In Situ Permittivity of Canine Brain: Regional Variations and Postmortem Changes

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Abstract—A new probe-based measurements system was used to study dielectric properties of brain *in situ*, under conditions of induced physiological and pathological changes. Comparative measurements were made as a function of time for 30 min prior to euthanasia and for 90-min post-mortem on the pia, the dura (both normal and anoxic), and in grey and white matter. All measurements were performed at 2450 MHz using a probe of diameter comparable to a 16-gauge hypodermic needle.

Both conductivity and dielectric constant gradually decrease with time following $CaCl_2$ or KCl injection; however, following $CaCl_2$ induced cardiac arrest, values increased transiently upon injection, with subsequent decrease similar to KCl euthanasia. This indicates that the $CaCl_2$ injection causes a stronger and more abrupt change in blood flow to the brain, as expected from the different mechanisms by which the K^+ and Ca^{2+} ions cause cardiovascular arrest.

Values of dielectric properties in homogenized brain—containing all tissue types—lay within the range of values recorded for different tissue types. Lower values for deeper tissue (white matter) reflect the reduced blood flow in comparison to that of the cortex (grey matter) and possible tissue differences. These regional differences are significant in determining absorption patterns for microwave exposure of the head.

I. INTRODUCTION

IT IS WELL KNOWN THAT the interaction of an electromagnetic (EM) field with a biological system is largely determined by the system's dielectric properties. Accurate *in situ* dielectric property information would be of significant benefit in many ways. Real-time *in situ* measurement of living tissues could be used for the detection of pathophysiological conditions in tissues, for measuring changes in certain normal physiological processes, for differentiating between normal and diseased tissues, or for elucidating pharmaco-physiological effects due to drugs. Specific differences or changes of *in situ* dielectric properties within a single tissue type or among tissues suggest the ability of EM diagnostic imaging methods to discern the existence of pathophysiological conditions in intact tissues, organs, or organisms. Differences between *in situ* living tissue properties and *in vitro* properties are of key importance in dosimetry determinations (in both magnitude and distribution) via EM imagery. In dosimetry determinations with respect to potential EM radiation hazards and in treatment planning for cancer patients using hyperthermia induced by RF or microwave fields, an accurate knowledge of the respective *in situ* tissue dielectric properties is essential to an accurate determination of absorbed power.

The determination of the dielectric properties of biological tissues has in the past been limited to measurements over restricted frequency ranges on separate excised tissue samples [4], [5], [9]. These previous results served to validate simple electrical impedance models of tissue structure, but were not capable of yielding information on the physiological variation of *in situ* tissue dielectric properties, especially those due to changes in regional blood flow. In addition, the influence of surrounding tissue organization, blood perfusion, and the existence of pathological conditions could not be ascertained from *in vitro* measurements. The recent development of small dielectric measurement probes [1]–[3] provides the opportunity for obtaining *in situ* dielectric data for a variety of physiological conditions and offers the potential of using dielectric measurements for the detection of local tissue pathology.

The importance of *in situ* tissue dielectric property data as opposed to data obtained by measurements from excised tissues has long been of concern to investigators. As early as 1922, Osterhout described significant changes in the dielectric characteristics of biological materials following death due to the loss of membrane function and the breakdown of cellular structure [4]. Rajewsky's low-frequency measurements showed a deterioration of the dielectric properties concomittant with a significant decrease in metabolic rate [5]. However, the reported change did not begin until approximately one day following death of the organism. Recent *in situ* low-frequency measurements by Burdette *et al.* [6] revealed changes in electrical conductivity of the liver within an hour following death, while one day was required for the observation of changes in the dielectric permittivity. The observed changes in low-frequency properties are caused by a counterion relaxation and a breakdown of cellular membranes, which are primarily responsible for the low-frequency characteris-

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tic properties (i.e., α and β dispersions). In other measurements, Larsen, Jacobi, and Krey [7] have reported changes in permittivity dispersion over the 3–30-MHz frequency range associated with physiological and drug-induced pathophysiological changes in cellular membranes in living cell suspensions. Schwan and Foster [8] state that ultra-high-frequency data are relatively unaffected by death of the tissue because, at those frequencies, the dielectric characteristics of tissue are predominantly due to the water and protein contents of the tissue. However, some of their data [8], [9] do show magnitude changes in dielectric properties following death. Changes in the tissue, such as blood loss and dessication, also occur upon excision and may affect its dielectric properties.

It is true that at high frequencies the tissue dielectric characteristics largely reflect those of water. However, in measurements performed *in situ*, changes in the dielectric characteristics of brain tissue at microwave frequencies were seen immediately upon termination of the experimental animal [10], [11]. These initial changes were followed by a slower, gradual reduction in permittivity and conductivity over a longer period of time (two hours). The initial change was attributed to blood flow, while the slower changes were attributed to a combination of tissue water loss and autolysis. From those *in situ* studies of permittivity, there appear to be significant physiologic influences on tissue dielectric characteristics at microwave frequencies, in spite of the small reactance presented by the cell membrane.

II. Methods

A. Probe Dielectric Measurement System

A small diameter (2.2 mm) probe uniquely suited to the measurement to the *in vivo* dielectric properties of tissues has been developed and tested by Burdette, Seals, and Cain [2]. The basic concept of this probe system relies on an antenna modeling theorem [13] which states that a change in the terminal impedance of an antenna inserted into a lossy medium can be related to the dielectric properties of that medium. Because the details of these analyses have been previously reported [2], [12], only a brief synopsis of the theory is given here.

Simply stated, the antenna modeling theorem equates the terminal impedance of an antenna operating at frequency $n\omega$ in a dielectric material to the antenna's terminal impedance in free space at complex frequency $n\omega$. In a nonmagnetic material ($\mu = \mu_0$), the theorem is expressed mathematically as [13]

$$\frac{Z(\omega,\epsilon^*)}{\eta} = \frac{Z(n\omega,\epsilon_0)}{\eta_0} \tag{1}$$

where

$\omega = 2\pi f$,
ϵ_0 = permittivity of free space,
ϵ^* = complex permittivity of the dielectric medium,
η = the complex intrinsic impedance of the dielectric medium,
η_0 = the intrinsic impedance of free space, and
n = the complex index of refraction of the dielectric medium relative to that of air.

If an analytical expression for the impedance of the antenna is known in both a reference medium and in the medium under study, this modeling theorem may be used to determine the dielectric properties of the unknown medium. Because the impedance of a very short monopole antenna is easily described analytically, this type of antenna may be used as a small coaxial needle-like probe that can be inserted into living tissue and thus permit measurements of the tissue's dielectric properties.

For probe antennas one-tenth wavelength or less in length, the terminal impedance is given by

$$Z(\omega,\epsilon_0) = A\omega^2 + \frac{1}{jC\omega} \tag{2}$$

where A and C are constants determined by the physical dimensions of the antenna [14]. From a knowledge of the above constants and the complex terminal impedance A (ω, ϵ^*) of the probe antenna in a dielectric material, the complex permittivity, and thus the relative dielectric constant conductivity, and loss tangent values can be obtained from the theorem of (1) by substitution. Utilizing the form of antenna impedance given in (2), one obtains

$$Z(\omega,\epsilon^*) = A^{\omega^2}\sqrt{\frac{\epsilon^*}{\epsilon_0}} + \frac{1}{\left(\frac{\epsilon^*}{jC\omega\epsilon_0}\right)}. \tag{3}$$

Equation (3) relates the complex impedance of a lossy dielectric medium at a frequency ω to the relative complex dielectric constant of the medium. In terms of relative dielectric constant and loss tangent, (3) becomes

$$Z(\omega,\epsilon^*) = A\omega^2\sqrt{K(1-j\tan\delta)} + \frac{1}{jC\omega[K(1-j\tan\delta)]} \tag{4}$$

which is a restatement of the theorem of (1) for a short monopole.

For probes whose center conductor approaches zero length, the probe impedance in free space is totally reactive. In this case, the probe is an open-circuit transmission line having only a fringing field. Thus, the minimum sample volume necessary to obtain accurate measurement results is primarily dependent upon the distance between the tightly-coupled center and outer conductors of the probe. Required sample volume for a 2.2-mm-diam probe is approximately 10 mm^3. The free-space impedance of the open-circuited probe is simply

$$Z(\omega,\epsilon_0^*) = \frac{1}{jC\omega} \tag{5}$$

where C is as indicated in (2). Expanding this impedance expression in the antenna modeling theorem yields the

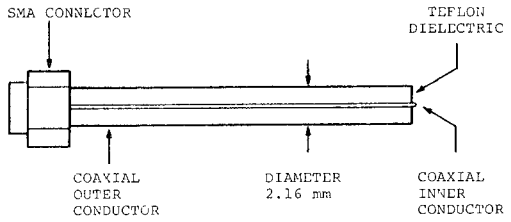

Fig 1. Diagram of the coaxial dielectric measurement probe.

result

$$Z(\omega,\epsilon^*) = \frac{1}{jC\omega[K(1-j\tan\delta)]} \tag{6}$$

which is the same expression as the imaginary part of (4) above. Therefore, for the case of an open-circuit transmission line, the antenna modeling theorem reduces to (6).

A variety of probe configurations were investigated. The length of the extended center conductor of an open-ended coaxial line [1], [2], [12] ranged from zero to 1.0 cm, and probe outside diameters ranged from the size of a 19-gauge hypodermic needle (approximately 1 mm) to 3.6 mm. The dielectric measurement probe used in the described studies is illustrated in Fig. 1. The probe was fabricated from 2.2-mm-diam semi-rigid coaxial cable. Use of the small-diameter probe reduces tissue trauma. Probes were gold-plated before assembly which minimized possible chemical reactions between the probe and the tissue being measured. For high-loss dielectric (muscle, brain), the minimum sample volume containing the probe's fringing field is 0.01 cm^3, which results in an effective measurement depth of 0.2 cm.

The impedance measurement instrumentation employed to measure the terminal impedance of the probe is schematically illustrated in Fig. 2. The key components of the measurement system are the probe and a network analyzer. The relative amplitude and phase difference between the reference and reflected signal channels is measured by the network analyzer, which yields the terminal impedance of the probe in terms of magnitude and phase angle of the reflection coefficient. These data are used as input data to a computer algorithm which corrects systemic measurement errors and computes the dielectric property information. A semi-automated data acquisition/data processing system, key components of which are an analog/digital converter and microprocessor, is used to increase the rate of acquisition and processing of *in situ* permittivity measurement data. In most experiments, the sampling interval was 1 min. During antemortem/postmortem experiments at the time of injection, the sampling interval was reduced to 2 s.

When a network analyzer system is used for performing microwave measurements, certain inherent measurement errors exist. These can be separated into two categories: instrument errors and test set/connection errors. Instrument errors are measurement variations due to noise, imperfect conversions in such equipment as the frequency converter, cross-talk, inaccurate logarithmic conversion, nonlinearity in displays, and overall drift of the system.

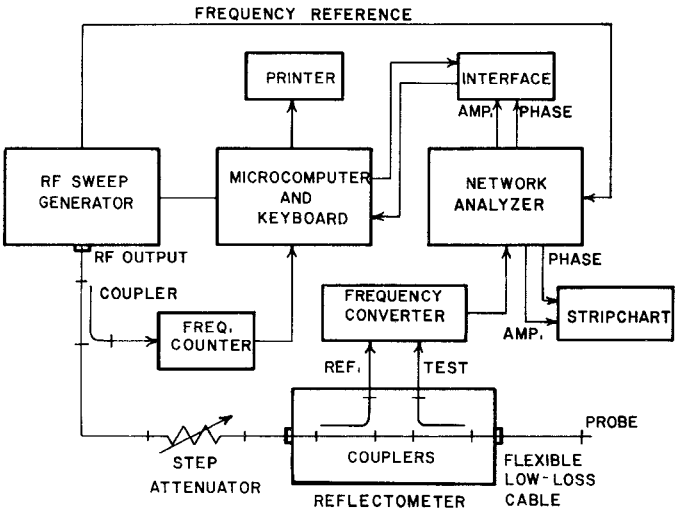

Fig. 2. Block diagram of microcomputer-controlled impedance measurement instrumentation used for the *in vivo* dielectric measurements.

Test set/connection errors are due to the directional couplers in the reflectometer, imperfect cables, and the use of connector adapters. The instrument errors exhibited by modern network analyzers are relatively small.

The primary source of measurement uncertainty is due to test set/connection errors at UHF and microwave frequencies. These uncertainties are quantified as directivity, source match, and frequency tracking errors. An analytical model to account for test set/connection errors has been developed by Hewlett-Packard for correcting reflectivity measurements on their semi-automatic network analyzer system [15]. This model has been implemented for use with the *in vivo* measurement probe, and equations which correct for the open-circuit fringing capacitance of the probe are included in the dielectric property computation algorithm.

The accuracy of the coaxial probe system was determined through measurements of standard dielectric material and of normal biological tissues [2]. Deionized water, 0.1-M saline, methanol, and ethylene glycol were studied in the frequency range from 10 MHz to 10 GHz. The relative dielectric constant and electrical conductivity determined for these liquids agreed to within ± 5 percent of the values reported by other researchers [16]–[19] and within ± 3 percent of the theoretical values [20].

The most important factor that must be controlled while performing tissue dielectric measurements is the contact between tissue and probe. Other factors which can affect the accuracy and/or repeatability of probe measurements include tissue dehydration, accumulation of excess fluid in the measurement area, formation of a dried film of tissue fluids on the probe, and changes in tissue temperature. Each of the above factors constitutes a potential error source during the performance of the dielectric measurements, and therefore steps to minimize these factors were taken.

During antemortem/postmortem dielectric studies in dog brain, we recognized that probe/tissue contact pressure also influenced accuracy and repeatability of measured

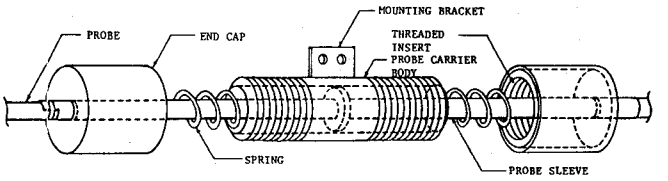

Fig. 3. Schematic diagram of spring-loaded *in situ* probe holder.

results. Following cessation of blood flow, the brain receded, resulting in a change in probe contact pressure and a concomittant change in dielectric properties. A six-percent change in dielectric constant was measured as a result of 4-mm depression of the pia. A four- to five-percent change in conductivity was also observed. To minimize effects of probe contact pressure variation on measured tissue dielectric properties, a spring-loaded probe holder was designed to maintain the probe contact on the tissue at a constant or nearly constant pressure. The contact pressures used were not sufficient to cause blanching/occulsion of pia vessels. Using the spring-loaded probe holder, the probe contact-induced variations in measured *in situ* dielectric properties were on the order of one percent.

B. Animals and Surgical Procedures

Useful results were obtained from fifteen mongrel dogs (12–19 kg) maintained NPO overnight prior to surgery. Each dog was initially anesthetized with 30-mg/kg body weight of pentobarbital sodium (Nembutal), and supplemental dosages of 30–60 mg were administered as necessary to maintain a constant level of anesthesia at Geudel's Stage III, Level 3 [24]. The femoral vessels were cannulated to allow monitoring of arterial and venous blood pressures. Electrocardiogram (ECG) needle electrodes were placed in a Lead II configuration to record heart rate and ECG. A thermistor temperature probe was inserted rectally to the level of the colon to measure systemic temperature.

With the dog in a prone position, the head was placed in a David Kopf Model 1504 stereotaxic apparatus as shown in Fig. 4. A midline incision was made through skin from the eyes to a point 2–3 cm behind the lamboidal ridge. The skin and muscle layers were resected until most of the top left side of the skull was exposed. Using a 3/4-in trephine, a hole was drilled through the skull at a location midway between the eyes and the lamboidal ridge and about 2 cm left of midline. The pial membrane on the surface of the brain was exposed by carefully puncturing and cutting away the tough outer dural membrane and allowing the intervening cerebrospinal fluid (CSF) to drain away. At this point, the arachnoid was removed and the pial surface was covered with saline-moistened gauze pads and the animal's skin condition allowed to stabilize while the probe measurement system was calibrated. A previously calibrated miniature thermistor temperature sensor was placed on the pial surface at the edge of the circular opening of the skull and the *in situ* measurement probe was positioned on the pia 30 min prior to euthanasia.

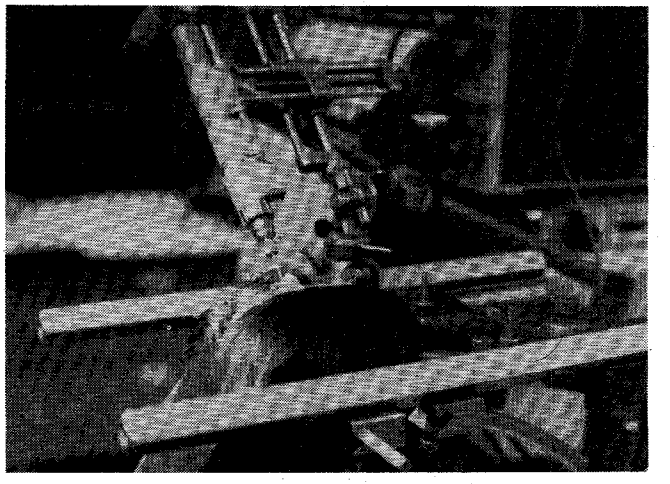

Fig. 4. Dog's head positioned in stereotaxic unit (David Kopf 1504) during *in situ* dielectric measurements of brain tissue performed using dielectric measurement probe.

C. Experimental Measurement Procedures

During each experiment, numerous variables were measured simultaneously. Some were recorded continuously; others were recorded at discrete time increments. The physiological parameters recorded continuously were arterial and venous blood pressures, electrocardiogram (ECG), and systemic temperature. Blood pH, P_{O_2}, and P_{CO_2} were also recorded at periodic intervals.

The network analyzer system was calibrated using standard terminations to correct for test set/connection errors. All measurements were performed as a function of time at 2450 MHz using a 2.2-mm-diam probe. The frequency, the amplitude and phase of the complex reflection coefficient, and the computed dielectric properties —relative dielectric constant, conductivity, and loss tangent—of the tissue contacted by the probe were recorded on digital storage media as functions of time. The quantities of drugs administered to the experimental animal were also recorded.

D. In Situ Brain Permittivity — Regional Studies

Four types of *in situ* measurements made according to the probe antenna location: dural, pial, grey matter (shallow), and white matter (deep). Dural measurements were made on the surface of the dura mater, the outermost membrane covering the brain; pial measurements were made on the pia mater, the innermost covering. The dura, a thick, tough membrane, is separated from the thin pia by cerebrospinal fluid (CSF) in the areas where measurements were performed. The pia is very thin, elastic, and conforms to the surfaces of the brain. Pial measurements may thus be considered as taken on the brain's surface. Measurements were also performed with the probe at two relative depths in brain tissue. The probe tip was less than 1.3 cm below the surface for shallow brain (grey matter) measurements and between 2.0 and 2.5 cm for deep brain (white matter) measurements. At both depths, the probe was inserted 30 min before euthanasia and measurements commenced 10–15 min later. Not as many data were recorded

for locations beneath the surface (grey and white matter) as for surface measurements due to emphasis placed on minimally invasive measurements with respect to brain tissue.

E. Antemortem/Postmortem Measurements

To study differences in dielectric properties of brain tissue, consequent to circulatory arrest, measurements were made before, during and after lethal injection of pentobarbital, calcium chloride ($CaCl_2$), or potassium chloride (KCl). In two animals euthanaized with pentobarbital overdoses, measurements were made with the probe in brain tissue.

In each, if the antemortem/postmortem experiments involving euthanasia by either KCl or $CaCl_2$, measurement of the *in situ* dielectric properties of dog brain were performed with the dura mater and arachnoid removed and the probe placed directly on the epipial layer of the pia mater over the ectosylvian gyrus.

In situ permittivity measurements were performed over a 2-h period. Both dielectric property data and physiological data were recorded for a period of approximately 30 min to ensure stability of all measured parameters prior to euthanasia performed by injecting a 30-cc bolus of saturated KCl or $CaCl_2$, or 15-cc pentobarbital solution into the femoral vein. All electrical and physiological parameters were monitored for 90-min postmortem for KCl or $CaCl_2$ sacrifice and 55-min postmortem for pentobarbital euthanasia. Cardiac arrest was defined to be the time at which all systemic pressures were zero.

After postmortem data had been collected for a short period, the left hemisphere of the brain was removed and homogenized for *in vitro* measurements of dielectric properties. This was accomplished by enlarging the hole in the skull with rongeurs, excising the brain tissue, homogenizing it first with a syringe and then with a tissue homogenizer, and placing the homogenized brain tissue in a beaker. The beaker was partially immersed in a temperature-controlled water bath, and the probe tip was immersed in the homogenized tissue. Measurements were performed at a frequency of 2.45 GHz as a function of temperature from 25°C to 40°C.

F. Brain Blood Flow Studies

The surgical procedure for exposing the brain for measurement of blood-flow effects was identical to that used in the antemortem/postmortem studies. This fact, and the desire to minimize the number of animals euthanaized, allowed us to obtain both types of measurements from the same group of subjects. Microvasculature blood flow effects on dielectric properties were measured in eight animals over a combined frequency range of 0.1–4 GHz, including data collected at 2.45 GHz where postmortem data were measured.

Two conditions were measured in these studies: presence and absence of blood flow in epipial microvasculature in the pial layer of the menenges. To measure the "blood flow present" condition, the probe was placed directly over a small vessel (0.5 mm diam) on the pial surface of the brain. Comparison measurements were made with the probe on the pial surface beside the vessel, but with no vessel under the probe tip, to represent the second condition—absence of the flow through macroscopic vasculature.

TABLE I
DIELECTRIC PROPERTIES OF HOMOGENIZED CANINE BRAIN AT 2450 MHz

N	TEMPERATURE (°C)	K ±	S.E.	σ ± (mmho/cm)	S.E.
1	25	46.88	-	16.75	-
3	26	42.64	2.39	14.73	1.01
3	27	43.32	2.07	15.13	0.90
4	28	42.94	1.81	14.98	0.75
3	29	43.88	1.96	15.18	0.89
4	30	43.39	1.69	15.16	0.75
4	31	43.37	1.69	15.16	0.75
4	32	43.40	1.65	15.16	0.75
4	33	43.49	1.65	15.17	0.75
4	34	43.49	1.62	15.17	0.74
4	35	43.59	1.58	15.32	0.68
4	36	43.60	1.55	15.32	0.67
4	37	43.63	1.52	15.44	0.67
4	38	43.59	1.43	15.58	0.67
4	39	43.62	1.38	15.58	0.66
2	40	41.53	0.54	14.95	0.54
Mean (all temperatures)	26–40	43.30	0.29	15.20	0.12

III. RESULTS

A. In Situ Brain Permittivity — Regional Differences

The mean of multiple dural site measurements at 2450 MHz in one animal for relative dielectric constant ranged from 45.3 to 53.9 and the conductivity mean ranged from 18.4 to 23.5 mmho/cm. The variance in dielectric properties for the dura were probably due to different thicknesses of the dura itself rather than to interanimal differences since measured values were distinctly different for two locations (anterior and posterior) in the same animal when this variability was studied. The measured properties of the dura were also influenced to a certain extent by the underlying CSF. This was demonstrated in one set of measurements in which the CSF was drained from beneath the measurement site through a small dural hole located a few millimeters away. For this condition, the measured dielectric constant was 44.0 ± 6.1 (mean $\pm$S.D) reduced from 58.1 ± 1.7 measured with the CSF present. Only small differences in conductivity, with overlapping sample values, were observed. Based on these results, dielectric properties on the dura would probably best be measured in a sample of dura alone. However, the results of such measurements would not necessarily reflect *in situ* conditions.

At various pial sites, the mean of multiple measurements performed on each animal for dielectric constant was 57.2

TABLE II
IN SITU DIELECTRIC MEASUREMENTS
LIVING CANINE BRAIN
MEAN VALUES ± SEM

DURA MATER	
$K' = 49.9 \pm 1.9$	$\sigma = 20.7 \pm 1.3$
PIA MATER	
$K' = 52.7 \pm 0.9$	$\sigma = 19.3 + 0.7$
*SHALLOW BRAIN (GREY MATTER)	
$K' = 43.0$	$\sigma = 17.4$
DEEP BRAIN (WHITE MATTER)	
$K' = 32.3 \pm 1.7$	$\sigma = 12.1 \pm 0.8$

*N = 1 DOG

± 1.35; for conductivity, the mean was 20.3 ± 1.74 mmho/cm. The pial measurements are not as patterned among animals as the dural measurements. Generally, the values for typical measurements are slightly greater than those obtained for the dural measurements. Additional pial data are discussed subsequently.

At grey matter sites in the brain cortex, the mean relative dielectric constant (43.0) and the mean conductivity (17.4 mmho/cm) are smaller than values for the respective property for both dural and pial measurements. At white matter or subcortical brain sites, the mean values of relative dielectric constant (33.9 and 30.6) and of conductivity (12.8 mmho/cm and 11.3 mmho/cm) are even smaller. Thus, there seems to be a pattern of small dielectric constant and smaller conductivity with increasing distance below the surface of the brain.

Data on freshly excised homogenized brain were measured at 1°C intervals from 26°C to 40°C at a frequency of 2450 MHz. The permittivity profile (from four dogs) was nearly flat over this temperature range; the mean relative dielectric constant was 43.3 ± 0.29 (mean ± SEM) and the mean conductivity was $15.2 + 0.12$ mmho/cm. These mean dielectric property values for the 26°–40°C temperature range are very near their mean values at 37°C ($K' = 43.5$; $\sigma = 15.4$). The mean dielectric property data are presented as a function of temperature in Table I. *In situ* mean values of $K = 32.3$ and $\sigma = 12.1$ corresponding to deep brain (white matter), $K = 57.2$ and $\sigma = 20.3$ corresponding to pia mater were found (Table II). As expected, the values measured for homogenized brain tissue lie near in this range, since all tissue types were present in the homogenized samples. The lower values found for the tissue at deeper locations in the brain can be associated with the fact that blood flow is somewhat reduced in deep brain with respect to cortex. These lower values may also be influenced by differences in tissue composition, particularly the myelin of the deeper white matter. Since the homogenized tissue was measured almost immediately after excision, it is unlikely that significant water loss occurred due to exposure of the tissue (water loss would be reflected as a decrease in measured *in vitro* dielectric constant and conductivity).

B. In Situ Measurements — Antemortem/Postmortem Results

Two animals were euthanaized with pentobarbital overdoses and measurements made with the probe in brain tissue. Figs. 5 and 6 show the results from these two experiments. The data for one animal were obtained with the probe in a white matter site (Fig. 5), and in the other animal data were obtained with the probe in a grey matter site (Fig. 6). Each data point for the white matter position is the average of three to six measurements taken within 1 min of each other. Data points for the grey matter position represent single measurements taken at 1-min intervals.

The time at which blood flow to the head stopped in these two experiments was taken as that time when the arterial blood pressure went to zero. In both experiments, the dielectric constant and conductivity increased after the blood flow stopped. In the grey matter, all dielectric property values began to increase within one minute of the cessation of blood flow. For the deep position, the increase in dielectric constant occurred between seven and ten minutes after the cessation of blood flow. Statistically, values of both dielectric constant and conductivity are significantly lower for white matter as compared to grey matter. This can be expected if the myelin of the deeper white matter is a major factor in the overall dielectric constant of the tissue at 2450 MHz. For the deep position, all the values increased monotonically until the end of the experiment. For the shallow position, the values increased for the first seven to eight minutes, leveled off for about six minutes, and then decreased until the end of the experiment at 55 min after cessation of blood flow.

A comparison of the results obtained from animals euthanaized with KCl and $CaCl_2$ may be found in Tables III and IV. The relative dielectric constant k and conductivity, (both measured at 2.45 GHz) in each case are given as functions of time elapsed after cardiac arrest. Both the relative dielectric constant and the conductivity are seen to decrease gradually after death occurs. This change appears more rapid in cases of $CaCl_2$ euthanasia, however.

Before intravenous administration of the lethal injection of either KCl or $CaCl_2$, the mean arterial blood pressure was 174/130 mmHg with a SEM of 3.2/3.6 in thirteen dogs. Mean venous blood pressure was 11.4/4.2 mmHg ± 0.8/0.7 SEM and mean heart rate was 162 beats/min ± 7 SEM.

The average antemortem values from all dogs in both groups taken together were a relative permittivity of 57.10 ± a standard error of 1.35, and a conductivity of 21.65 mmho/cm ± a standard error of 1.04 mmho/cm. This indicates the small variability among baseline values (measured over 30-min antemortem). Note that standard errors in Tables III and IV would be influenced by both the variation among baseline values and the variation among the dogs' responses to the injections. Since it was desired to look at postmortem effects separately, a normalization procedure was adopted. For each individual dog, the individual baseline value was subtracted from all postmortem

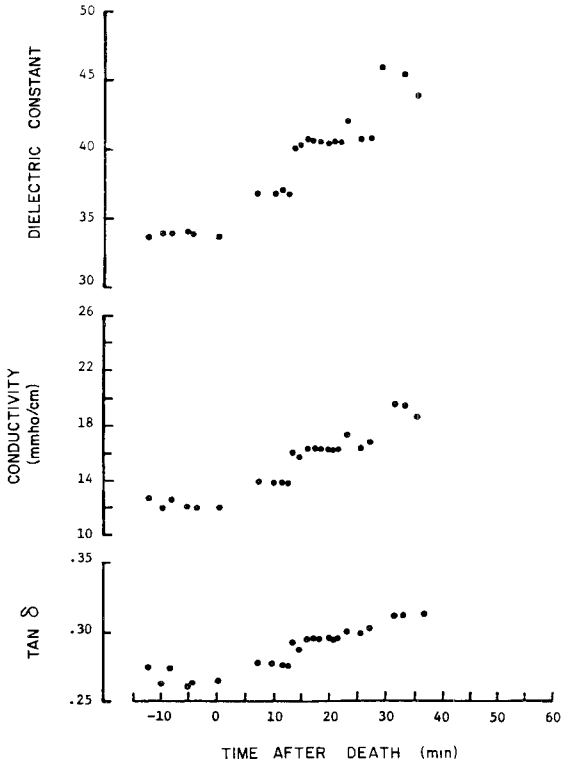

Fig. 5. Measured dielectric properties of *in situ* deep canine brain (white matter) at 37.5±1.0°C as a function of time postmortem. Euthanasia by pentobarbital overdose (from [10]).

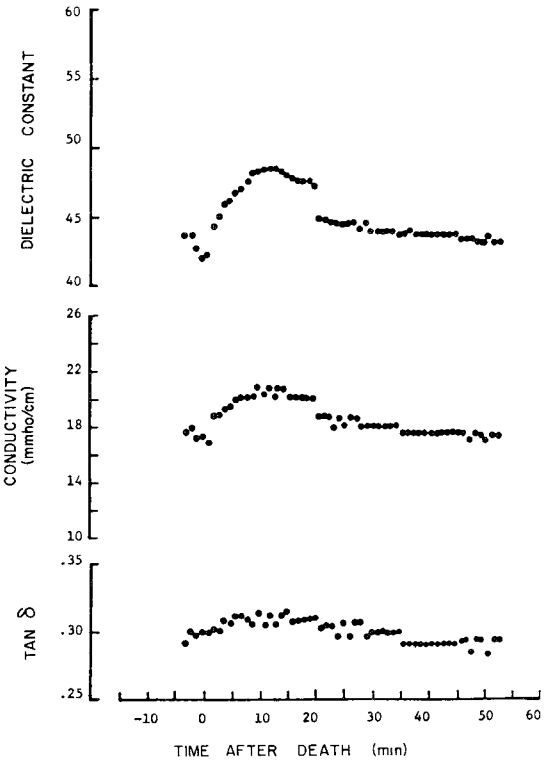

Fig. 6. Measured dielectric properties of *in situ* shallow canine brain (grey matter) as a function of time postmortem. Euthanasia by pentobarbital overdose (from [10]).

TABLE III
SUMMARY OF POSTMORTEM *IN SITU* DIELECTRIC STUDIES WITH KCL SACRIFICE†

Time After Injection (min)	Dielectric* Constant	Conductivity* (mmho/cm)	Brain Temperature (°C) ± 5.0	Colonic Temperature (°C) ± 5.0
0.1	58.15	20.41	36.4 ± 1.2	36.1 ± 1.0
0.2	57.72	20.38	-	-
0.4	57.53	20.43	-	-
0.6	57.16	20.13	-	-
1.0	57.64	20.36	36.2 ± 1.1	36.1 ± 1.2
3.0	58.51	20.66	36.3 ± 1.2	36.0 ± 1.3
10	58.63	19.56	36.5 ± 1.5	36.0 ± 2.1
20	56.66	18.34	36.0 ± 1.5	35.9 ± 2.1
40	54.63	17.12	35.6 ± 1.7	35.6 ± 2.3
60	52.08	16.60	35.7 ± 1.6	34.9 ± 2.6
90‡	52.32	17.59	35.4 ± 1.7	33.6 ± 2.2

† Average values from 8 dogs.

‡ Average values from 5 dogs.

* Standard deviation is shown in Figures 6 and 7.

values. The resulting data represented a plus or minus change from baseline. These normalized data were averaged and plotted in Figs. 7 and 8. Thus, the graphs represent the average changes caused by each mode of euthanasia and the error bars are a measure of the variability of the responses to each type of injection. Variations caused by individual baseline differences have been eliminated from these plots.

Fig. 7 shows the effects of $CaCl_2$ injection on observed dielectric properties. Ca^{2+} injection is associated with a surge of blood to the brain. This corresponds to a sudden, rapid rise in the values of these properties. Fig. 7(a) shows

TABLE IV
SUMMARY OF POSTMORTEM *IN SITU* DIELECTRIC STUDIES WITH $CaCl_2$ SACRIFICE†

Time After Injection (min)	Dielectric * Constant	Conductivity * (mmho/cm)	Brain Temperature (°C) ± 5.0	Colonic Temperature (°C) ± 5.0
0.1	59.91	25.74	40.0 ± 1.3	37.9 ± 0.8
0.2	62.22	26.46	-	-
0.4	58.80	24.74	-	-
0.6	58.35	24.49	-	-
1.0	57.50	24.13	38.7 ± 2.5	37.7 ± 0.0
3.0	55.09	23.05	37.5 ± 2.1	37.7 ± 0.7
10	54.06	22.04	35.5 ± 3.5	37.4 ± 0.2
20	53.36	21.56	36.3 ± 2.4	37.3 ± 0.3
40	53.19	20.97	37.9 ± 0.4	37.1 ± 0.1
60	53.05	21.22	37.1 ± 1.3	36.8 ± 0.1
90	52.57	20.09	36.4 ± 1.7	36.3 ± 0.1

† Average values from 5 dogs.
* Standard deviation is shown in Figures 4 and 5.

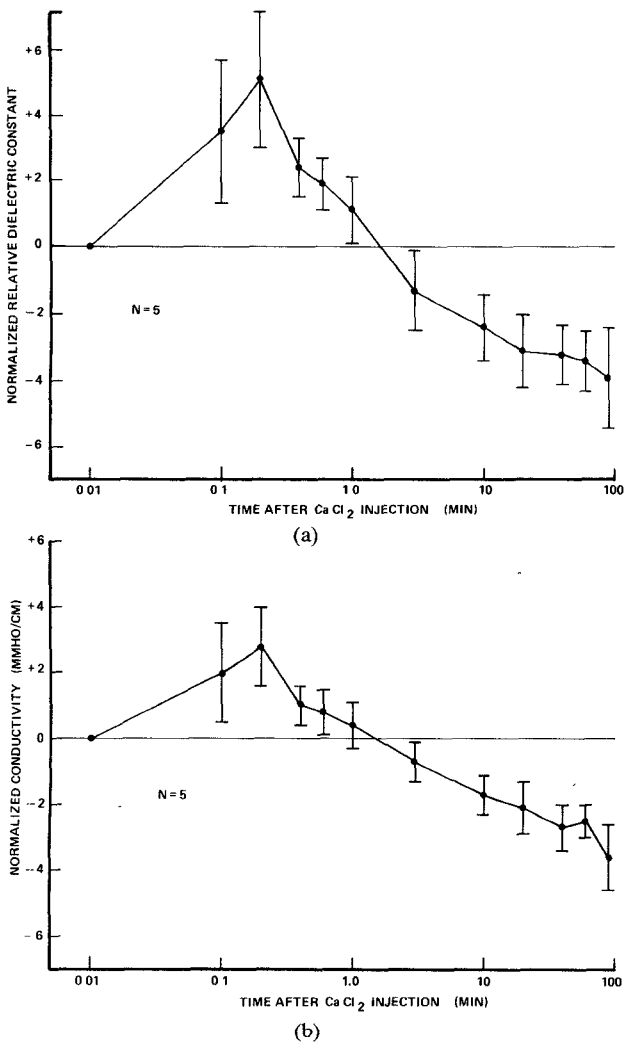

Fig. 7. (a) Mean normalized relative dielectric constant of pial surface of dog brain measured as a function of time after injection of $CaCl_2$. Bars indicate plus or minus one standard deviation. Refer to text for details. (b) Mean normalized conductivity of pial surface of dog brain measured as a function of time after injection of $CaCl_2$. Bars indicate plus or minus one standard deviation. Refer to text for details.

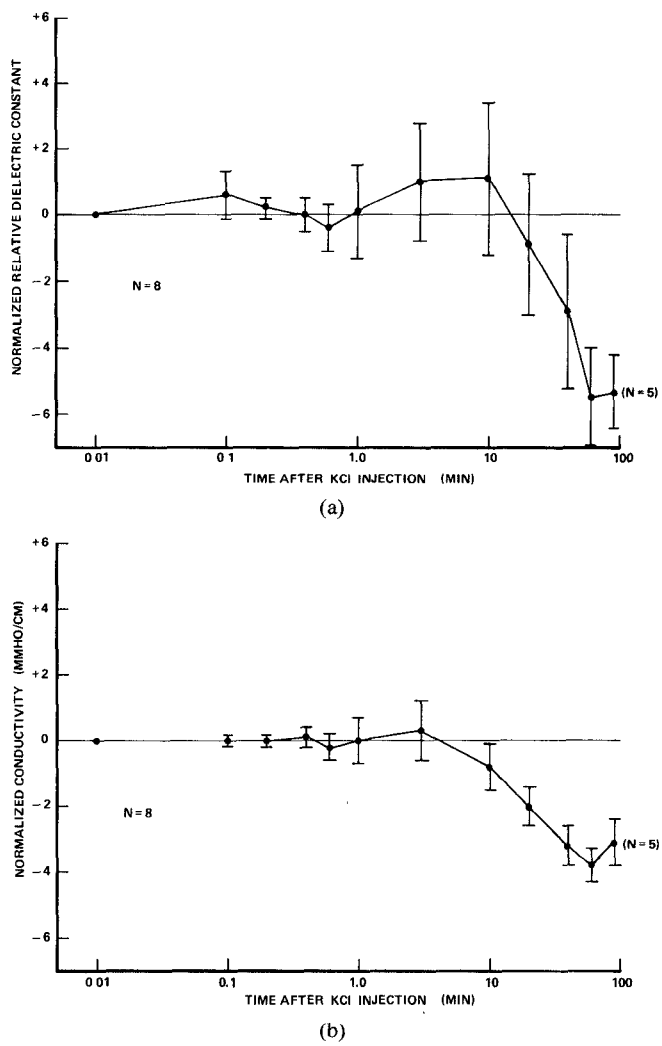

Fig. 8. (a) Mean normalized relative dielectric constant of pial surface of dog brain measured as a function of time after injection of KCl. Bars indicate plus or minus one standard deviation. Refer to text for details. (b) Mean normalized conductivity of pial surface of dog brain measured as a function of time after injection of KCl. Bars indicate plus or minus one standard deviation. Refer to text for details.

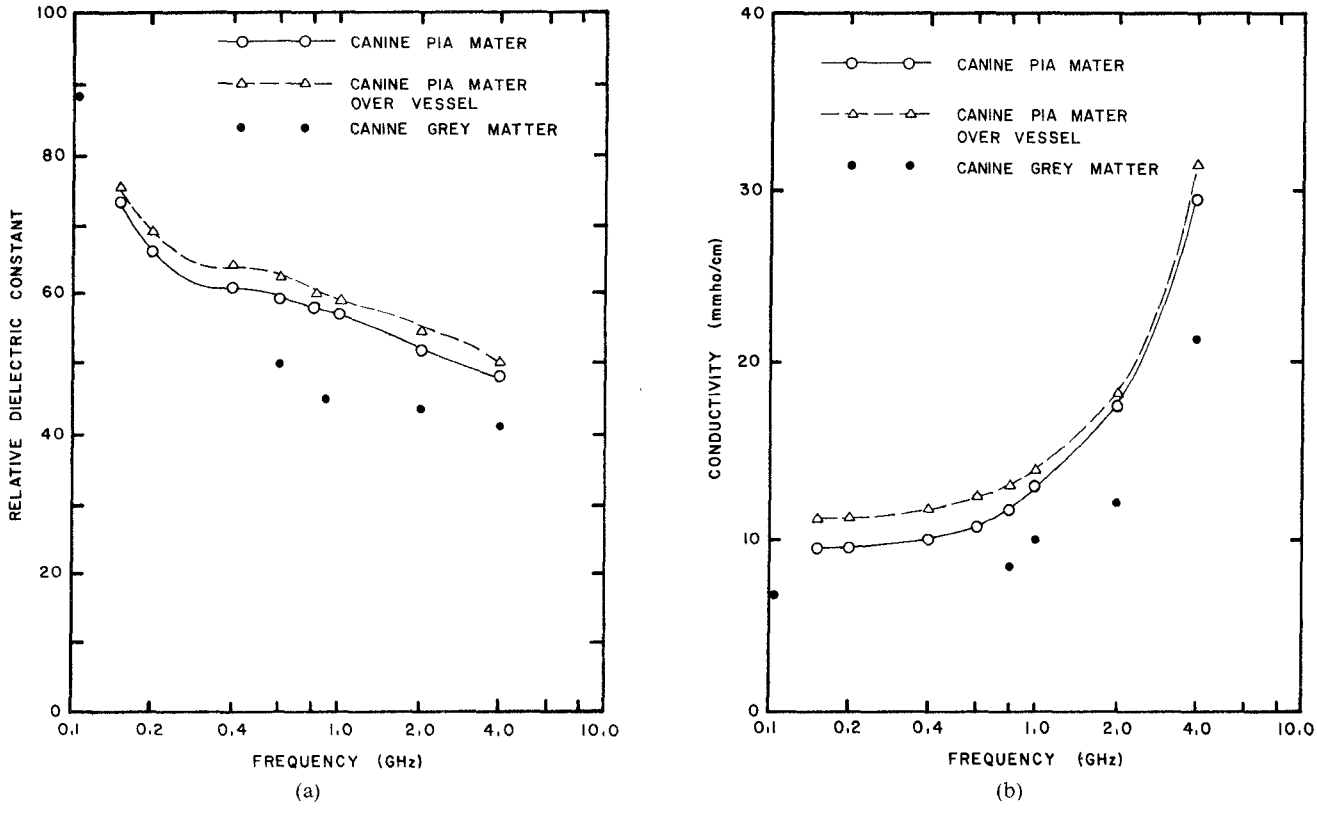

Fig. 9. (a) Relative dielectric constant of *in situ* canine brain (pia mater) at 36°C compared to 37°C *in vitro* canine brain (grey matter) data from [23]. (b) Conductivity of *in situ* canine brain (pia mater) at 36°C compared to 37°C *in vitro* canine brain (grey matter) data from [23].

that, following injection, K increases by an average of 5.1 relative dielectric units in just 12 s after the injection is initiated. Over the course of the following 90 min, the dielectric constant falls to a value 3.9 relative dielectric units below baseline, or a total drop of 9.0 units from its peak value. Similarly, as shown in Fig. 7(b), the conductivity experiences a rapid initial rise of 2.8 mmho/cm, and then gradually drops to a value 3.6 mmho/cm below baseline and 6.4 mmho/cm below its peak values.

Fig. 8(a) shows that, approximately 10-min postmortem, the relative dielectric constant fell to 5.5 units below the mean baseline value. The small initial rise of one dielectric unit was not statistically significant. Fig. 8(b) shows that the conductivity of canine pial tissue as a function of time elapsed after KCl sacrifice exhibited the same type behavior as the dielectric constant. After a statistically insignificant rise of 0.3 mmho/cm, it dropped to 3.8 mmho/cm below its mean baseline *in vivo* value.

C. Effects of Local Blood Flow Differences

Results of *in situ* pial dielectric property measurements performed over the 0.1–4.0-GHz frequency range under two different states of local blood flow are displayed in Fig. 9. Data for canine grey matter measured *in situ* are included for comparison. When a small vessel (0.5 mm diam) was present within the measurement volume of the dielectric probe, a rise of about 3 relative dielectric units was noted. Similarly, as shown in Fig. 9(b), the presence of a small vessel in the measurement field is associated with a conductivity about 2 mmho/cm higher than the conductivity with no vessel present. In general, the conductivity increases with frequency from near 10 mmho/cm at 150 MHz to nearly 30 mmho/cm at 4.0 GH. In the same frequency range, the relative dielectric constant for both conditions decreases from approximately 75 to near 50.

IV. Discussion

There exist little published experimental data with which to compare data obtained in the majority of the experiments described. Using the probe technique developed in our laboratory, we have measured live rat brain in a location equivalent to the pial measurements described here [12], [27]. At 2450 MHz, a dielectric constant of 54 and a conductivity of 20 mmho/cm were measured, both of which are in good agreement with the pial values shown in Table III. The *in vivo* dielectric properties of normal tissues (skeletal muscle, kidney, fat, brain, and blood) from dog and rat [1], [2], [12] generally agreed with previously published *in vitro* results [9], [21]–[23], but significant quantitative differences between *in vivo* and *in vitro* tissue dielectric properties were observed.

A pattern of smaller dielectric constant and conductivity at increased depths within the brain was observed. This relationship is consistent with the greater blood perfusion

of grey matter located near the surface of the brain [25]. It should be noted that our shallow- and deep-brain data reveal a relative difference between grey and white matter similiar to that of recently published results [23] for freshly excised canine grey and white matter. These site-dependent dielectric differences are potentially significant in accurately determining microwave power absorption patterns in the head.

Measurements on homogenized brain tissue, using a slotted line, have been made 2–24 h after removal from the animals [22]. The reported average dielectric constant was 30–35 and the average conductivity ranged from 15 to 20 mmho/cm with a large amount of scatter in the data. This average dielectric constant is similar to the value for live deep brain and dead pia, but smaller than our data for homogenized brain. The average conductivity is comparable to live pia and shallow brain and to our homogenized brain data, but it is larger than antemortem deep brain and postmortem pia. The differences between those data [22] and the data measured in our laboratory could be attributed to the difference between viable and postmortem brain tissue or to the averaging effect of homogenizing the tissue (considering that the homogenized brain used in those measurements could have had a larger volume percentage of white matter than our homogenized brain tissue).

The differences in the time courses of dielectric changes observed following euthanasia with pentobarbital overdose could be due to the different types of brain tissue measured. The type of neural tissue may determine not only the static dielectric properties, but also the changes in these properties due to physiological states. Alternatively, the differences in time courses may be related to blood flow changes in the tissue [25], [26]. Blood flow through the grey matter (shallow) is known to be several times larger than the blood flow through white matter (deep). Thus, the effect of a cessation of blood flow to the brain would be expected to have more rapid and larger effect on grey matter than white matter. Changes in dielectric properties could be the direct result of the lack of blood flow or, because of the greater metabolic activity of grey matter, they could be the result of changes in metabolic processes caused by the lack of nutrients in the grey matter [26]. A comparison of the changes in dielectric properties of grey and white brain matter may be a sensitive test for analyzing the effects of blood flow on dielectric properties.

The spring-loaded probe holder proved extremely useful in monitoring antemortem and postmortem dielectric changes which occurred in the brain as a result both of the method of euthanasia and/or vascular shifts from the brain following cessation of arterial pressure. Following euthanasia by $CaCl_2$ injection intravenously, the initial forceful cardiac myofibril contraction resulted in a rapid expansion of the brain with the surge of blood, followed by a less rapid recession as the blood slowly leaves the brain (due to gravity). Thus, the spring-loaded probe holder largely eliminated probe/sample contact variation by enabling the measurement probe to track the brain's surface through a displacement of several millimeters. Without the mobile capability provided by the spring-loaded probe holder, such tracking would have been impossible.

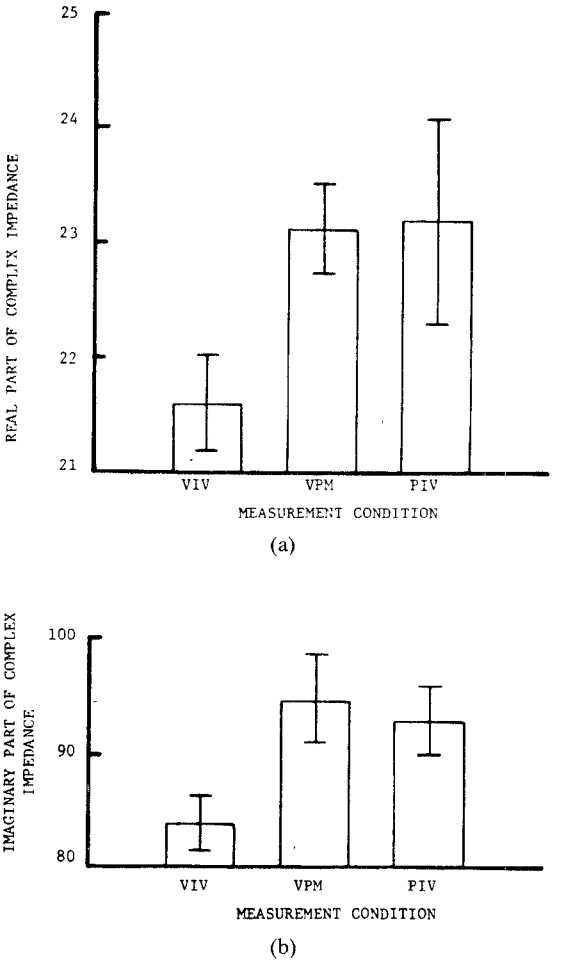

Fig. 10. Canine brain complex impedance measured *in vivo* and *in situ* postmortem on the pia at a frequency of 2450 MHz. Measurement conditions consisted of probe on small (0.5 mm diam) vessel *in vivo* (VIV), probe on vessel postmortem (VPM), and probe on pia *in vivo* (PIV) with no vessel beneath probe. (a) Real part of measured complex impedance. (b) Imaginary part of measured complex impedance.

Because the postmortem studies were done at 2.45 GHz, a comparison of the effect of vessel present/no vessel present conditions on *in vivo* electrical properties was also done at this single frequency. Taken together with postmortem data, an interesting pattern emerges, as illustrated in Fig. 10. This figure compares complex impedances, from which dielectric properties are computed. As was expected, a significant difference was found between complex impedances measured at sites over a blood vessel and sites not over a blood vessel. This difference appears to diminish with increasing frequency, owing to the increasing dominance of "free" water over bound water. (Free water is that which is unassociated with larger molecules in a solution, and bound water is that which is associated with proteins, enzymes, or other macromolecules.) In addition, the post-

mortem condition immediately after euthanasia, which was measured at a site over a small vessel, was found to be remarkably similar to the living tissue when no vessel was present. Presumably this is because blood was not in the vessel in the postmortem case. Thus, the electrical differences measured in the pia can most easily be attributed to the presence or lack of blood flow in the measurement region included within the probe's fringing field.

Data from the antemortem/postmortem experiments summarized in Table III illustrate the measured electrical property changes which occur immediately following KCl injection. The dielectric constant increased rapidly from a mean of 57.8 to 60.9, followed by a slow decrease to 52.3 over a 90-min period postmortem. In a similar fashion, the conductivity rapidly increased from 20.3 mmho/cm to 21.1 mmho/cm upon KCl injection and slowly decreased to 17 mmho/cm.

Results of dielectric measurements performed during cardiac dysrhythmia when a concentrated aqeous $CaCl_2$ solution was used as the agent of euthanasia are presented in Table IV. The arterial blood pressure increased immediately upon this injection and then decreased to zero within 20 s after the injection. This drop of blood pressure to zero was more rapid than seen in the experiments using overdoses of pentobarbital, but less rapid than the rate observed following administration of KCl. In this respect, the results of experiments performed using KCl or $CaCl_2$ euthansia should be more indicative of the effects of an abrupt cessation of blood flow. As indicated by the data in Table IV, there was a rapid, very large increase in the relative dielectric constant and conductivity to 67.3 and 31.5, respectively, following injection. The brain expanded during this period, corresponding to the increase in blood pressure. Subsequent to the blood pressure increase, a rapid return to values similar to those prevailing before the injection was observed, followed by a gradual decrease in both properties.

$CaCl_2$ euthanasia produced an immediate 17-percent increase in measured dielectric constant, occurring 6–10 s before systemic pressures reached zero. KCl euthanasia, on the other hand, produced a total initial change of about 4 percent. This indicated that the $CaCl_2$ injection causes a stronger and more abrupt change in blood flow to the brain, as would be expected from the different mechanisms by which the K^+ and Ca^{2+} ions cause cardiac arrest. The measured dielectric property changes most likely were due to blood flow rather than the Ca^{2+} and K^+ ions per se, because any change in the systemic concentration of these ions resulting from their injection was too small to affect the tissue's dielectric characteristics.

Parallels can be drawn among the physiological action of each ion species used for euthanasia, its effect on blood flow to the brain, and resulting changes in dielctric properties. The presence of an excessive concentration of Ca^{2+} ions causes the cardiac myofibrils to undergo a forceful, sustained contraction. The subsequent surge of blood also accounts for the sharp increase in dielectric properties immediately after injection of $CaCl_2$.

In contrast to the results observed following $CaCl_2$ euthanasia, responses measured in dogs euthanaized by KCl injection did not exhibit this sudden sharp rise. An excessive presence of K^+ ions has the physiological effect of interfering with the propagation of the action potential in the myocardium. In cases where KCl is injected for euthanasia, sufficient concentration is used to cause both SA block and AV block, followed by fibrillation and myocardial arrest. Thus, when K^+ ions are used as the agent of euthanasia, one sees neither the sharp increase of blood volume in the brain nor the associated rise in dielectric property values.

Regardless of the method of euthanasia, however, both groups of dogs used in this experiment exhibited the same long-term trend (dielectric property value decrease) from about 3-min postmortem until the end of the observation period at about 90-min postmortem. The fact that this trend appeared in both sets of dogs, regardless of whether caused by K^+ ions or Ca^{2+} ions, indicates that postmortem decreases are due to 1) blood flow changes and 2) concomittant metabolic changes associated with cerebral ischemia itself rather than the mode of action of the ion species used for euthanasia.

In these investigations, significant dielectric changes were measured as a function of induced physiological change; however, it is not appropriate to infer that similar dielectric changes are necessarily indicative of a specific physiological modification. Physiological changes (e.g., blood flow variations) do have an effect on tissue dielectric characteristics, and it may be possible that real-time monitoring of such characteristics could be used to follow changing physiological events [6]. But in these studies, however, the physiological changes were drastic and the variation in dielectric properties, although significant, was relatively small.

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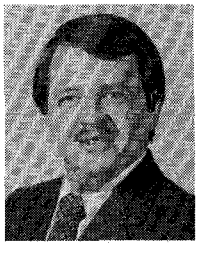

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