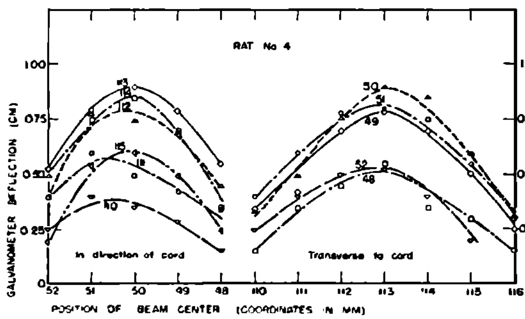

FIG. 4. Rat No. (4). Deflection of galvanometer at termination of a 1.0-second acoustic pulse as a function of the relative position of thermocouple junction and beam center. The thermocouple junction was drawn into the cord by threading the constantan wire through the cord.

[7] See, for example, G. D. Ludwig, J. Acoust. Soc. Am. 22, 862 (1950).

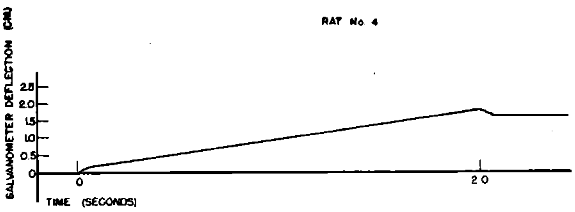

FIG. 5. Rat No. (4). Trace of a recording of galvanometer deflection as a function of time for an acoustic pulse length of 2.0 seconds.

similar to those just presented were obtained. The average temperature rise for a 1.0-sec pulse at an incident intensity of 64 watts/cm² is 2.9°C.

The temperature of the saline bath in contact with the dorsal surface of the cord was 28°C for this rat when the thermocouple was in position (a). From Fig. 1 a value of 30°C is obtained for the temperature in the cord near the ventral surface. Therefore, the maximum temperature attained in this region of the cord for a 1.0-second pulse of acoustic radiation at an incident intensity of 67 watts/cm² was about 33°C.

Temperature measurements were made in one rat cord (rat 4 of Table I) by means of a thermocouple which had been drawn into the tissue by threading the constantan wire transversely through the cord. The position of the thermocouple in the tissue was determined by following the procedure indicated above. The junction was located on the transverse diameter, i.e., half-way through the cord in the dorsal-ventral direction, approximately $\frac{1}{3}$ of the length of the diameter from the lateral surface of the cord.

Figure 4 is a graph of galvanometer deflection as a function of the relative position of the thermocouple junction and the axis of the focused beam for this arrangement. Figure 5 is a trace of a record of the galvanometer deflection for a two-second pulse with the junction centered on the beam axis. The peak deflection in Fig. 4 is 0.90 cm. The rapid response deflection obtained from Fig. 5 is 0.10 cm. Therefore, the galvanometer deflection associated with the temperature change resulting from acoustic absorption in the tissue (thermocouple absent) for a one-second pulse of sound at an incident intensity of 63 watts/cm² is 0.80 cm. This value multiplied by the thermocouple sensitivity

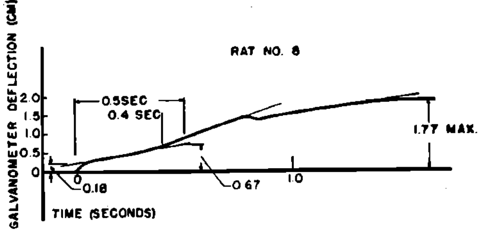

FIG. 6. Rat No. (8). Deflection of galvanometer as a function of time for an 0.8-second pulse of acoustic radiation at an incident intensity of 73 watts/cm². The thermocouple junction is in close proximity to the bone.

in degrees Centigrade per cm deflection yields the value 3.3°C of Table I. The value 0.23 for the intensity absorption coefficient μ falls within the range of values computed from measurements obtained by using thermocouples of the other type.

The results of measurements of the temperature changes under acoustic irradiation in the spinal cords of six living rats are summarized in Table I. From a measurement of the initial time rate of change of temperature, a value for the intensity absorption coefficient μ is computed. As indicated above, a value of ρC_p equal to 1.00 calorie/cm³ is used in the calculations. The values of μ cover a range from 0.19 to 0.23 a total spread of about 20 percent. This is not significantly greater than the variation with position in a single animal as shown by the values for rat No. (3). Part of this variation may be the result of disturbance of the traveling wave field by reflections from the bone underlying the cord. In computing μ a pure traveling wave is assumed. There may also be a variation of the acoustic absorption coefficient with position of the thermocouple in the cord.

The temperature rises which results after periods of 1.0 and 2.0 seconds are also tabulated. In some cases

TABLE II.

Rat No.	I watts/cm²	ΔT in 1 sec (deg. C)	ΔT in 1.5 sec (deg. C)	ΔT in 2 sec (deg. C)
1	68	15	20	23
7	58	12	15	18
8	73	7 (0.8 sec)		
4	60	12		
9	69	11		

the temperature rose linearly for the entire two second interval. In others a distinct deviation from linearity occurs indicating an approach to equilibrium.

When the thermocouple junction is placed in positions in the cord which are in close proximity to bone or between the dura and the bone, the temperature changes which occur during a time interval of the order of one second are determined, to an appreciable extent, by the heat which enters the region of the thermocouple by conduction from the bone. Figure 6 illustrates this effect for a sound pulse of 0.8-second duration and an incident intensity of about 73 watts/cm², rat No. (8) of Table II. The thermocouple was inserted into the cord until the tip just preceding the junction touched the bone. This curve exhibits, in addition to the characteristics of the curve of Fig. 2, a deviation from the initial linear rise associated with the absorption of acoustic energy by the tissue of the cord during the latter part of the irradiation period. The deviation from the initial linear rise occurred about 0.4 sec after initiation of the acoustic pulse. Some time after the acoustic pulse is terminated, the temperature reaches a second maximum which in this case is higher than the first. Both of these additional features are the result of the conduction of heat from the bone. Figure 7 is a trace of a recording of galvanometer deflection as a function of time for a two-second pulse of acoustic radiation at an incident intensity of about 68 watts/cm². The thermocouple junction was placed between the dura and the periosteum of the vertebra of rat No. (1) of Table I. To accomplish this, the cord was laterally displaced slightly while the thermocouple was inserted. In this location the temperature deviated from its initial linear rise in about 0.1 second. Heat conducted from the bone became important after this first 0.1 sec in determining the time rate of temperature change. The temperature then increased more rapidly and at termination of the acoustic pulse had practically reached an equilibrium value. The temperature rise, thermocouple absent, is computed as before. The galvanometer deflection as a function of the relative position of thermocouple junction and beam center is illustrated graphically in Fig. 8. The temperature rise at equilibrium in this location between dura and periosteum, under an incident intensity of radiation of 68 watts/cm², is 23°C. In Table II values are tabulated for the temperature changes after 1 sec and 1.5 seconds of radiation at this intensity. These are readily computed from the record in Fig. 7.

Observations were made on another rat, No. (7) of Table II, with the thermocouple junction placed in position in a fashion similar to that just described for rat No. (1). The record obtained, for galvanometer deflection as a function of time, for a 2.0-second acoustic pulse at an incident intensity of 58 watts/cm² shows that temperature equilibrium would have been practically realized with a sound pulse several tenths of a second longer than 2.0 seconds. The temperature rises recorded on this animal are in good agreement with the values for rat No. (1) when correction is made for the difference in the intensities of irradiation. Temperature changes on rats No. (4) and (9) with the thermocouple junction close to the bone are also given in Table II. Data for 1.0-sec acoustic pulses only were obtained.

4. CONCLUSION

The measurements reported in this paper show that consistent values of the temperature changes occurring in tissue during high intensity ultrasonic irradiation can be obtained by using thermocouples inserted into the tissues. This has been demonstrated by measurements made on the rat spinal cord. The particular preparation serves to illustrate the relative importance of the heat conduction process in contributing to the temperature changes depending upon the proximity of the region to bone and the time interval following initiation of the exposure. These direct measurements of temperature change during acoustic irradiation have been performed while the tissue is subjected to sound intensities up to approximately 80 watts/cm² at a frequency of 980 kc and under atmospheric pressure for acoustic pulse durations up to two seconds. The data presented in this paper can be used to obtain values for acoustic

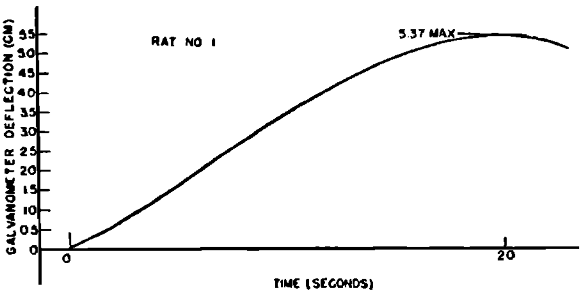

FIG. 7. Rat No. (1). Galvanometer deflection as a function of time for a 2.0-second pulse at an incident intensity of 68 watts/cm². The junction is placed between the dura and periosteum of a vertebra.

absorption coefficients of the tissue. The initial time rate of change of the temperature $(dT/dt)_0$ resulting from absorption of acoustic energy in the tissue is basic to this evaluation. It can be determined directly from the initial, linear portions of the records of galvanometer deflection, Figs. 2, 5, and 6. The range of values obtained for the intensity absorption coefficient μ for a number of rat spinal cords and positions in the cord from the data given in this paper is 0.19 to 0.23. As indicated above, part of this variation may be the

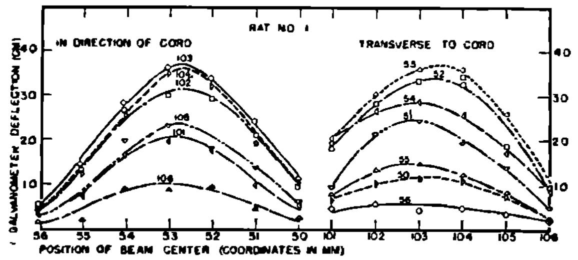

FIG. 8. Rat No. (1). Maximum deflection of galvanometer following exposure of the cord to a 1.0-second acoustic pulse as a function of the relative position of the thermocouple junction and the beam center. The thermocouple junction is placed between the dura and the periosteum of a vertebra.

result of deviations in the sound field from the traveling wave form caused by reflections from the bone underlying the cord. It is interesting to note that Hüter's[8] value for the "white matter" of excised hog brain, extrapolated to a frequency of 0.98 mc, is 0.15.

[8] T. F. Hüter, Naturwiss. 39, 21 (1952).