

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION
SPONSORED PROJECT INITIATION

Date: October 26, 1976

Project Title: *Research & Engineering Studies for Electromagnetic Thawing of Large Organs*

Project No: *B-474*

Project Director: *Dr. H. A. Ecker*

Sponsor: *National Science Foundation*

Agreement Period: From 9/1/76 Until 31 Aug 81
~~2/28/79*~~

*24 months budget period plus 6 months for flexibility, submission of required reports, etc.

Type Agreement: *Grant ENG76-10124*

Amount: *\$68,500 NSF Funds (GIT Institutional Cost Sharing applicable)*

Reports Required: *Annual Technical Letters; Final Report.*

Sponsor Contact Person (s):

Technical Matters

*Dr. Norman Caplan
Division of Engineering
National Science Foundation
Washington, D. C. 20550
Phone: (202) 632-5881*

Contractual Matters

*(thru OCA)
Mr. F. G. Naughten
Grants Manager, Area 4
National Science Foundation
Washington, D. C. 20550
Phone: (202) 632-5965*

Defense Priority Rating: *None*

Assigned to: *Applied Engineering Laboratory* (School/Laboratory)

COPIES TO:

Project Director
Division Chief (EES)
School/Laboratory Director
Dean/Director-EES
Accounting Office
Procurement Office
Security Coordinator (OCA)
Reports Coordinator (OCA)

Library, Technical Reports Section
Office of Computing Services
Director, Physical Plant
EES Information Office
Project File (OCA)
Project Code (GTRI)
Other _____

SPONSORED PROJECT TERMINATION SHEETDate 3/10/82Project Title: Research & Engineering Studies for Electromagnetic Thawing
of Large Organs

Project No: B-474

Project Director: J. C. Toler

Sponsor: National Science Foundation

Effective Termination Date: 8/31/81Clearance of Accounting Charges: 8/31/81

Grant/Contract Closeout Actions Remaining:

- ☐ Final Invoice and Closing Documents
- ☒ Final Fiscal Report
- ☐ Final Report of Inventions, N/A
- ☐ Govt. Property Inventory & Related Certificate
- ☐ Classified Material Certificate
- ☐ Other _____

Assigned to: ECSL/BRD (~~SEKXOM~~/Laboratory)COPIES TO:

Administrative Coordinator
Research Property Management
Accounting
Procurement/EES Supply Services

Research Security Services
Reports Coordinator (OCA)
Legal Services (OCA)
Library

EES Public Relations (2)
Computer Input
Project File
Other _____

ANNUAL SUMMARY REPORT

RESEARCH AND ENGINEERING STUDIES FOR ELECTROMAGNETIC
THAWING OF LARGE ORGANS

Grant No. ENG-7610124

Prepared By

J. C. Toler

Submitted to
National Science Foundation
Washington, DC 20550


Submitted by
Biomedical Research Group
Electromagnetic Effectiveness Division
Systems and Techniques Laboratory
Engineering Experiment Station
Atlanta, GA 30332

FOREWORD

The research efforts described in this annual report were undertaken by personnel in the Biomedical Research Group in the Electromagnetic Effectiveness Division of Georgia Tech's Engineering Experiment Station. These efforts were sponsored by the National Science Foundation under Grant No. ENG-7610124, and were designated by Georgia Tech as Project B-474. The period of performance was the first year of a two year program, extending from 1 September 1976 through 1 September 1977. During this time, the primary efforts were engineering studies concerned with compiling a base of dielectric property data for cryogenically-preserved canine kidneys and evaluating thermometry devices for use at cryogenic temperatures where electromagnetic fields are used for heating.

The report format is such that a summary of program activities is first provided, followed by a brief technical description of specific studies. These are then followed by a description of significant research accomplishments made during the year. Finally, the personnel supported by the program are listed, and information on a technical paper presented as a result of program activities is presented.

Respectfully Submitted,



J. C. Toler
Program Director

Approved:



F. L. Cain, Chief
EM Effectiveness Division

TABLE OF CONTENTS

	Page
I. SUMMARY	1
II. TECHNICAL DESCRIPTION OF RESEARCH ACTIVITY AND RESULTS	2
III. SIGNIFICANT RESEARCH ACCOMPLISHMENTS	7
IV. PERSONNEL SUPPORTED BY GRANT	10
V. PAPER PUBLICATIONS	11

I. SUMMARY

Research and engineering studies during this initial year were concerned with two technical areas of crucial importance to the long-range goal of providing an electromagnetic system for rapidly and uniformly thawing cryogenically-preserved large organs. The two areas were (1) establishing a base of dielectric property data that will subsequently govern the design parameters of a thawing system and (2) investigating temperature measurement techniques for use under conditions that simultaneously involve cryogenic temperatures and electromagnetic waves. Progress in these two areas is summarized below.

A priori knowledge of tissue dielectric properties is essential because these properties directly influence the interaction between the electromagnetic wave applied for thawing and the organ to be thawed. Technical efforts during the year resulted in the definition and assembly of equipment suitable for measuring dielectric properties. Also, a methodology was established for providing liquid solutions to reduce tissue sample temperatures to cryogenic levels. The equipment configuration and liquid solutions were then used with 29 cryogenically-preserved canine kidneys to establish a base of dielectric constant, loss tangent, and conductivity data. These data are presented as a function of temperature (-80 to $+20^{\circ}\text{C}$), cryoprotectant level (0, 5, and 10% dimethyl sulfoxide concentrations), and tissue type (kidney cortex and medulla).

Satisfactory temperature measurement techniques for use under simultaneous conditions of cryogenic temperature and electromagnetic waves have not been available. Technical efforts during the year resulted in the assembly and evaluation of thermometry devices consisting of ultra-small thermistors with small-diameter wire leads and improved circuits for control and monitoring purposes. With the leads loosely twisted, these thermometry devices yielded temperature values accurate to within 1°C in the presence of electromagnetic waves with field strengths comparable to those used in thawing cryogenically-preserved organs.

II. TECHNICAL DESCRIPTION OF RESEARCH ACTIVITY AND RESULTS

A nation-wide system of banks in which human organs could be stored in readiness for implantation has long been recognized as a capability that would substantially enhance health care delivery in the United States. Research studies directed to transforming this capability into a reality have focused on investigating techniques by which organs can be satisfactorily received, typed, stored for long time periods, and rapidly recovered for implantation. The techniques for organ receipt and typing are generally available; consequently, the major research studies have been concerned with developing the more difficult techniques associated with organ storage and recovery.

During the past several years, collaborative research programs underway at the Georgia Institute of Technology and the Medical College of Georgia have been investigating organ storage and recovery techniques. These programs have used rabbit and canine kidneys to study electromagnetic thawing as a method of recovering organs that have been stored at cryogenic temperatures. The studies have been highly multidisciplinary and have advanced to the point that the feasibility of cryogenic storage followed by electromagnetic recovery has been demonstrated first for rabbit kidneys and now for canine kidneys (which are comparable in size and function to human kidneys).

Studies conducted during the initial year (1 September 1976 to 1 September 1977) of this two-year Grant have supported, in several crucial engineering areas, the research concerned with cryogenic storage and electromagnetic recovery of organs. These engineering areas have included:

- Providing dielectric property data essential in designing an electromagnetic system to rapidly and uniformly thaw cryogenically preserved kidneys, and
- Investigating thermometry techniques that make possible the accurate measurement of temperature over a -80 to $+20^{\circ}\text{C}$ range and in the presence of an electromagnetic field.

Results from the studies in each of these engineering areas are summarized in the following paragraphs.

A. Study of Large Organ Dielectric Properties

An a priori knowledge of dielectric properties is essential in engineering efforts concerned with designing an electromagnetic system for thawing cryogenically-preserved organs. The importance of this knowledge is evident when it is recognized that these properties are fundamental in determining

- how much of the incident electromagnetic radiation is coupled into, as opposed to reflected from, the organ, and
- how much of the electromagnetic energy in the coupled radiation is converted into heat energy during propagation of the energy.

The dielectric properties of primary interest are dielectric constant K , loss tangent δ , and conductivity σ . The dielectric constant is the property of tissue that defines the capability for storing energy during exposure to an electric field. The dielectric property of tissue that defines the energy dissipation capabilities relative to the energy storage capabilities is the loss tangent. Conductivity is the dielectric property of tissue that defines energy loss due to the frictional rotation of molecular dipoles and the migration of charged particles.

In view of the fundamental importance of these properties, an engineering study was undertaken for the purpose of measuring the dielectric constant, loss tangent, and conductivity of kidney tissue as a function of temperature, frequency, tissue type, and cryoprotectant level. With these data available, an adequate system for rapidly and uniformly thawing large organs can be designed during the second year of engineering effort. Canine kidneys were used for the measurement of dielectric properties since they are highly representative of human kidneys. Frequencies of 918 and 2450 MHz were used because their characteristics are electrically suitable for medical heating applications. The temperature range of interest was -80 to $+20^{\circ}\text{C}$, and properties of both cortex and medulla tissue were measured.

The initial efforts involved arranging a configuration of equipment suitable for measuring dielectric properties at 918 MHz and 2450 MHz and over the -80 to $+20^{\circ}\text{C}$ temperature range. The final equipment arrangement consisted of a coaxial slotted line fed by an appropriate signal generator and terminated in a special holder for disk-shaped tissue samples. With

the output of the slotted line connected to a standing wave indicator, it was possible to observe the shapes and relative positions of voltage maxima and minima along the coaxial line. Changes in the shape and position of voltage minima when the air reference medium was replaced by tissue were recorded. These changes were then used in a computer program to calculate the tissue dielectric properties that had to exist in order to cause the observed changes.

Once an equipment configuration for measuring the dielectric properties of kidney tissue was defined, attention was directed to developing a means by which stable temperatures within the -80 to $+20^{\circ}\text{C}$ range could be conveniently provided. This resulted in the use of a cupric chloride and distilled water solution whose freezing point was determined by the cupric chloride concentration. The temperature of this solution was then reduced to its freezing point by immersion in a bath of acetone and dry ice. When the desired temperature of the cupric chloride/distilled water solution was reached, it was removed from the acetone/dry ice bath and positioned such that it engulfed the tissue sample holder. After an appropriate time delay during which the tissue sample temperature reached that of the surrounding cupric chloride/distilled water solution, the data necessary to determine the dielectric properties of the tissue were measured. These data were used in a computer program developed specifically to calculate dielectric constant, loss tangent, and conductivity properties.

As a result of these measurements and computations, dielectric properties of 29 cryogenically-preserved canine kidneys (provided by the Medical College of Georgia) were defined as a function of temperature (-80 to $+20^{\circ}\text{C}$), cryoprotectant level (0, 5, and 10% concentrations of dimethyl sulfoxide), and tissue type (kidney cortex and medulla). Knowledge of these properties will provide engineering information essential to the second-year effort of designing an adequate system for electromagnetically recovering cryogenically-preserved large organs.

B. Study of Thermometry Techniques

Thermometry devices capable of accurately measuring cryogenic temperatures in the presence of an electromagnetic field and over a wide dynamic range are not presently available. Yet devices with these capabilities are essential in research studies concerned with the electromagnetic recovery of cryogenically-preserved organs. Such devices would typically consist of a small temperature sensor connected to control/monitoring circuitry via an electromagnetically transparent lead.

Conventional thermometry devices such as thermistors and thermocouples are made of conductive materials and therefore interact with the electromagnetic field. This interaction causes distortion of the field and localized heating. The recently-developed fiber-optic, liquid-crystal probes are operational over a narrow temperature range and are too large for convenient implantation in tissue. Several new and somewhat exotic thermometry devices are under development, but none are near the point of commercial availability.

In view of this situation, a study was undertaken to determine whether ultra-small thermistors, which have recently become available, could be used as the temperature sensor in thermometry devices designed to operate in the presence of an electromagnetic field and over a -80 to $+20^{\circ}\text{C}$ range. Four ultra-small thermistors were purchased and arrangements were made with a microcircuitry laboratory to have No. 38 Gage wire leads attached. The thermistors and their wire leads were connected to bridge circuits of the type normally used for temperature monitoring and control. Temperature measurements made with this arrangement were inaccurate because the current provided to the thermistor by the bridge circuit both induced self-heating in the thermistor and varied as the thermistor resistance changed. An improved control/monitoring circuit utilizing operational amplifiers and feedback paths was then designed and breadboarded. This circuit provided a much lower current magnitude to the thermistor and maintained this magnitude at a constant level even when the thermistor resistance was changing. These two features of the circuit eliminated the previous data inaccuracy problems caused by thermistor self-heating and variable current magnitude.

Using this thermometry device configuration (ultra-small thermistors connected to improved control/monitoring circuits via straight wire leads), temperature measuring capabilities were evaluated during exposure to a variety of electromagnetic field conditions. These evaluations revealed that temperature errors of 8.8°C could result when this configuration is used in organ thawing applications. The wire leads connecting the control/monitoring circuit to the thermistor were then twisted, and the evaluations were repeated. Under these conditions, temperature errors less than 1°C resulted. Errors of this magnitude are acceptable in studies concerned with electromagnetic recovery of cryogenically-preserved organs. Further, they are generally acceptable in many of the research studies concerned with electrohyperthermia as a cancer treatment modality.

Once efforts to reduce temperature measurement errors to tolerable levels were successful, the thermometry study was directed to identifying techniques by which the thermistor could be implanted. This resulted in a procedure for inserting the thermistor beads and their twisted leads in a sheath of small-diameter, teflon tubing. Epoxy cement was used to secure the thermistor bead in a position such that it extends barely beyond the distal end of the tubing. The teflon tubing is then positioned in a hypodermic needle and inserted into either phantom modelling materials or living tissues. If the hypodermic needle is metal, it is removed from the volume-to-be-heated by withdrawing it back over the tubing. A hypodermic needle made of nonconductive materials can be either withdrawn or left in place during heating.

Although the evaluation of this thermometry device is still considered preliminary, there are positive indications that it will prove adequate for use in engineering studies concerned with electromagnetic recovery of cryogenically-preserved organs.

III. SIGNIFICANT RESEARCH ACCOMPLISHMENTS

The engineering studies conducted during this initial year resulted in significant research accomplishments in the following two areas:

- A large base of canine kidney dielectric property data was obtained as a function of temperature, cryoprotectant level, tissue type, and frequency, and
- A thermometry device suitable for use at cryogenic temperatures and in the presence of electromagnetic fields was designed, assembled, and evaluated.

Both of these accomplishments are absolutely essential to the overall effort of providing an electromagnetic system for recovering, i.e., thawing, large organs that have been cryogenically-preserved; however, both accomplishments also have a much broader applicability in that they provide answers to major problems hindering technical efforts concerned with (1) electrohyperthermia as an adjunct treatment modality for cancer in human patients, (2) biological hazards of human exposure to electromagnetic environments, etc.

Over the past decade, repeated studies have been undertaken for the purpose of investigating protocols for recovering cryogenically-preserved human organs in a condition acceptable for implantation. Several of these studies have considered electromagnetic heating as a recovery technique; however, the complex parameters that influence electromagnetic interaction with tissue have been neither fully understood nor accounted for. As a result, several efforts have been made to thaw frozen organs simply by using commercially-available microwave ovens.

The principal parameters that must be known and used in designing an electromagnetic thawing system are the dielectric properties known as dielectric constant, loss tangent, and conductivity. Without knowledge of these properties, there can be no a priori prediction of how much of the incident electromagnetic energy will be coupled into the cryogenically-preserved organ or how much of the coupled energy will be converted into heat. Therefore, it is impossible for an electromagnetic system to be designed for the specific purpose of rapidly and uniformly thawing cryogenically-preserved organs.

During this initial year's effort, extensive and precise measurements were made to determine the dielectric constant, loss tangent, and conductivity properties of cryogenically-preserved canine kidneys. Preceding the measurements were efforts to (1) assemble a configuration of electronic equipments which would yield accurate and repeatable data at both normal and cryogenic temperatures and (2) establish a methodology by which tissue sample temperatures could be reduced to and maintained at discrete cryogenic levels. Dielectric property data were then determined for 29 cryogenically-preserved kidneys as a function of the following variables:

- temperature (-80 to $+20^{\circ}\text{C}$),
- frequency (918 and 2450 MHz),
- cryoprotectant level (0, 5, and 10 percent dimethyl sulfoxide level), and
- tissue type (cortex and medulla).

Each of the three dielectric properties were plotted versus these variables to yield a family of curves that clearly reveal the behavior of the property in response to factors associated with electromagnetic recovery. For example, an extensive base of canine kidney dielectric property data in both the frozen and thawed state is now available. These data clearly show the temperature at which the tissue changes from one state to the other.

Thermometry techniques at cryogenic temperatures and in the presence of electromagnetic fields have been a problem for studies concerned with electromagnetic heating of tissue. The problem stems from the difficulty in providing a temperature sensor with both a wide dynamic range and transparency to electromagnetic fields. Several exotic temperature sensing techniques are now under investigation and a technique with a limited dynamic range (the fiber-optic liquid-crystal probe) is commercially available. In order to be useful in studies concerned with electromagnetic recovery of cryogenically-preserved organs, a thermometry device must (1) operate over a -80 to $+20^{\circ}\text{C}$ temperature range, (2) be transparent to the electromagnetic fields, (3) be small enough in size to permit implantation, and (4) offer accurate, repeatable, and reliable temperature data.

During this initial year's efforts, new ultra-small thermistors were investigated to determine whether they could be configured as a satisfactory thermometry device. The thermistors were connected to small-gauge enameled

wire leads which were in turn coupled to a control and monitoring device. The control and monitoring device consisted of a specially-designed circuit using operational amplifiers and feedback paths to assure a constant current to the thermistor. The evaluation of this thermometry device consisted of exposing it to a variety of electromagnetic fields while monitoring the resulting temperature indications. It was noted that temperature errors of approximately 9°C were produced during exposure of the device to fields used in studies concerned with the electromagnetic recovery of cryogenically-preserved organs. These errors were traced to interaction between the exposure field and the thermistor leads. When these leads were loosely twisted, this interaction was greatly reduced. Under these conditions, the errors in temperature data were less than 1°C. Errors of this magnitude can be accepted when working with an overall temperature range of -80 to +20°C; therefore, a simple and relatively inexpensive thermometry device for studies concerned with electromagnetic thawing of large organs is now available.

IV. PERSONNEL SUPPORTED BY GRANT

The following persons have been partially supported by the Grant during this initial year:

Name: J. C. Toler

Title: Principal Research Engineer

Contribution: Planning and directing project activities

Name: J. Seals

Title: Assistant Research Engineer

Contribution: Measurement of tissue dielectric properties

Name: V. Bernard

Title: Graduate Research Assistant

Contribution: Evaluation of thermometry devices and measurements of tissue dielectric properties

V. PAPER PUBLICATIONS

The following technical paper was presented as a direct result of research studies conducted under this Grant:

"An Investigation of Thermistors for Temperature Mapping of Biological Specimens During EM Radiation," 1977 International Symposium on the Biological Effects of Electromagnetic Waves, October 30 - November 4, 1977, Airlie, VA.

Additional data have now been added to this paper, and it is being prepared as a review manuscript for the IEEE Transactions on Engineering in Medicine and Biology.

ANNUAL SUMMARY REPORT

RESEARCH AND ENGINEERING STUDIES FOR ELECTROMAGNETIC
THAWING OF LARGE ORGANS

Grant No. ENG-7610124

Prepared by

J. Toler, J. Seals, and W. Berry

Submitted to

NATIONAL SCIENCE FOUNDATION
Washington, D.C. 20550

Submitted by

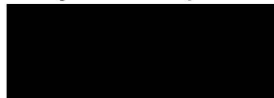
BIOMEDICAL RESEARCH BRANCH
Electronics Technology Laboratory
Georgia Institute of Technology
Engineering Experiment Station
Atlanta, GA 30332

FORWORD

The research efforts described in this report were undertaken by personnel in the Biomedical Research Branch in the Electronics Technology Laboratory of Georgia Tech's Engineering Experiment Station. These efforts were sponsored by the National Science Foundation under Grant No. ENG-7610124, and were designated by Georgia Tech as Project B-474. The period of performance was the third year of a four-year program, extending from 1 June 1979 to 1 June 1980. During this time, the primary technical efforts were concerned with (1) designing and constructing an engineering model of a multi-channel, computer-controlled, thermistor-based thermometry system for use during electromagnetic recovery of cryogenically-preserved organs and (2) defining tissue-equivalent modelling materials that accurately simulate kidney tissue at cryogenic temperatures.

The report format is such that a summary of program activities is first provided, followed by a brief technical description of specific studies. These are followed by a description of significant research accomplishments. Finally, the personnel supported by the program are listed, and information on a technical paper to be presented as a result of program activities is provided.

Respectfully submitted,



J. C. Toler
Program Director

Approved:



F. L. Cain
Associate Director
Electronics Technology Laboratory

TABLE OF CONTENTS

<u>Section</u>	<u>Page</u>
I. SUMMARY	1
II. TECHNICAL DESCRIPTION OF RESEARCH ACTIVITY AND RESULTS	2
III. SIGNIFICANT RESEARCH ACCOMPLISHMENTS	11
IV. PERSONNEL SUPPORTED BY GRANT	13
V. PUBLICATIONS	14

I. SUMMARY

Research and engineering studies were concerned with two technical areas of crucial importance to the long-range goal of providing an electromagnetic system for rapidly and uniformly thawing cryogenically-preserved large organs. The two areas were (1) design, construction, and evaluation of a 12-channel, computer-controlled, thermistor-based thermometry system and (2) definition of recipes for modelling materials that simulate the dielectric properties of cryopreserved canine kidneys. Progress in these two areas is summarized below.

The development of electromagnetic techniques for recovering cryogenically-preserved organs requires the ability to measure temperature levels and profiles at various locations in the organ during thawing. This dictates a multi-channel thermometry capability with temperature sensors that do not interact with the electromagnetic field. A 12-channel system to provide this capability was designed and constructed using thermistors as the temperature sensors. The interconnection between thermistors and the system electronics was made via conductive plastic leads. The 12-channel thermometry system was interfaced with a desk-top computer that stored and displayed real-time temperature information. This system was evaluated during electromagnetic thawing of cryogenically-preserved canine kidneys.

Data describing the dielectric properties of canine kidneys were measured during earlier phases of this grant. During this grant phase, recipes for modelling materials that duplicate these kidney dielectric properties were defined. This required measuring the dielectric properties of many different modelling material recipes as a function of temperature and cryoprotectant. Once a satisfactory recipe was defined, a mold that formed kidney-shaped models instrumented for 12 temperature measurements was constructed. This mold was then used to provide satisfactory canine kidney models for evaluating the thermometry system and the electromagnetic instrumentation used in the thawing process.

II. TECHNICAL DESCRIPTION OF RESEARCH ACTIVITY AND RESULTS

A nation-wide system of banks in which human organs can be stored in readiness for implantation has long been recognized as a capability that would substantially enhance health care delivery in the United States. Research studies directed to transforming this capability into a reality have focused on investigating techniques by which organs can be satisfactorily received, typed, stored for long time periods, and rapidly recovered for implantation. Techniques for organ receipt and typing are generally available; consequently, the major research studies have been concerned with developing the more difficult techniques associated with organ storage and recovery.

During the past several years, collaborative research programs underway at the Georgia Institute of Technology and the Medical College of Georgia have been investigating organ storage and recovery techniques. These programs have used rabbit and canine kidneys to study electromagnetic thawing as a method of recovering organs that have been stored at cryogenic temperatures. The studies have been highly multidisciplinary and have advanced to the point that the feasibility of cryogenic storage followed by electromagnetic recovery has been demonstrated first for rabbit kidneys and now for canine kidneys (which are comparable in size and function to human kidneys).

Studies conducted during this reporting period (1 June 1979 to 1 June 1980) have supported, in several crucial engineering areas, research concerned with cryogenic storage and electromagnetic recovery of organs. These engineering areas have included:

- the design and construction of a multi-channel, computer-controlled, thermistor-based thermometry system capable of measuring temperature elevations and profiles in cryogenically-preserved organs during electromagnetic thawing, and
- the definition of a tissue-equivalent modelling material for simulating the dielectric properties of canine kidneys at cryogenic temperature and with different concentrations of cryoprotectant.

Engineering efforts undertaken in designing/constructing the thermometry system and in defining the new recipe for modelling material are described in the following paragraphs.

A. Design and Construction of a Thermometry System

At present, no multi-channel, computer-controlled thermometry system capable of measuring cryogenic temperatures in the presence of electromagnetic fields is commercially available. Yet, real-time knowledge of temperature levels and distributions at multiple organ locations during the thawing process is mandatory in order to assess both the viability of thawed organs and the adequacy of electromagnetic thawing systems. During earlier tasks under this Grant, initial efforts were undertaken to determine whether individual ultra-small thermistors could be used as temperature sensors in thermometry devices that must operate in the presence of intense electromagnetic fields and over temperature ranges of approximately -80°C to $+20^{\circ}\text{C}$. Such thermistors and their associated leads must

- not perturb the electromagnetic field,
- yield data accurate to within approximately 0.2°C .
- be small enough to be inserted into organs without appreciable tissue damage, and
- not self-heat in the presence of the electromagnetic field.

Four ultra-small thermistors were purchased and arrangements were made with a microcircuitry laboratory to have No. 38 Gage wire leads attached. The thermistors and their wire leads were connected to bridge circuits of the type normally used for temperature monitoring and control. Temperature measurements made with this arrangement were inaccurate because the current provided to the thermistor by the bridge circuit both induced self-heating in the thermistor and varied as the thermistor resistance changed. An improved control/monitoring circuit utilizing operational amplifiers and feedback paths was then designed and breadboarded. This circuit provided a much lower current magnitude to the thermistor and maintained this magnitude at a constant level even when the thermistor resistance was changing. These two features of the circuit eliminated the previous data inaccuracy problems caused by thermistor self-heating and variable current magnitude.

Using this thermometry configuration (ultra-small thermistor connected to an improved control/monitoring circuit via straight wire leads), temperature measuring capabilities were evaluated during exposure to a variety of electromagnetic field conditions. These evaluations revealed that temperature errors of 8.8°C could result when this configuration was used in organ thawing applications. The wire leads connecting the control/monitoring circuit to the thermistor were then twisted, and the evaluations were repeated. Under these conditions, temperature errors of approximately 1°C resulted.

During this third year of the Grant, engineering improvements in the design of the thermometry device have been developed, and 12 devices have been configured as a multi-channel, computer-controlled system. These efforts were undertaken in four tasks as described below.

Task 1 - Construction of Thermistor Sensors

Small-diameter (0.095 inches OD) thermistor beads were used to construct temperature sensors for the thermometry system. The construction involved use of suitable lengths of conductive plastic leads to interconnect the thermistor beads and the thermometry system. The conductive plastic leads minimized the interaction between the thermistor and the electromagnetic field since their conductivity much more nearly approximated that of tissue rather than metal leads. Initially, problems were encountered in maintaining reliable electrical contact between the thermistors and the conductive plastic leads. This was solved by eliminating the varnish used to insulate the electrical connection. Twelve thermistors with conductive plastic leads were then constructed and used with conventional circuitry to demonstrate that reliable and accurate temperature measurements could be made.

Task 2 - Multi-channel Temperature Transducer

A multi-channel temperature transducer was designed and constructed. The purpose of this unit was to convert the resistance changes experienced by the thermistors into useful electric signals. Various design possibilities were evaluated. The design finally selected utilized operational amplifiers

configured to function as non-inverting feedback amplifiers. Thermistors were connected to this configuration in a manner that caused the amplifiers to have temperature-dependent gains. By driving the amplifiers with fixed and known input signals and then measuring the ensuring output signals, it was possible to compute the thermistor's resistance and hence the desired temperatures. The 12-channel transducer was tested by evaluating its ability to measure the values of a wide range of fixed resistors of known values. Results of this evaluation in terms of the equivalent temperature error are presented in Figure 1.

Task 3 - Computer Interface

A desk-top computer (Commodore PET-2001) was employed to control the operation of the 12-channel thermometry system. A computer-controlled, analog-digital converter digitized the analog signals outputted by the multi-channel temperature transducer so that they could be inputted by the computer. The analog signals measured were (1) the fixed reference voltage used to drive the 12 channels of the temperature transducer and (2) the output voltages determined by the temperature-dependent gain of the 12 channels. Once appropriate information was inputted into the computer, a variety of software routines performed the operations necessary to obtain the desired temperature information. In its present form, the computer's software has provisions for printing the measured temperature results on either the computer's CRT or on an external printer.

Task 4 - Preliminary Testing of System

A preliminary evaluation of the thermometry system was performed using the configuration shown in Figure 2. In this evaluation, thermistor probes were inserted into a frozen kidney model (bottom, end and top) and used to monitor the temperature of the model as it was thawed at an output power level of approximately 400 watts. These tests showed that initially there was a very uniform temperature distribution throughout the frozen model. This temperature distribution remained uniform (± 2 degrees centigrade) until a temperature of approximately -40 degrees centigrade was reached. At this point, the bottom of the frozen kidney

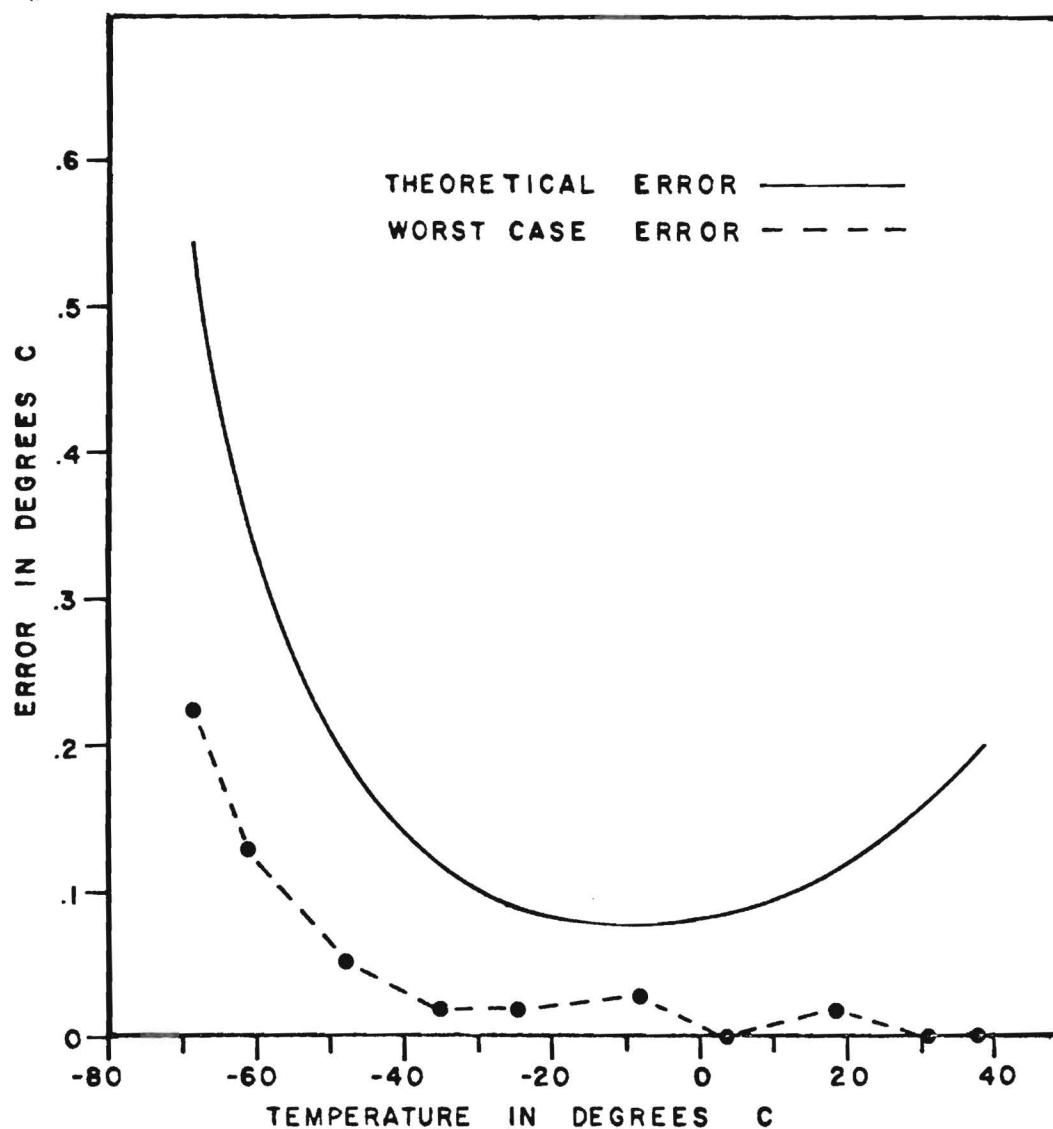


Figure 1. Comparison of theoretically predicted error and measured error (worst case of 8 trials) for simulated temperature measurements using fixed resistors.

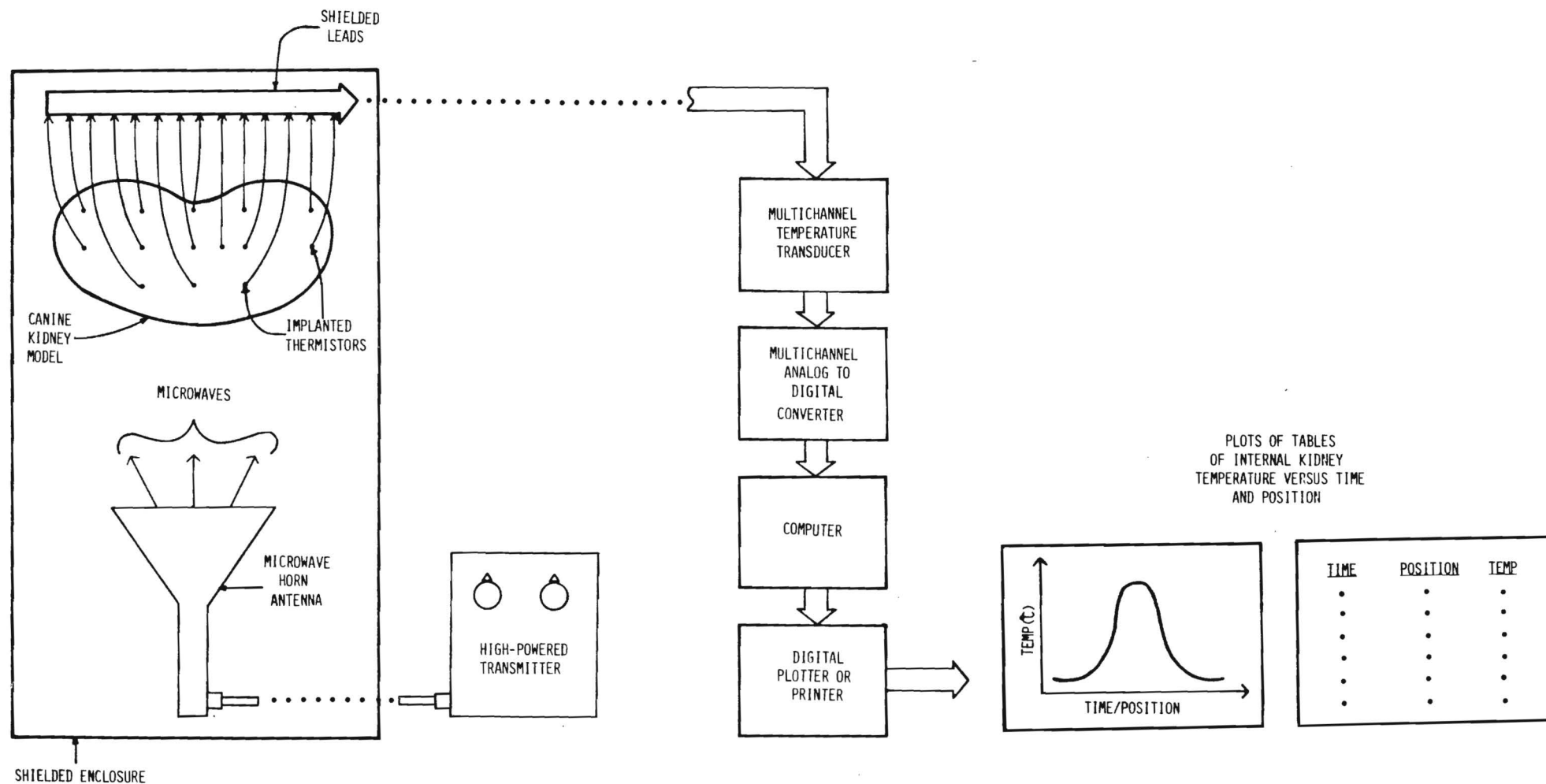


Figure 2. Configuration used to evaluate thermometry system during kidney thawing experiments.

model (which was facing the incident electromagnetic field) began to warm more rapidly. The evaluation was terminated when the bottom of the model reached approximately -30 degrees centigrade while the top of the model remained at approximately -40 degrees centigrade. Further evaluations using thermistors in different locations in the model will be conducted once the design of the horn antenna has been modified to provide a more acceptable radiation pattern at its aperture.

A photograph of the thermometry system, including the chassis housing the 12 thermistor circuits, the computer, and the analog-to-digital converter, is shown in Figure 3.

B. Definition of Tissue-Equivalent Modelling Materials

Most of the studies conducted while developing electromagnetic techniques for recovery of cryogenically-preserved organs will necessarily involve the use of tissue-equivalent modelling materials. The dielectric properties of these materials (which determine how much of the electromagnetic energy is converted to heat energy as the field travels through the tissue) vary as a function of temperature and cryoprotectant concentration. Therefore, it is necessary to define modelling material recipes that exhibit the same dielectric properties as cryopreserved tissues. During this study, a two-task effort was conducted to define such modelling materials for canine kidneys.

Task 1 - Recipe for Tissue-Equivalent Modelling Materials

Since the interaction of any material with electromagnetic energy is determined by the material's dielectric properties, it was necessary to measure the dielectric properties of many versions of the basic tissue-equivalent modelling material recipe (consisting of a gelling medium, powdered polyethylene and saline) in order to identify a suitable receipt. During these measurements, the effect of variables such as temperature, level of cryoprotectant, etc. were evaluated. Results of these measurements indicated that a suitable material could be obtained if the saline used in the basic recipe was replaced with a physiological

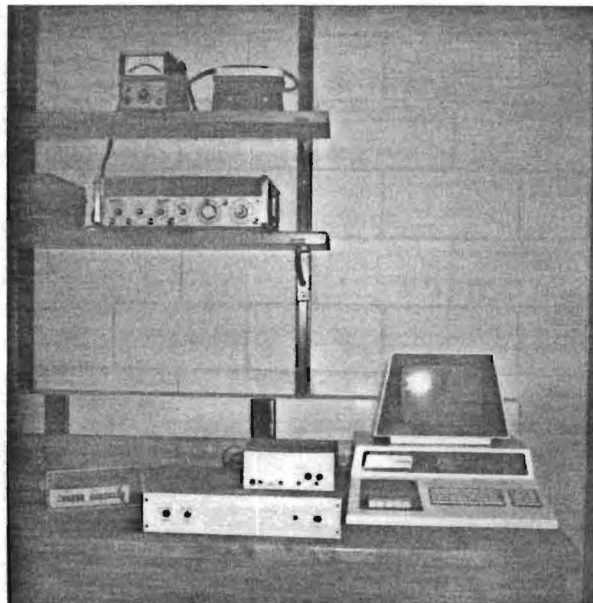


Figure 3. Photographs of the 12-channel thermometry system with its A/D converter and control computer.

perfusion solution (the same solution normally used to perfuse actual canine kidneys prior to freezing) containing a small amount of the cryoprotectant dimethyl-sulfoxide (DMSO).

Task 2 - Construction of Kidney Models

Recipes formulated in Task 1 were used to construct tissue-equivalent kidney models. A mold made from Dow Corning RTV compound was used to give the kidney models the desired shape. Holes drilled into the mold allowed insertion of thermistor sensors. The entire configuration (mold, kidney model and thermistors) can readily be frozen to cryogenic temperatures, then positioned on the horn antenna for electromagnetic thawing.

In summary, an engineering model of a 12-channel, computer-controlled thermometry system using thermistors with conductive plastic leads was designed, constructed, and evaluated. Additionally, the dielectric properties of several different tissue-equivalent modelling material recipes were measured as a function of temperature and cryoprotectant concentration. From these measurements, a new modelling material recipe was defined. This new recipe adequately simulates the dielectric properties of cryogenically-preserved kidneys.

III. SIGNIFICANT RESEARCH ACCOMPLISHMENTS

The engineering studies conducted during this third year resulted in significant research accomplishments in the following two areas:

- Design, construction, and evaluation of a 12-channel, computer-controlled, thermistor-based thermometry system and
- Definition of a tissue-equivalent modelling material recipe that duplicates the dielectric properties of canine kidneys at cryogenic temperatures and at different concentrations of cryoprotectant.

Both of these accomplishments are absolutely essential to the overall effort of providing an electromagnetic system for recovering, i.e., thawing, large organs that have been cryogenically preserved; however, both accomplishments also have a much broader applicability in that they provide answers to major problems hindering technical efforts concerned with (1) electrohyperthermia as an adjunct treatment modality for cancer in human patients, (2) biological hazards of human exposure to electromagnetic environments, etc.

Over the past decade, repeated studies have been undertaken for the purpose of investigating protocols for recovering cryogenically-preserved human organs in a condition acceptable for implantation. Several of these studies have considered electromagnetic heating as a recovery technique; however, complex parameters in the form of dielectric properties influence electromagnetic interactions with tissue. During earlier phases of this study, these dielectric properties were thoroughly defined for canine kidneys. During this phase of the study, efforts have been concerned with using these properties to take additional steps toward the ultimate goal of providing protocols for electromagnetically recovering cryogenically-preserved human organs. One of these steps involved designing, constructing, and evaluating a 12-channel, computer-controlled, thermistor-based thermometry system capable of accurately measuring temperatures over a range of -80°C to $+20^{\circ}\text{C}$ in the presence of an intense electromagnetic field. Such a system is essential in assessing the adequacy of electromagnetic

devices used for thawing cryogenically-preserved organs and in determining the viability of cryogenically-preserved organs that have been electromagnetically thawed.

A second major step toward the goal of providing protocols for electromagnetically recovering cryogenically-preserved organs was the definition of a recipe for tissue-equivalent modelling materials that duplicate the dielectric properties of canine kidneys as a function of cryogenic temperatures and cryoprotectant concentrations. These materials make it possible to use models instead of actual kidneys in future studies to evaluate the adequacy of electromagnetic systems, the uniformity of thawing, etc.

IV. PERSONNEL SUPPORTED BY GRANT

The following persons have been partially supported by the Grant during this reporting period:

Name:	J. C. Toler
Title:	Principal Research Engineer
Contribution:	Planned and managed project activities
Name:	J. Seals
Title:	Research Engineer II
Contribution:	Directed laboratory efforts with thermometry system and modelling materials
Name:	Walter Barry
Title:	Co-op Student
Contribution:	Conducted laboratory measurements, set up equipment, etc. associated with evaluating the thermometry system and defining the modelling material recipe.

V. PUBLICATIONS

A proposal has been prepared for evaluation by the Publications Office of the Institute of Electrical and Electronic Engineers (IEEE). The proposal describes a text titled

Beneficial Applications of Electromagnetic Waves in
Medicine and Biology

to be published by the IEEE press. A major section of the text will be devoted to engineering efforts concerned with the goal of providing a nation-wide system of banks in which cryogenically-preserved organs are stored in readiness for electromagnetic thawing and implantation. The engineering efforts in this section of the text will be a presentation of the research accomplished under this Grant.

ANNUAL TECHNICAL REPORT
PROJECT B-474

RESEARCH AND ENGINEERING STUDIES FOR ELECTROMAGNETIC THAWING OF LARGE ORGANS

By
J. Toler, J. Seals, and E. McCormick

Prepared for
NATIONAL SCIENCE FOUNDATION
WASHINGTON, D.C. 20550
GRANT NO. ENG-76-10124

Submitted by
BIOMEDICAL RESEARCH GROUP
ELECTROMAGNETIC EFFECTIVENESS DIVISION
SYSTEMS AND TECHNIQUES LABORATORY

MAY 1979

GEORGIA INSTITUTE OF TECHNOLOGY

**Engineering Experiment Station
Atlanta, Georgia 30332**



1979



TECHNICAL REPORT

Project B-474

RESEARCH AND ENGINEERING STUDIES FOR ELECTROMAGNETIC
THAWING OF LARGE ORGANS

February 1979

National Science Foundation

Grant No. ENG-76-10124

Prepared by

J. Toler, J. Seals, and E. McCormick

Submitted to

National Science Foundation
Washington D.C. 20550

Submitted by

Biomedical Research Group
Electromagnetic Effectiveness Division
Engineering Experiment Station
Georgia Institute of Technology
Atlanta, Georgia 30332

FOREWORD

The research and engineering study described in this report was conducted by the Biomedical Research Group in the Electromagnetic Effectiveness Division of Georgia Tech's Engineering Experiment Station. The study was sponsored by the National Science Foundation under Grant No. ENG-76-10124, and was designated by Georgia Tech as Project B-474. The period of performance was 1 September 1976 through 1 September 1978.

The purpose of the study was to determine the electrical properties of tissue as a function of variables that affect the electromagnetic recovery of cryogenically-preserved large organs. During the study, the theoretical basis for the interaction between electromagnetic waves and tissue was clarified. Then a procedure for measuring pertinent characteristics of tissue samples was developed. This procedure involved defining and arranging an equipment configuration, designing a technique for preparing tissue samples suitable for measurement, providing a means by which tissue samples could be reduced to and maintained at cryogenic temperatures during measurements, and designing improved instrumentation for measuring cryogenic temperatures in the presence of electromagnetic waves. Using this procedure, tissue sample characteristics were measured and used in a computer program to calculate electrical properties as a function of frequency (918 MHz and 2450 MHz), temperature (-68°C to $+20^{\circ}\text{C}$), cryoprotectant concentration (0, 5, and 10 percent dimethyl sulfoxide), and tissue type (cortex and medulla). Electrical properties of primary interest were dielectric constant, loss tangent, and conductivity. Knowledge of these properties is now available for a priori use in designing electromagnetic instrumentation capable of thawing cryogenically-preserved large organs. The availability of such instrumentation will enhance significantly the possibility of a nationwide system of banks in which cryogenically-preserved large organs can be stored in readiness for implantation.

The authors gratefully acknowledge the technical consultation provided by Dr. Armand Karow, Jr. of the Medical College of Georgia Department of Pharmacology, and Mr. Clif Burdette of the Georgia Tech Biomedical Research Group. Also, the extensive laboratory assistance provided by Mr. Victor Bernard and Mr. Doug Fuller, students at Georgia Tech, is gratefully acknowledged.

Respectfully submitted,



James C. Toler
Project Director

Approved:



Fred L. Cain
Chief,
EM Effectiveness Division

TABLE OF CONTENTS

<u>Section</u>	<u>Page</u>
I. NON-TECHNICAL SUMMARY.	1
II. TECHNICAL SUMMARY.	3
III. SIGNIFICANT RESEARCH ACCOMPLISHMENTS	6
IV. PERSONNEL SUPPORTED BY GRANT.	9
V. PUBLICATIONS	10
VI. STUDY APPROACH AND ORGANIZATION.	11
VII. BIOLOGICAL TISSUE AND ELECTROMAGNETIC WAVE INTERACTION MECHANISMS	15
VIII. ELECTRICAL PROPERTY DETERMINATIONS	26
IX. THERMOMETRY DEVICE INVESTIGATIONS.	52
X. ELECTRICAL PROPERTY VALUES	58
XI. CONCLUSIONS AND RECOMMENDATIONS.	74
XII. REFERENCES.	80

LIST OF FIGURES

<u>Figure</u>		<u>Page</u>
1.	Penetration depth as a function of frequency for several tissue types.	24
2.	Wave interactions in short-circuited line with sample material in place	28
3.	Holder designed especially for disk-shaped tissue samples	32
4.	Steps in the procedure for preparing tissue samples: sample cutter	33
5.	Steps in the procedure for preparing tissue samples: tissue disks	34
6.	Diagram of device used to measure sample thickness.	36
7.	Tissue sample holder immersed in low-temperature bath	38
8.	Diagram of constant temperature bath.	39
9.	Standing wave pattern inside short-circuited coaxial line (a) coaxial line empty and (b) coaxial line containing sample.	41
10.	Block diagram of the short-circuited coaxial line measurement system.	44
11.	Photograph of the short-circuited coaxial line measurement system.	45
12.	Cross-sectional view of sample holder main body	47
13.	Thermistor size in relation to pin head	54
14.	Thermistor temperature sensor mounted in Teflon tubing and inserted in hypodermic needle	56
15.	Five thermistors mounted in-line in Teflon tubing sheath.	57
16.	Relative dielectric constant of cortex tissue at 2450 MHz.	68
17.	Relative dielectric constant of cortex tissue at 918 MHz	69
18.	Loss tangent of cortex tissue at 2450 MHz	70
19.	Loss tangent of cortex tissue at 918 MHz.	71
20.	Electrical conductivity of cortex tissue at 2450 MHz.	72
21.	Electrical conductivity of cortex tissue at 918 MHz	73
22.	Penetration depth of cortex tissue at 2450 MHz.	76
23.	Penetration depth of cortex tissue at 918 MHz	77

LIST OF TABLES

<u>Table</u>	<u>Page</u>
I. ELECTRICAL PROPERTIES OF DEIONIZED WATER.	51
II. SUMMARY OF TEST CONDITIONS.	59
III. ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 2450 MHz AND WITH A 0 PERCENT PERFUSATE CONCENTRATION	60
IV. ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 2450 MHz AND WITH A 5 PERCENT PERFUSATE CONCENTRATION	61
V. ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 2450 MHz AND WITH A 10 PERCENT PERFUSATE CONCENTRATION.	62
VI. ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 918 MHz AND WITH A 0 PERCENT PERFUSATE CONCENTRATION	63
VII. ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 918 MHz AND WITH A 5 PERCENT PERFUSATE CONCENTRATION	64
VIII. ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 918 MHz AND WITH A 10 PERCENT PERFUSATE CONCENTRATION.	65
IX. ELECTRICAL PROPERTIES OF MEDULLA TISSUE AT 2450 MHz AND WITH A 5 PERCENT PERFUSATE CONCENTRATION	66
X. ELECTRICAL PROPERTIES OF MEDULLA TISSUE AT 2450 MHz AND WITH A 10 PERCENT PERFUSATE CONCENTRATION.	67

SECTION I

NON-TECHNICAL SUMMARY

Research and engineering studies were undertaken in two technical areas of crucial importance to the long-range goal of providing an electromagnetic system for rapidly and uniformly thawing cryogenically-preserved large organs. The two areas were (1) establishing a base of tissue electrical property data that can be used to indicate design parameters for the electromagnetic thawing system and (2) investigating temperature measurement techniques that can be used under conditions which simultaneously involve cryogenic temperatures and electromagnetic waves. Engineering progress made in these two areas is presented in this report.

An a priori knowledge of tissue electrical properties is essential because these properties govern the interaction between the electromagnetic wave and the cryogenically-preserved organ. Engineering efforts during this study clarified the theoretical relationship between tissue electrical properties and electromagnetic waves, and then provided instrumentation with which electrical properties could be measured as a function of frequency (918 MHz and 2450 MHz), tissue type (kidney medulla and cortex), cryoprotectant concentration (0, 5, and 10 percent dimethyl sulfoxide), and temperature (-68°C to $+20^{\circ}\text{C}$). Results of these measurements, which were made using tissue samples from 50 individual canine kidneys, are presented.

Satisfactory temperature measurement techniques for use under simultaneous conditions of cryogenic temperature and electromagnetic waves have not been available. Engineering efforts during this study resulted in the assembly and evaluation of a thermistor-based thermometry system with improved electronic control circuitry. This system yielded temperature values accurate to within 1°C in the presence of electromagnetic waves and at cryogenic temperatures. The electromagnetic waves were comparable in magnitude to those used for organ thawing. Operation and performance of this thermometry system are described.

Using the thermistor-based thermometry system design and the electrical property data (dielectric constant, loss tangent, and conductivity), the design of an electromagnetic system for rapidly and uniformly thawing large organs is discussed.

SECTION II

TECHNICAL SUMMARY

The surgical transplantation of human organs is a developing clinical procedure that promises substantial improvement in the delivery of health care in the United States; however, at the current time, transplantation is infrequently used because no reliable methodology for providing functioning organs at the time of need is available. In order to provide functioning organs on demand, tissue preservation techniques must exist in which metabolism can be reversibly terminated. Theoretically, reversibly-terminated metabolism can be achieved by either physical or chemical means; however, under the present state-of-the-art, long-term tissue preservation is feasible only by a physical means in which organ temperature is reduced to cryogenic levels. Numerous studies have been undertaken for the purpose of defining freeze-induced injury, perfusion dynamics, suitable warming and cooling rates, appropriate cyroprotectant levels, etc., associated with cryopreservation procedures. One of the results of these studies has been the fact that, almost without exception, it is not possible to thaw cryogenically-preserved organs too rapidly. Knowledge of this fact has highlighted the need for a thawing technique that is rapid, uniform, and hygienic.

Thawing techniques studied over the past several years include convection heat, high pressure, perfusion, and electromagnetic waves. With the exception of electromagnetic waves, these thawing techniques have proven to be inefficient and technically difficult. As a consequence, there is significant interest in solving the remaining engineering and medical problems that prevent electromagnetic waves from providing a satisfactory technique for recovering cryogenically-preserved large organs.

During this study, crucial engineering problems associated with the electromagnetic recovery of cryogenically-preserved large organs were investigated. The following resulted from these investigations:

- Tissue electrical property data essential to the design of electromagnetic instrumentation for rapidly and uniformly thawing cryogenically-preserved kidneys were provided, and
- Thermometry techniques that make possible the reliable measurement of temperature over a -68°C to $+20^{\circ}\text{C}$ range and in the presence of electromagnetic waves were evaluated.

The electrical properties of primary interest were the dielectric constant, loss tangent, and conductivity. Initial efforts involved assembling a configuration of electromagnetic instrumentation capable of measuring electrical properties at frequencies of 918 MHz and 2450 MHz. This instrumentation consisted of a coaxial slotted line fed by appropriate signal sources and terminated in a specially-designed holder for ring-shaped tissue samples. A special device for preparing tissue samples with the precision and uniformity required by the measurement procedure was also provided.

Once electromagnetic instrumentation for measuring the electrical properties of tissue was defined, a means for providing stable tissue temperatures over the -68°C to $+20^{\circ}\text{C}$ temperature range was assembled. This involved the use of a cupric chloride/distilled water solution, the temperature of which was controlled by immersion in a bath of acetone and dry ice. The sample holder, with the tissue sample in place, was positioned in the chilled cupric chloride/distilled water solution during the measurement of electrical properties.

Changes in voltage maxima and minima, as measured using the coaxial slotted line, were used with a computer program to determine electrical properties of tissue samples from 50 canine kidneys (provided by Dr. Armand Karow, Jr., of the Medical College of Georgia). Electrical properties of primary interest were the dielectric constant, loss tangent, and conductivity. These properties were determined as a function of frequency (918 MHz and 2450 MHz), temperature (-68°C to $+20^{\circ}\text{C}$), cryoprotectant level (0, 5, and 10 percent dimethyl sulfoxide), and tissue type (cortex and medulla).

The investigation of thermometry techniques considered the possibility of using ultra-small thermistors as sensors suitable for

temperature measurements in the presence of electromagnetic waves and over a -68°C to $+20^{\circ}\text{C}$ range. Four thermistors were purchased and small, No. 38 gauge, wire leads were attached. When this configuration was evaluated using conventional electronic circuitry, difficulties arose because the current provided to the thermistors by the circuitry induced self-heating and varied as the thermistor resistance changed. Improved circuitry using operational amplifiers and feedback paths was designed and breadboarded. This circuitry eliminated the previous problems and resulted in an ability to measure temperatures with an error of less than 8.8°C when electromagnetic waves were present and a range of -68°C to $+20^{\circ}\text{C}$ was used. Further experimentation revealed that these errors could be reduced to less than 1°C by loosely twisting the leads connecting the thermistors to the electronic circuitry.

Techniques suitable for inserting the thermistors in tissue or modelling materials were then investigated. The resulting technique involved inserting thermistors and their leads in a sheath of small-diameter Teflon tubing. Epoxy was used to secure the thermistor such that it barely extended beyond the distal end of the tubing. The Teflon tubing was inserted in a hypodermic needle and pushed into the tissue or modelling material. The needle was then removed from the volume to be heated by withdrawing it back over the tubing. With the thermistor in place, the electromagnetic field was applied, the material was heated, and the temperature was satisfactorily measured. With multiple thermistors positioned in the Teflon sheath and inserted in the material to be heated, it appears feasible to accurately measure temperature profiles in the presence of electromagnetic waves and over broad temperature ranges.

Using the thermistor-based thermometry system design and the electrical property data (dielectric constant, loss tangent, and conductivity), the design of an electromagnetic system for rapidly and uniformly thawing large organs is discussed.

SECTION III

SIGNIFICANT RESEARCH ACCOMPLISHMENTS

The engineering efforts undertaken during this study resulted in significant research accomplishments in the following two areas:

- A large base of canine kidney electrical property data was obtained as a function of temperature, cryoprotectant level, tissue type, and frequency, and
- A thermometry device suitable for use at cryogenic temperatures and in the presence of electromagnetic waves was designed, assembled, and evaluated.

Both of these accomplishments are absolutely essential to the overall effort of providing electromagnetic instrumentation for recovering large organs that have been cryogenically preserved; however, both accomplishments also have a much broader applicability in that they provide answers to major problems hindering technical efforts concerned with (1) electrohyperthermia as an adjunct treatment modality for cancer in human patients, (2) biological hazards of human exposure to electromagnetic environments, etc.

Over the past decade, repeated studies have been undertaken for the purpose of investigating protocols for recovering cryogenically-preserved human organs in a condition acceptable for implantation. Several of these studies have considered electromagnetic heating as a recovery technique; however, the complex parameters that influence electromagnetic interaction with tissue have been neither fully understood nor accounted for. As a result, several efforts have been made to thaw frozen organs simply by using commercially-available microwave ovens.

The principal tissue parameters that must be known and used in designing an electromagnetic thawing system are the electrical properties known as dielectric constant, loss tangent, and conductivity. Without knowledge of these properties, there can be no a priori prediction of how much of the incident electromagnetic wave will be

coupled into the cryogenically-preserved organ or how much of the coupled wave will be converted into heat; therefore, it is impossible for an electromagnetic system to be designed for the specific purpose of rapidly and uniformly thawing cryogenically-preserved organs.

During this study, extensive and precise measurements were made to determine the dielectric constant, loss tangent, and conductivity properties of cryogenically-preserved canine kidneys. Preceding the measurements were efforts to (1) assemble a configuration of electronic equipment which would yield accurate and repeatable data at both normal and cryogenic temperatures, (2) provide a technique by which suitable tissue samples could be prepared, and (3) establish a methodology by which tissue sample temperatures could be reduced to and maintained at discrete cryogenic levels. Electrical property data were then determined for 50 cryogenically-preserved kidneys as a function of the following variables

- temperature (-68°C to $+20^{\circ}\text{C}$),
- frequency (918 and 2450 MHz),
- cryoprotectant level (0, 5, and 10 percent dimethyl sulfoxide), and
- tissue type (cortex and medulla).

Each of the three electrical properties was plotted versus these variables to yield a family of curves that clearly reveal the behavior of the property in response to factors associated with electromagnetic recovery. As a result, an extensive base of canine kidney electrical property data in both the frozen and thawed state is now available. These data clearly show tissue behavior during thawing and can be used to design instrumentation by which cryogenically-preserved organs can be electromagnetically recovered.

Thermometry techniques at cryogenic temperatures and in the presence of electromagnetic waves have been a problem for studies concerned with electromagnetic heating of tissue. The problem stems from the difficulty in providing a temperature sensor with both a wide dynamic range and transparency to electromagnetic waves. Several exotic

temperature sensing techniques are now under investigation and a technique with a limited dynamic range (the fiber optic liquid-crystal probe) is commercially available. In order to be useful in studies concerned with electromagnetic recovery of cryogenically-preserved organs, a thermometry device must (1) operate over a -80°C to $+20^{\circ}\text{C}$ temperature range, (2) be transparent to electromagnetic waves, (3) be small enough in size to permit implantation, and (4) offer accurate, repeatable, and reliable temperature data.

During this study, new ultra-small thermistors were investigated to determine whether they could be configured as satisfactory thermometry devices. The thermistors were connected to small-gauge enameled wire leads which were in turn coupled to a control and monitoring device. The control and monitoring device consisted of a specially-designed circuit using operational amplifiers and feedback paths to assure a constant current to the thermistor. The evaluation of this thermometry device consisted of exposing it to a variety of electromagnetic waves while monitoring the resulting temperature indications. It was noted that temperature errors of approximately 9°C were produced during exposure of the device to fields used in studies concerned with the electromagnetic recovery of cryogenically-preserved organs. These errors were traced to interaction between the exposure field and the thermistor leads. When these leads were loosely twisted, this interaction was greatly reduced. Under these conditions, the errors in temperature data were less than 1°C . Errors of this magnitude can be accepted when working with an overall temperature range of -80°C to $+20^{\circ}\text{C}$; therefore, a simple and relatively inexpensive thermometry device for studies concerned with electromagnetic thawing of large organs is now available.

SECTION IV
PERSONNEL SUPPORTED BY GRANT

The following persons were partially supported by this Grant during its two-year period of performance:

Name:	J. Toler
Title:	Principal Research Engineer
Contribution:	Planning and directing project activities
Name:	J. Seals
Title:	Assistant Research Engineer
Contribution:	Planning project activities, measurement of tissue electrical properties, and data analysis
Name:	E. McCormick
Title:	Co-op Student
Contribution:	Measurement of tissue electrical properties and data analysis
Name:	D. Fuller
Title:	Co-op Student
Contribution:	Measurement of tissue electrical properties
Name:	V. Bernard
Title:	Graduate Research Assistant
Contribution:	Evaluation of thermometry devices and measurement of tissue electrical properties

SECTION V
PUBLICATIONS

The following publications were a direct result of research studies conducted under this Grant:

"An Investigation of Thermistors for Temperature Mapping of Biological Specimens During EM Radiation," 1977 International Symposium on the Biological Effects of Electromagnetic Waves, October 30 - November 4, 1977, Airlie, VA.

"Technical Aspects of Electromagnetic Techniques for Recovering Cryogenically-Preserved Large Organs," Accepted for Presentation at the 1979 International IEEE/AP-S Symposium and National Radio Science Meeting, June 18-20, 1979, Seattle, WA.

SECTION VI

STUDY APPROACH AND ORGANIZATION

The surgical transplantation of human organs is a developing clinical procedure that promises substantial improvement in the delivery of health care in the United States. However, at the present time, transplantation is infrequently performed because reliable techniques are not available for providing viable donor organs at the time of recipient need. If these techniques were available, a nationwide system of banks could be established in which organs were received, typed, stored for extended time periods, and then recovered as needed for implantation. Since organ receipt and typing problems have generally been resolved, the more recent transplantation studies have been concerned with making available techniques for long-term organ storage and rapid organ recovery.

Storage of organs for extended time periods requires tissue preservation techniques in which metabolism is reversibly terminated. Theoretically, reversibly-terminated metabolism can be achieved by either chemical or physical means; however, the only feasible means for long-term preservation currently available is physical, and involves reducing organ temperature to cryogenic levels where metabolism is arrested [1]. Generally, cryogenic preservation of organs is a six-step procedure as follows [2]:

- Step 1: Acquire and flush the organ.
- Step 2: Perfuse the organ with a cryoprotectant.
- Step 3: Freeze the organ at a cryogenic temperature.
- Step 4: Store the organ for the desired time period.
- Step 5: Recover the organ via thawing.
- Step 6: Remove the cryoprotectant and ready the organ for implantation.

Ideally, each of these steps are performed in a manner that is non-injurious to the organ. In current practice, however, both toxicity associated with the cryoprotectant and the formation of ice crystals are

problem areas [3,4] to the extent that cryopreservation must be performed in a manner that injures the organ as little as possible. The overall objective, therefore, has become one of assuring that the cumulative injury of all six steps is maintained within tolerable bounds. To meet this objective, numerous in vitro studies have been conducted to define perfusion dynamics, freeze-induced injury, suitable cooling and warming rates, appropriate cryoprotectant drugs, etc. [5,6,7,8].

From the above discussion, it is obvious that a key requirement in organ cryopreservation is the ability to thaw biological material efficiently and without damage. With minor exceptions (i.e., mouse embryos), most investigators believe that it is impossible to thaw too quickly. When thawing is slow, small, innocuous, intra-cellular crystals undergo recrystallization with disastrous results for the cells. Also, prolonged thawing makes chemical injury possible as a result of cell exposure to high concentrations of solutes at relatively high temperatures. These high solute concentrations are created during the freezing process since, as liquid water is converted to ice, the concentration of solutes rises until the eutectic temperature is reached. In general, a thawing rate greater than 20°C per minute is desirable, but this is technically difficult to realize in organs with relatively large tissue masses.

A variety of different thawing methods have been studied over the past several years. These methods include conduction heat [9], high pressure [10], perfusion [9], vascular perfusion [9], and electromagnetic waves [11]. With the exception of electromagnetic waves, these different thawing methods have been technically difficult and inefficient. Electromagnetic thawing is sophisticated and requires engineering knowledge of the interaction between electrical, thermal, and biological properties of organs. In spite of its sophistication, however, this method currently offers the possibility of rapid, uniform, and hygienic thawing of cryopreserved organs. If this possibility can be realized, the major obstacle in the way of a nationwide system of organ banks will have been removed.

Under this grant, research and engineering studies were undertaken to define the electrical properties of cryogenically-preserved large organs. A priori knowledge of these properties is essential in designing an effective electromagnetic system for organ thawing. The importance of these properties is evident in the fact that they are fundamental influences in determining

- how much of the incident electromagnetic wave is coupled into, as opposed to being reflected from, the organ, and
- how the electromagnetic wave coupled into the organ is transformed into heat energy.

The electrical properties of primary interest are the dielectric constant, loss tangent, and conductivity. The dielectric constant is the property that defines the tissue's capability for storing energy during exposure to an electric field. The property of tissue that defines energy dissipation capabilities relative to energy storage capabilities is the loss tangent. Conductivity is the electrical property of tissue that defines energy loss due to frictional rotation of molecular dipoles and the migration of charged particles.

The approach used in this study to define the electrical properties of cryopreserved organs began with efforts to better understand interaction mechanisms between tissue and electromagnetic waves. Configurations of precision equipment were then assembled and used to measure the electrical properties of 50 canine kidneys at both normal and cryogenic temperatures (-68°C to $+20^{\circ}\text{C}$). These measurements were made at two different frequencies (918 MHz and 2450 MHz), on two different types of kidney tissue (medulla and cortex), and for three different concentrations of cryoprotectant (0, 5, and 10 percent dimethyl sulfoxide). As a part of these measurements, engineering methods were developed for

- preparing samples of kidney tissue in the special shape and with the precise dimensions required by the sample holder,
- providing a controllable means by which the temperature of tissue samples could be reduced to and maintained at cryogenic levels, and

- measuring tissue temperatures in the presence of electromagnetic waves.

The 918 MHz and 2450 MHz frequencies were used during this study because electromagnetic waves at these frequencies couple effectively into biological materials. Also, the availability of electronic components at these two frequencies cause them to be highly probable choices for an electromagnetic thawing system. The -68°C to $+20^{\circ}\text{C}$ temperature range was used because it encompassed the major temperature variations that a cryogenically-preserved organ goes through as it is thawed. The use of canine kidney tissue was based on the fact that this organ is of considerable interest from a cryopreservation point-of-view. Also, canine kidney tissue is physiologically comparable to human kidney tissue. Use of three different perfusate concentrations provided an opportunity to assess the effects of a commonly-used cryoprotectant on kidney tissue under conditions of freezing and thawing. Interest in the two different tissue types arose because of their structural differences, and the possibility that these differences could cause non-uniformity in heating profiles during electromagnetic thawing.

Data resulting from this study were analyzed and prepared in tables and graphs that reveal the electrical properties of tissue comprising a large organ such as the kidney.

SECTION VII

BIOLOGICAL TISSUE AND ELECTROMAGNETIC WAVE INTERACTION MECHANISMS

When electromagnetic waves are used to heat biological tissue, a priori knowledge of temperature profiles and energy absorption is desirable so precise control of the heating process can be assured. This is especially true when electromagnetic waves are used to recover cryogenically-preserved organs because non-uniform thawing can rapidly occur and cause severe tissue damage. Accurate knowledge of the mechanisms which govern the interaction between biological tissue and electromagnetic waves is therefore essential. This knowledge begins with an understanding of the electrical properties that characterize the response of tissue exposed to electromagnetic waves.

A. Electrical Property Definitions

Interactions between tissue and electromagnetic waves result from the presence of particles within the tissue that can be affected by the electrical force field of the electromagnetic wave. These particles include free charges, such as ions that possess a net electrical charge, and bound charges, such as polar molecules that possess a dipole moment even though they are electrically neutral. The electrical properties of tissue reflect the presence of free and bound particles within the tissue, and hence, provide an a priori indication of the tissue's response to an electromagnetic wave.

A variety of parameters is commonly used to characterize a material's electrical properties. These parameters include the permittivity, dielectric constant, loss factor, conductivity, and loss tangent. Because these parameters are closely inter-related and may be defined differently depending on the physical process involved, there is often confusion concerning the interpretation of a given electrical property. This situation can be clarified by analyzing the electrical current induced in a material by an electromagnetic wave.

An electromagnetic wave induces electric current in a material by imparting motion to the free and bound charges present within the

material. In biological materials, various disassociated ions (e.g., sodium, chlorine, potassium, calcium, etc.) constitute free charges. At microwave frequencies, water is the predominate source of bound charges in biological materials. Definitions for the various electrical properties can be established by analyzing the electromagnetically-induced current; however, these definitions will depend on the interpretation given to components of the induced current. One interpretation involves analyzing the induced current as the sum of a conduction current and a displacement current. The conduction current is the induced motion of free charges and is analogous to electronic conduction in a metal wire. The displacement current is the induced rotational motion of bound charges. In this interpretation, the conductivity of a material is defined in relation to the conduction current while the permittivity of the material is defined in relation to the displacement current. This interpretation of electromagnetically-induced current within a material as the sum of conduction and displacement currents can be described mathematically by Ampere's Circuital Law. If it is assumed that the electric and magnetic field intensities of the applied electromagnetic wave are of the form $\vec{E} \exp(j\omega t)$ and $\vec{H} \exp(j\omega t)$, respectively, the differential form of Ampere's Circuital Law may be expressed as

$$\nabla \times \vec{H} = \sigma_T \vec{E} + j\omega \epsilon_T \vec{E}, \quad (1)$$

where ∇ = mathematical operator,

\vec{H} = magnetic field intensity,

\vec{E} = electric field intensity,

σ_T = conductivity,

ϵ_T = permittivity, and

ω = angular frequency.

The units of this equation are electric current density. The first quantity on the right side of the equation represents conduction current in the material while the second quantity on the right side represents displacement current in the material. The subscript, T, denotes the

fact that, when electrical properties are defined in this manner, they are referred to as the "true" electrical properties since they reflect separate free-charge and bound-charge movement.

An alternate interpretation involves defining the electromagnetically-induced current in a material as the sum of dissipative and reactive currents. Electrical properties are then defined in relation to these dissipative and reactive currents. At first glance, it would appear that this alternate interpretation leads to definitions identical to those previously derived. In this case, the conduction and displacement currents in Equation (1) would correspond to dissipative and reactive currents, respectively. However, except for a vacuum, the permittivity of all materials is really a complex quantity of the following form

$$\epsilon_T^* = \epsilon_T' - j\epsilon_T'' \quad (2)$$

where the asterisk denotes that the permittivity is complex. This means that the displacement current in Equation (1) has both dissipative and reactive components. This is apparent if the complex permittivity in Equation (2) is substituted into Equation (1) as in the following expression:

$$\nabla \times \vec{H} = \sigma_T \vec{E} + j\omega(\epsilon_T' - j\epsilon_T'')\vec{E}, \quad (3)$$

where the terms are as previously defined.

Terms on the right side of Equation (3) can be regrouped in several different formats. Two possible formats are shown in Equations (4a) and (4b).

$$\nabla \times \vec{H} = (\sigma_T + \omega\epsilon_T'')\vec{E} + j\omega\epsilon_T'\vec{E}, \text{ and} \quad (4a)$$

$$\nabla \times \vec{H} = j\omega[\epsilon_T' - j(\epsilon_T'' + \sigma_T/\omega)]\vec{E}. \quad (4b)$$

The first quantity on the right side of Equation (4a), represents a dissipative current and the second term represents a reactive current

flow. An "effective" conductivity, σ_e , and "effective" permittivity, ϵ_e , can be defined in relation to the dissipative and reactive currents as follows:

$$\sigma_e = \sigma_T + \omega \epsilon''_T, \text{ and} \quad (5a)$$

$$\epsilon_e = \epsilon'_T. \quad (5b)$$

Equation (5a) shows that the effective conductivity sums all dissipative effects, and hence, it cannot be strictly associated with only free charge movements. Equation (5b) shows that the effective permittivity can still be strictly associated with bound charge movement. However, the effective permittivity is only a partial description of the bound charge movement since it only describes the reactive component of the total displacement current. It is noted that the effective permittivity is a real quantity. In order to avoid confusion over notation, the effective permittivity is usually referred to as the dielectric constant while the term permittivity is reserved for reference to the complex permittivity of a material. An "effective" permittivity, ϵ_e^* , can be defined from Equation (4b) as follows:

$$\epsilon_e^* = \epsilon'_e - j\epsilon''_e, \quad (6)$$

where $\epsilon'_e = \epsilon'_T = \epsilon_e$ and $\epsilon''_e = \epsilon''_T + \sigma_T/\omega$.

When electrical property measurements are made on a material, the parameters that are directly measured are the effective electrical properties shown in Equation (6). Therefore, the descriptive title "effective" is usually dropped and the complex permittivity, ϵ^* , dielectric constant, ϵ , and conductivity, σ , of the material are usually defined as follows:

$$\epsilon^* = \epsilon' - j\epsilon'' = \epsilon'_T - j(\epsilon''_T + \sigma_T/\omega), \quad (7a)$$

$$\epsilon = \epsilon'_T = \epsilon', \text{ and} \quad (7b)$$

$$\sigma = \sigma_T + \omega \epsilon''_T = \omega \epsilon''. \quad (7c)$$

Other widely used electrical properties include the relative dielectric constant (K' or K), the relative loss factor (K''), and the loss tangent ($\tan \delta$). These parameters can be expressed in terms of Equations (7a), (7b), and (7c) as follows:

$$K' = K = \epsilon' / \epsilon_0 = \epsilon / \epsilon_0, \quad (8a)$$

$$K'' = \epsilon'' / \epsilon_0 = \sigma / \omega \epsilon_0, \text{ and} \quad (8b)$$

$$\tan \delta = \epsilon'' / \epsilon' = \sigma / \omega \epsilon, \quad (8c)$$

where ϵ_0 (8.854×10^{-12} farads per meter) is the dielectric constant of free space. Because of the inter-relationships between the various electric properties, it is not necessary to specify values for each property to completely characterize a material's electrical properties. Combinations of properties that are commonly used include the following:

Relative dielectric constant and
relative loss factor (K and K''),

Relative dielectric constant and
conductivity (K and σ), and

Relative dielectric constant and
loss tangent (K and $\tan \delta$).

It is noted that either of these three combinations could be used to compute any of the other properties on the left sides of Equations (7a) through (8c).

Considerable emphasis has been placed on distinguishing between the "effective" and "true" electrical properties of biological tissues. The significance of this emphasis to biomedical studies involving electromagnetic waves is dependent on the specific goals of the studies. For example, when electromagnetically-induced heating is the primary concern, knowledge of the effective electrical properties should prove adequate; therefore, for the purpose of this study, the effective electrical properties were of primary interest. In studies where the actual mechanisms of interaction between biological tissue and an electromagnetic wave are of concern, knowledge of the true electrical properties would be of concern. An example of this latter concern would be studies to assess the possibility of non-thermal electromagnetic effects on living systems.

This discussion has clarified definitions for the terms commonly used to quantitate a material's electrical properties. It has also been noted that the electrical properties of a material play a significant role in determining the interaction that occurs between the material and an electromagnetic wave. The significance of this role is shown in the following paragraphs by examining how electrical properties influence electromagnetic wave propagation and energy dissipation within a material.

B. Significance of Electrical Properties

The significance of a material's electrical properties can be shown by examining electromagnetic wave propagation and energy dissipation within the material.

The point-of-departure for this examination is Maxwell's equations and how they are used to derive vector Helmholtz equations for the electric and the magnetic field intensities of the electromagnetic wave. These vector Helmholtz equations can then be solved to determine the electric and magnetic field intensities as functions of electrical properties of the material.

If the definitions in Equations (7a), (7b), and (7c) are employed, Maxwell's equations may be expressed in differential form as

$$\nabla \times \vec{E} = -\mu \partial \vec{H} / \partial t, \quad (9a)$$

$$\nabla \times \vec{H} = \epsilon^* \partial \vec{E} / \partial t, \quad (9b)$$

$$\nabla \cdot \vec{E} = 0, \text{ and} \quad (9c)$$

$$\nabla \cdot \vec{H} = 0. \quad (9d)$$

where μ denotes the permeability of the material. For non-magnetic materials such as biological tissue, μ is equal to μ_0 , the permeability of free space. By taking the curl of each side of Equations (9a) and (9b), and then using the results of Equations (9c) and (9d), the following vector Helmholtz equations for electric field intensity (\vec{E}) and magnetic field intensity (\vec{H}) can be obtained:

$$\nabla^2 \vec{E} + k^2 \vec{E} = 0, \text{ and} \quad (10a)$$

$$\nabla^2 \hat{H} + k^2 \hat{H} = 0. \quad (10b)$$

The parameter k is the complex wave number of the material and is related to the electrical properties of non-magnetic materials in the following manner:

$$k = \omega(\mu_o \epsilon^*)^{1/2}. \quad (11)$$

If it is assumed that the electromagnetic wave is propagating through the material in the $+z$ direction, it can be shown that there are solutions to Equations (10a) and (10b) of the form

$$\hat{E} = \hat{E}_o e^{-j(kz - \omega t)}, \quad \text{and} \quad (12a)$$

$$\hat{H} = \hat{H}_o e^{-j(kz - \omega t)}, \quad (12b)$$

where \hat{E}_o and \hat{H}_o are time-independent functions. To realize the objective of associating \hat{E} and \hat{H} with the electrical properties of materials, the complex propagation constant (γ) is defined in terms of the complex wave number as follows:

$$\gamma = \alpha + j\beta = jk = j\omega(\mu_o \epsilon^*)^{1/2}. \quad (13)$$

If γ is substituted into Equations (12a) and (12b), the electric and magnetic field intensities may be expressed in the following form,

$$\hat{E} = \hat{E}_o e^{-\alpha z} e^{-j(\beta z - \omega t)}, \quad \text{and} \quad (14a)$$

$$\hat{H} = \hat{H}_o e^{-\alpha z} e^{-j(\beta z - \omega t)}. \quad (14b)$$

Examination of Equations (14a) and (14b) reveals that the parameter α causes \hat{E} and \hat{H} to be exponentially attenuated as the electromagnetic wave propagates through the material. The parameter β simply causes a phase delay of the electromagnetic wave. Because of these effects, α and β are usually referred to as the attenuation constant and phase

delay constant of the material, respectively. Equation (13) indicates that α and β are dependent on the electrical properties of a material; therefore, it can be observed that the electrical properties will determine the attenuation and phase delay experienced by an electromagnetic wave as it propagates through a material. If Equation (13) is solved for α and β , these parameters may be represented in terms of the material's electrical properties as follows:

$$\alpha = \omega \sqrt{\frac{\mu_0 \epsilon'}{2}} \left[\sqrt{1 + (\epsilon''/\epsilon')^2} - 1 \right]^{1/2}, \text{ and} \quad (15a)$$

$$\beta = \omega \sqrt{\frac{\mu_0 \epsilon'}{2}} \left[\sqrt{1 + (\epsilon''/\epsilon')^2} + 1 \right]^{1/2}. \quad (15b)$$

The attenuation constant and phase delay constant could be expressed in several different formats by using other electrical properties that were defined previously; however, the format used in Equations (15a) and (15b) allows some interesting observations regarding the dependence of electromagnetic wave propagation in a material on the electrical properties of the material. For example, it can be noted that the ratio ϵ''/ϵ' appears in the expressions for both α and β . Generally, electrical properties are used to classify a material as being either "low-loss" or "lossy". For low-loss materials, the value of ϵ' is usually several orders of magnitude greater than the value of ϵ'' . Therefore, the ratio is very small (i.e., $\epsilon''/\epsilon' \ll 1$). Equations (15a) and (15b) reveal that for very small values of ϵ''/ϵ' , the attenuation constant is approximately zero and the phase delay constant is approximately equal to $\omega \sqrt{\mu_0 \epsilon'}$. It may be concluded that an electromagnetic wave propagating through a low-loss material will experience a phase delay as determined by β , but will be only minimally attenuated. For lossy materials such as biological tissues, the value of ϵ'' is comparable in magnitude to ϵ' . Therefore, the ratio ϵ''/ϵ' is significant. It can be seen that for low-loss and lossy materials having the same value of ϵ' , an electromagnetic wave will experience more phase delay in a lossy material than in a low-loss material. It can also be seen that the attenuation constant of a lossy material is

not equal to zero and that an electromagnetic wave will be exponentially attenuated as it propagates through a lossy material. The inverse of the attenuation constant, i.e., α^{-1} , is a measure of the depth at which the amplitude of the electromagnetic wave has decayed to 36.8 percent of its original value, and is defined as the penetration depth of a material. Figure 1 is a graphical representation of the penetration depth of several types of biological tissue as a function of frequency. This graph shows that there will be severe attenuation of an electromagnetic wave in the microwave frequency range as it propagates through tissues.

It has been shown that the electrical properties of a lossy material will exponentially attenuate an electromagnetic wave as it propagates through the material. This attenuation will result in heat dissipation in the propagating medium, and, as might be expected, this heat dissipation is dependent on the electrical properties of the material. This dependence can be evaluated by making use of the complex Poynting vector, \vec{S} , which is defined as

$$\vec{S} = \frac{1}{2} \vec{E} \times \vec{H}^*, \quad (16)$$

where the asterisk denotes the complex conjugate. The negative of the divergence of \vec{S} represents the complex volume density of the power being deposited at a point. This can be expressed mathematically as

$$-\nabla \cdot \vec{S} = -\frac{1}{2} \nabla \cdot (\vec{E} \times \vec{H}^*). \quad (17)$$

The real part of Equation (17) represents the rate per unit volume at which energy from the electromagnetic wave is being dissipated in a material as heat. Correspondingly, the imaginary part of Equation (17) describes the rate per unit volume of electromagnetic energy storage. Equation (17) can be represented as the sum of real and imaginary components by first making use of the expansion

$$\nabla \cdot (\vec{E} \times \vec{H}^*) = \vec{H}^* \cdot (\nabla \times \vec{E}) - \vec{E} \cdot \nabla \times \vec{H}^*, \quad (18)$$

and then substituting Equations (9a) and (9b) for the $\nabla \times \vec{E}$ and $\nabla \times \vec{H}^*$ terms. Since it was originally assumed that \vec{E} and \vec{H} were time harmonic

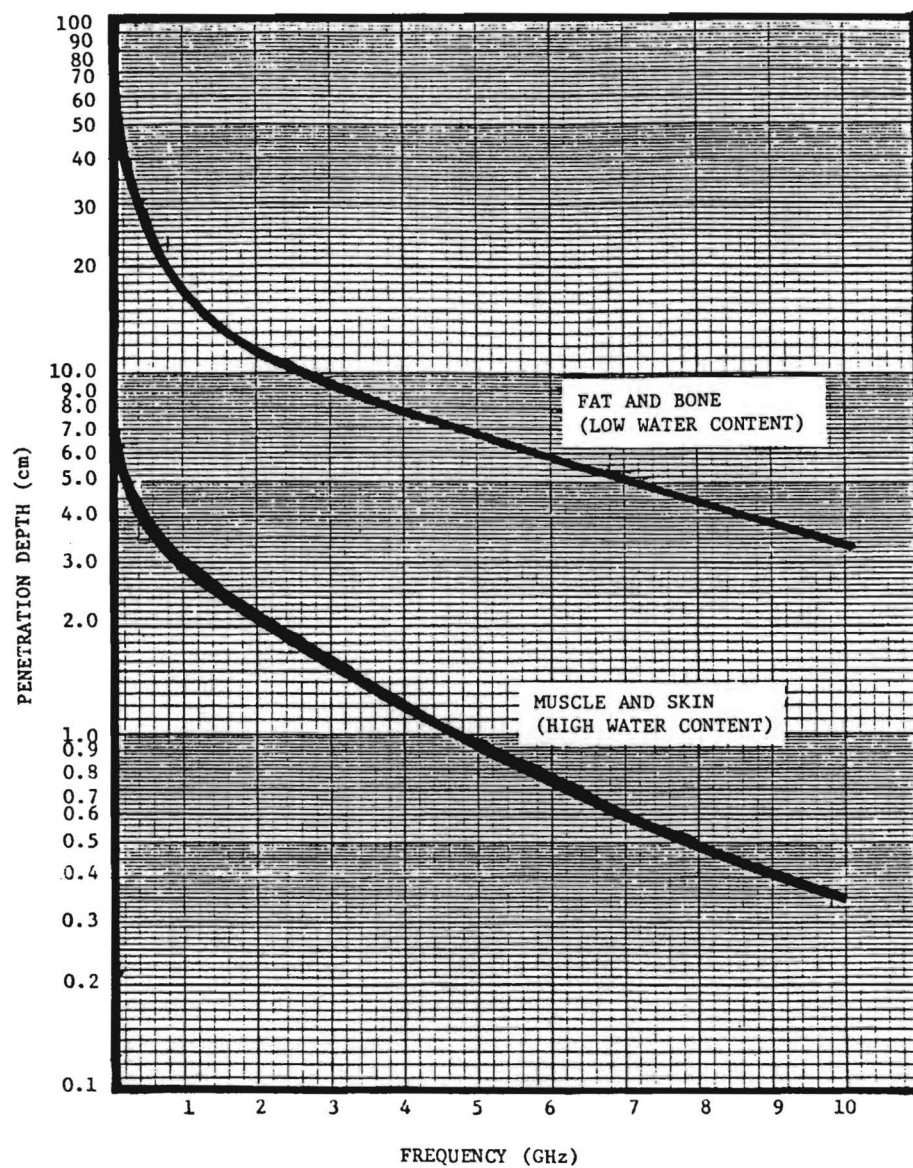


Figure 1. Penetration depth as a function of frequency for several tissue types.

functions, the results of these manipulations are expressed as follows:

$$-\nabla \cdot \vec{S} = \frac{1}{2} \left[(\omega \epsilon'' |\vec{E}|^2) + j\omega \left(\frac{1}{2} \mu |\vec{H}|^2 - \frac{1}{2} \epsilon' |\vec{E}|^2 \right) \right]. \quad (19)$$

From this equation, it can be seen that the rate per unit volume at which energy from the electromagnetic wave is being dissipated as heat in the material can be represented as follows:

$$P = \frac{1}{2} \omega \epsilon'' |\vec{E}|^2 = \frac{1}{2} \sigma |\vec{E}|^2, \quad (20)$$

where P is often designated the "heating potential" of the material. Equation (20) also shows clearly that the dissipation of electromagnetic energy in a material is dependent on the material's electrical properties.

SECTION VI

ELECTRICAL PROPERTY DETERMINATIONS

Techniques for determining the electrical properties of a material are based on measuring the effect a sample of the material has on a well-defined electromagnetic wave. This measured effect is then used with derived formulas to compute the electrical properties of the material. The measurement technique used during this study involved a standing wave pattern inside a short-circuited coaxial transmission line as the well-defined electromagnetic wave. A conventional slotted line with a probe and crystal detector mounted on a movable carriage provided the means for measuring characteristics of the standing wave pattern. Formulas derived by Roberts and von Hippel [12] were then used to compute electrical property values. These formulas were based on the fact that the terminating impedance of a short-circuited coaxial line can be described by two separate equations. One equation involves the standing wave pattern characteristics as measured by a slotted line. The second equation involves the unknown complex propagation constant of the sample material. By setting these two equations equal to each other, a solution for the unknown complex propagation constant can be defined. Once the value of the complex propagation constant is determined, it can be used to compute electrical properties of the sample material. Information regarding the theoretical basis and practical implementation of this technique for determining electrical property values is presented in the following paragraphs.

A. Theoretical Basis

It is a well-known fact that an impedance mismatch exists at the interface between two materials having different electrical properties. In general, an incident electromagnetic wave will be partially or possibly totally reflected and/or refracted when it encounters an impedance mismatch. This fact, coupled with the phase delay and attenuation experienced by an electromagnetic wave travelling through dielectric materials (discussed in Section VII), provide the theoretical basis for the short-circuited coaxial line measurement technique.

A simplified representation of a section of short-circuited coaxial line is depicted in Figure 2. The figure shows that the material sample is positioned at the end of the coaxial line adjacent to the short circuit. An electromagnetic wave with an electric field component \vec{E}_i propagates down the coaxial line in the negative s direction and is incident on the sample. This wave encounters two impedance mismatches -- one at the air/sample interface (Boundary 1) and another at the sample/short circuit interface (Boundary 2). At Boundary 1, a portion of the incident wave is reflected down the coaxial line in the positive s direction. The non-reflected portion of the wave is transmitted into the sample material where it experiences phase delay and attenuation as it propagates toward Boundary 2. At Boundary 2, the high conductivity of the short circuit causes an almost total reflection of the wave. This reflected wave then propagates back through the material (again experiencing phase delay and attenuation) in the positive s direction. Upon arrival at Boundary 1, a portion of the wave is transmitted through the interface and the remainder is reflected back into the material. The transmitted portion of the wave propagates down the coaxial line in the positive s direction while the reflected portion propagates back into the material. This reflection-transmission effect continues with the overall result being a large number of individual waves travelling down the coaxial line in a direction opposite the incoming wave. Collectively, these waves form a composite reflected wave traveling in the $+s$ direction. The parameter \vec{E}_r shown in Figure 2 represents the electric field component of this composite wave.

The ratio of the reflected wave to the incident wave is defined as the reflection coefficient, and this coefficient is expressed mathematically as

$$\Gamma = \frac{\vec{E}_r}{\vec{E}_i} = \Gamma_0 e^{-2\beta_0 s}, \quad (21)$$

where Γ = reflection coefficient,

Γ_0 = reflection coefficient at $s = 0$,

s = position along the coaxial cable, and

β = phase delay constant for the coaxial cable.

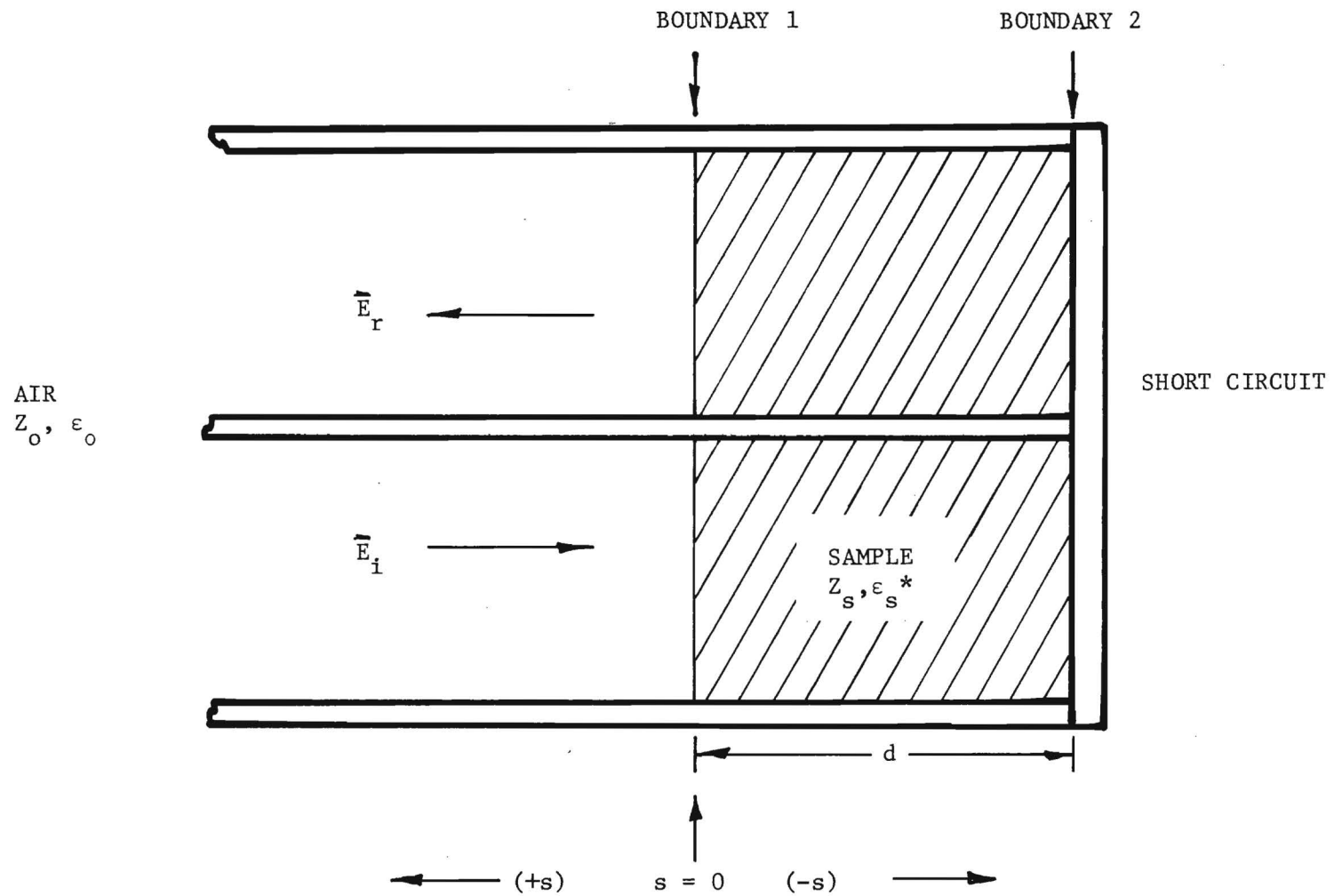


Figure 2. Wave interaction in short-circuited line with sample material in place.

In Figure 2, it is seen that Γ_o is the reflection coefficient at the air/material interface. In general, Γ_o is a complex quantity and its value can be experimentally determined by standing wave pattern measurements.

As previously noted, the short-circuit coaxial line measurement technique is based on the fact that two equations can be derived for the terminating impedance of the Figure 2 configuration. The first equation can be experimentally derived in terms of the parameter Γ_o as follows:

$$Z_{s=0} = Z_o \frac{1 + \Gamma_o}{1 - \Gamma_o} , \quad (22)$$

where Z_o is the characteristic impedance of the air-filled coaxial line. The second equation is dependent on the complex propagation constant and thickness of the material sample, and is defined mathematically as

$$Z_o = Z_s \tanh(\gamma_s d) , \quad (23)$$

where Z_s = characteristic impedance of the sample-filled portion of the coaxial line,

γ_s = complex propagation constant, and

d = sample thickness.

When Equations (22) and (23) are equated, the following result is obtained:

$$\frac{Z_s}{Z_o} \tanh(\gamma_s d) = \frac{1 + \Gamma_o}{1 - \Gamma_o} . \quad (24)$$

Equation (24) can be arranged in a more easily solved format by first noting that Z_o and Z_s are related to the intrinsic impedance of air and the sample material, respectively. The intrinsic impedance of non-magnetic materials is defined as

$$\eta = \left(\frac{\mu_o}{\epsilon} \right)^{1/2} = \frac{j\omega\mu_o}{\gamma} , \quad (25)$$

where the terms are as previously defined. For coaxial cables, the characteristic impedances Z_o and Z_s are linearly proportional to the

corresponding intrinsic impedances by identical proportionality factors; therefore, the ratio Z_s/Z_o can be redefined as

$$\frac{Z_s}{Z_o} = \frac{\eta_s}{\eta_o} = \frac{\gamma_o}{\gamma_s} \quad (26)$$

However, γ_o is the propagation constant of air and can be expressed in terms of λ_o , the wavelength inside the air-filled portion of the coaxial line, as follows:

$$\gamma_o = \frac{j2\pi}{\lambda_o} \quad (27)$$

If the results of Equations (26) and (27) are substituted back into Equation (24) and both sides are divided by the sample thickness d , the following result is obtained:

$$\frac{\tanh(\gamma_s d)}{\gamma_s d} = j \frac{\lambda_o}{2\pi d} \left(\frac{1 + \Gamma_o}{1 - \Gamma_o} \right) \quad (28)$$

This equation represents the desired results. Since the parameters Γ_o , λ_o , and d can all be experimentally determined, Equation (28) can be solved to yield the value for γ_s .

For coaxial cable, the complex permittivity ϵ_s^* of the sample material is related to γ_s in the following manner:

$$\epsilon_s^* = \epsilon'_s - j\epsilon''_s = -\epsilon_o \left(\frac{\lambda_o \gamma_s}{2\pi d} \right)^2 \quad (29)$$

Hence, once γ_s is determined from Equation (28), it is available for use in computing the electrical properties of the material.

It is noted that a slotted-line measurement system can not be used to measure Γ_o directly. It can, however, measure certain characteristics of the standing wave pattern inside the short-circuited coaxial line. Data from these measurements are then used with other procedures to compute Γ_o . These standing wave pattern measurements are described in the next subsection.

B. Measurement Procedure

The procedure used to measure the data necessary for determining the electrical properties of tissue was reasonably extensive and involved several separate activities. These activities included

- o Preparation of the tissue sample,
- o Measurement of tissue sample thickness,
- o Production of discrete cryogenic temperatures, and
- o Measurement of standing wave patterns.

Details applicable to each of these activities are presented in the following paragraphs.

1. Tissue Sample Preparation

Several different procedures were used before a satisfactory method was found for preparing the ring-shaped tissue samples necessary to fit in the specially-designed sample holder shown in Figure 3. Each of these procedures began by thawing a cryogenically-preserved kidney. A kidney immediately after thawing is shown in Figure 4a. After thawing, the capsule (a thin, transparent membrane encasing the entire kidney) and any fatty tissue were moved. The procedure finally adopted for preparing tissue samples involved the sequence of steps shown in Figures 4b through 5c. The device shown in Figures 4b and 4c was first used to section the kidney longitudinally. This device consisted of a Plexiglas cutting base and two surgical microtome blades attached to Plexiglas handles. The Plexiglas handles were designed to fit into the guide slots in the cutting base. With a kidney positioned in the base, the cutting tools were used with a guillotine action to provide tissue slices with uniform thickness as shown in Figure 4d. To alleviate the problems encountered in efforts to precisely slice tissue that is at room temperature, the kidneys were thoroughly chilled in a refrigerator prior to slicing.

Both cortex and medulla tissue was used for electrical property measurements. Cortex tissue was available from the outer or peripheral regions while medulla tissue was available from the inner or central

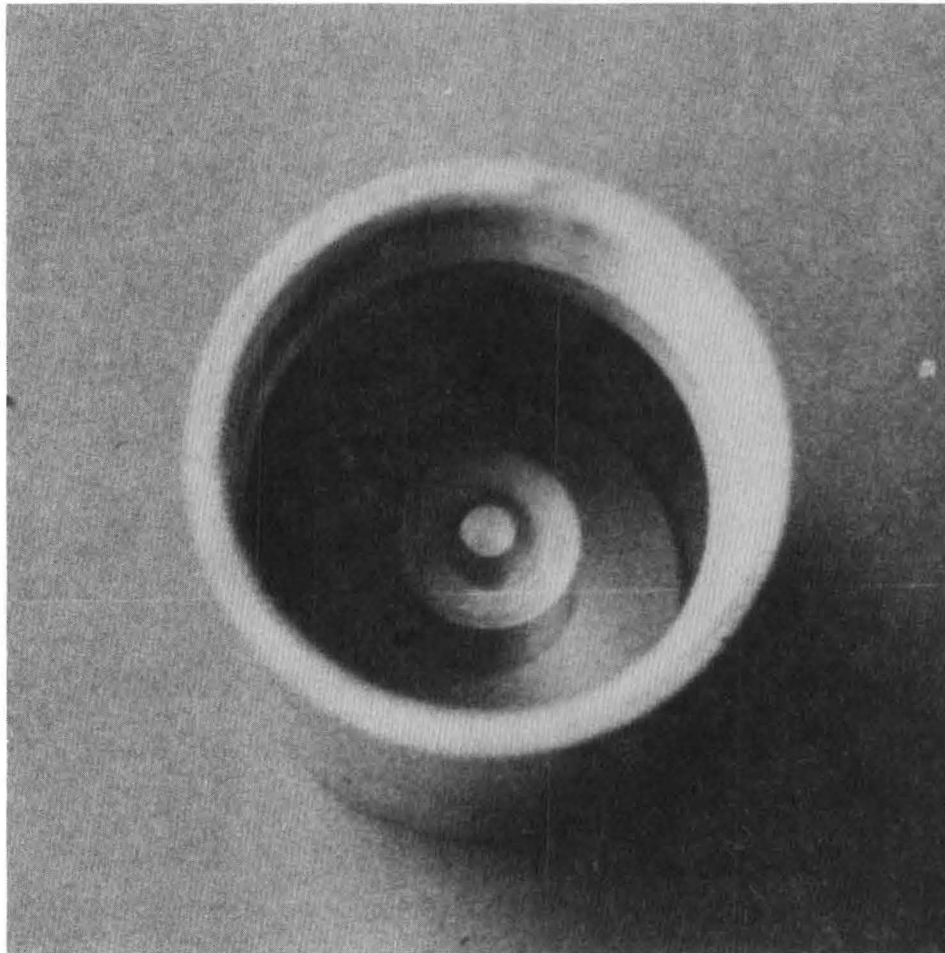
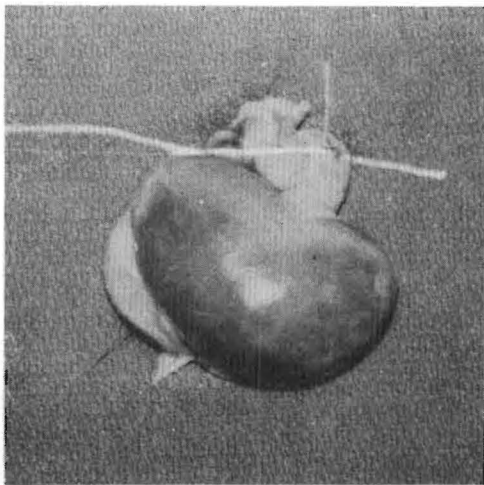
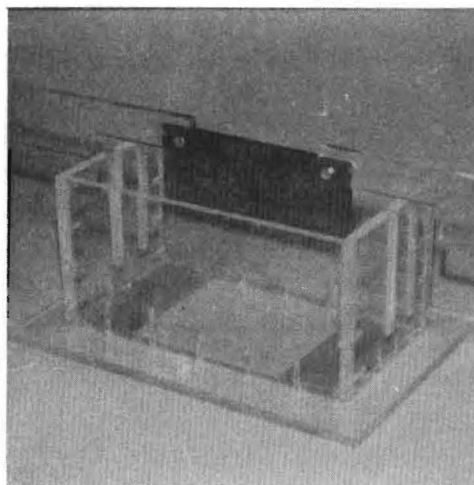


Figure 3. Holder designed especially for ring-shaped tissue samples.



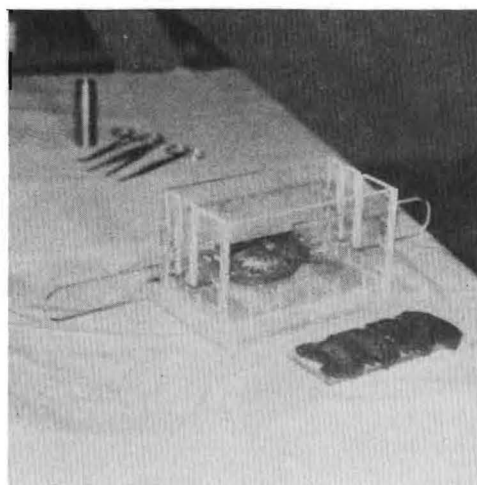
(4a)



(4b)

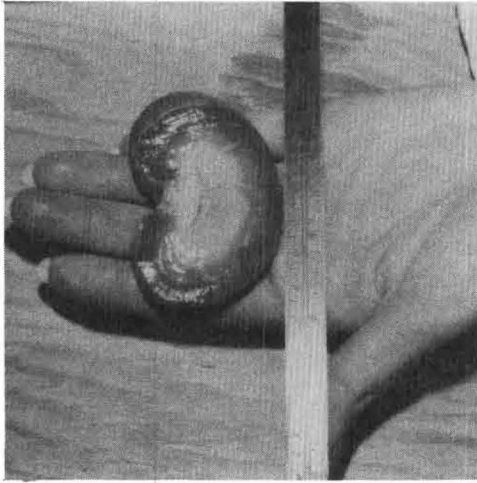


(4c)

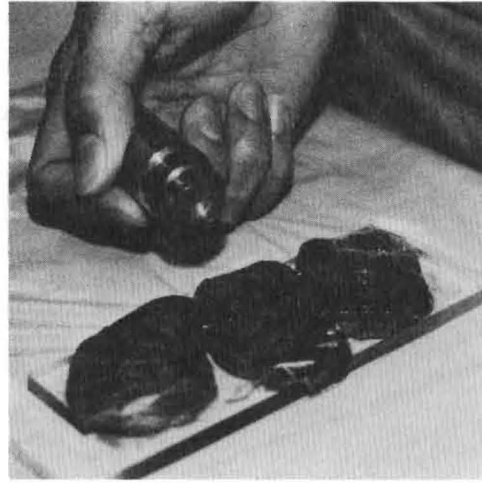


(4d)

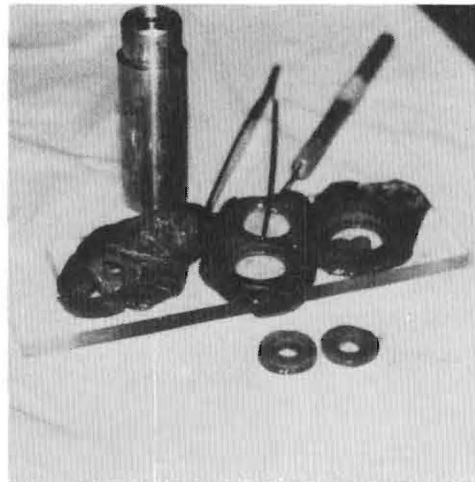
Figure 4. Steps in the procedure for preparing tissue samples:
sample cutter.



(5a)



(5b)



(5c)

Figure 5. Steps in the procedure for preparing tissue samples: tissue rings.

regions of the sectioned kidneys (see Figure 5a). Because of both the location and shape of the two tissue types, cortex tissue samples were much more easily obtained. In fact, it was not possible to obtain a sufficiently large sample of medulla tissue from many of the kidneys.

Once slices were obtained, they were chilled and the specially-designed cutter shown in Figure 5b was used to provide ring-shaped samples suitable for the sample holder (see Figure 5c). These ring-shaped samples were approximately 4 millimeters in thickness and the tissue thickness needed by the sample holder was 12 millimeters; therefore, three individual rings of tissue were stacked on top of each other in the sample holder.

2. Tissue Sample Thickness Measurement

When the three samples were stacked in the holder, their total thickness had to be measured with precision. As was evident in earlier sections that discussed the theory underlying the computations, even small errors in measuring sample thickness would cause appreciable inaccuracy in the final computations of electrical property values. Consequently, an extensive effort was devoted to providing an accurate method for tissue sample thickness measurement. The method that ultimately evolved used the device shown in Figure 6. Operation of this device was based on the fact that an ohmmeter could be used to indicate the initial contact between a needle probe and either the sample or its holder. The procedure required that the probe be slowly lowered into the holder until electrical contact with either the sample or the short-circuiting plate was indicated on the ohmmeter. The difference between probe depths needed to contact the sample and the short-circuiting plate was measured using a precision scale, and this difference represented the sample thickness. This procedure was generally repeated at five different locations on the sample, and the averaged thickness was used in the electrical property computations. Measurement accuracy was determined to be ± 0.3 millimeter for samples intended to have a 12 millimeter thickness.

3. Production of Discrete Cryogenic Temperatures

A major objective of this study was to determine the electrical properties of tissue as a function of temperature. This

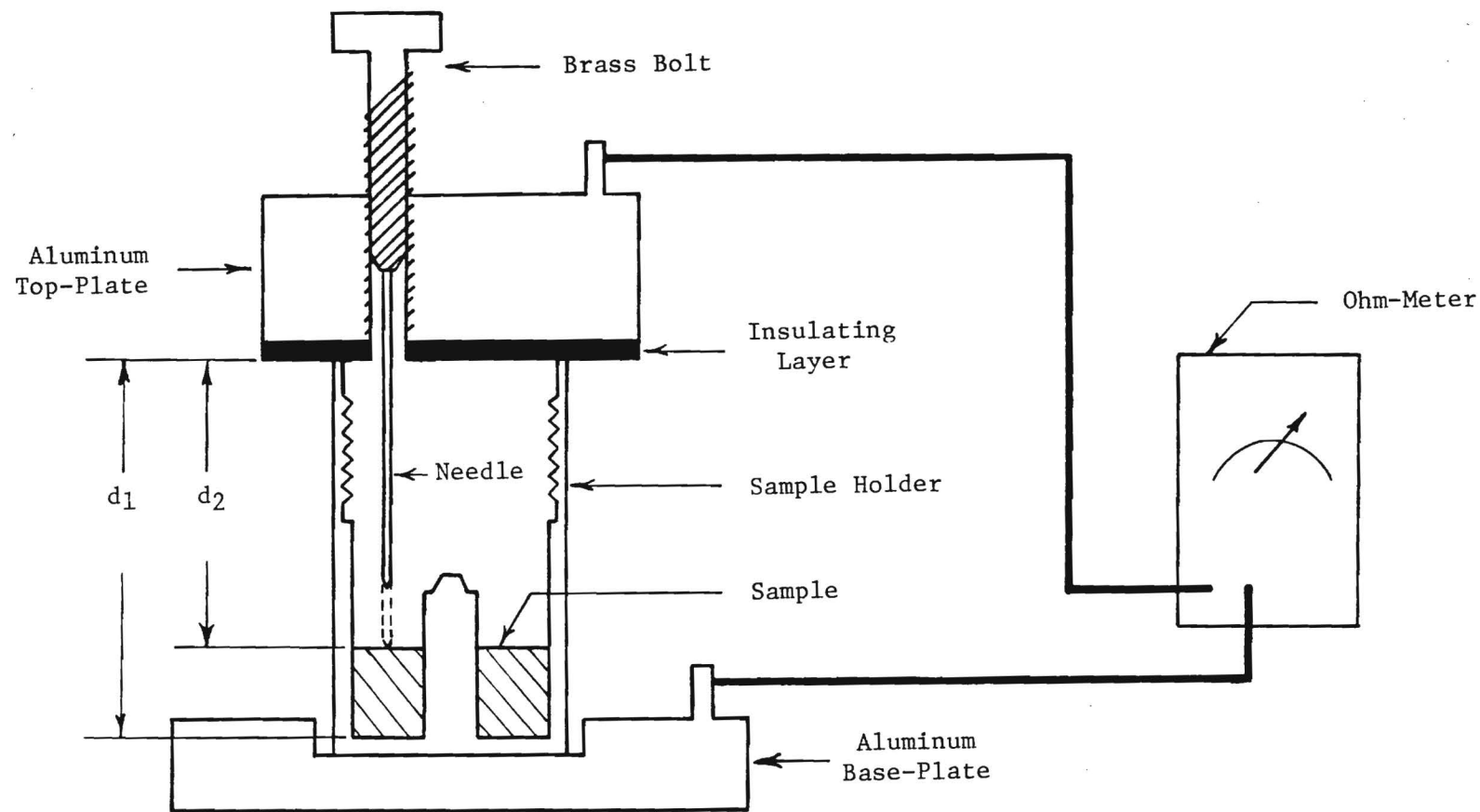


Figure 6. Diagram of device used to measure sample thickness.

objective was important in efforts to design an effective electromagnetic thawing system because existing data on the electrical properties of water (a major constituent of tissue) show marked changes within the temperature range where the phase change occurs (where water changes either from a liquid to solid or from a solid to liquid state). Similar electrical property changes were therefore expected within tissue, and must be carefully designed for in the thawing system if thermal runaway is to be avoided.

The method used to provide stable, discrete cryogenic temperatures for the tissue sample involved immersing the sample holder in a constant-temperature bath as shown in Figure 7. To assure temperature equilibration, the holder containing the tissue sample was maintained in the bath for approximately one-half hour prior to initiation of the measurements. Baths at different temperatures were provided by mixing solutions of either water and methanol or water and cupric chloride. By varying the water concentration in these solutions, different freezing points could be provided. These freezing points were realized by suspending the beaker containing the solution in a mixture of acetone and dry ice, whose freezing point was -79°C . The solutions were not allowed to freeze solid, but instead were maintained in the acetone/dry ice mixture until they became a semi-solid slush. In this phase-transitional state, the temperature could be maintained constant and equal to the freezing point of the solution. The individual beakers of semi-solid solution were mounted in an insulated container that was positioned such that the sample holder could be immersed in them. This arrangement is shown in Figure 8. The small pieces of dry ice between the beaker and the container wall helped maintain the temperature of the solution at the freezing point and to offset the initial warming when the sample holder was first immersed in the solution.

4. Measurement of Standing Wave Patterns

As noted in Paragraph A of this section, standing wave pattern measurements can be used to obtain values for Γ_0 , which may then be used to compute the electrical properties of materials. The actual measurements involve determining standing wave pattern characteristics

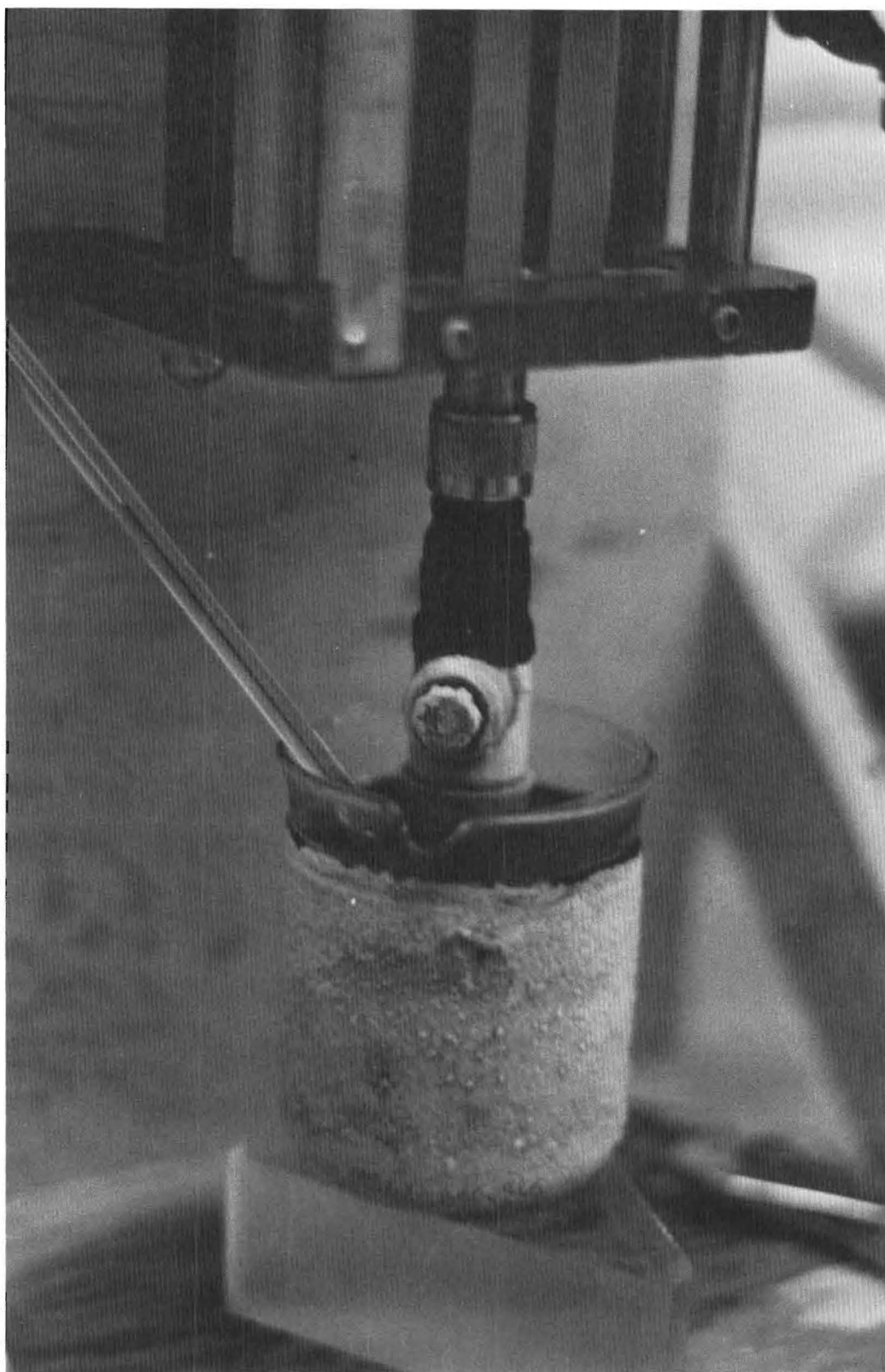


Figure 7. Tissue sample holder immersed in low-temperature bath.

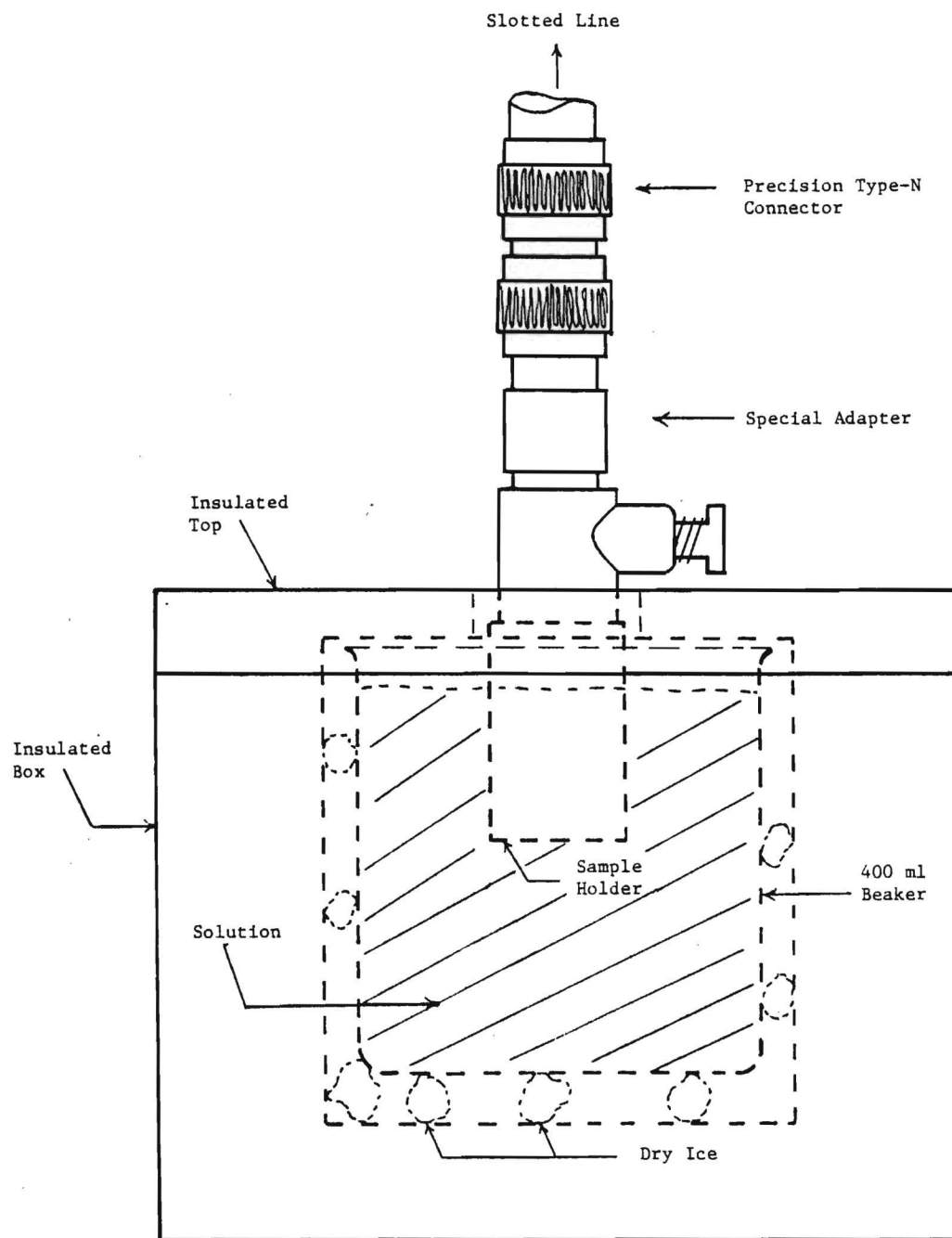


Figure 8 . Diagram of constant temperature bath.

for two cases, i.e., when the short-circuited coaxial line is empty and when it contains a sample of the test material. Measurements on the empty line provide air data for reference purposes. Typical standing wave patterns that might exist in a coaxial line are shown in Figure 9. Differences in the two patterns are due to phase delay and attenuation experienced by components of the composite reflected wave. Characteristics of the standing wave pattern needed to compute Γ_o are

- the distance between the air/sample material interface and the first minima in the air-filled portion of the coaxial line (denoted x_o in Figure 9b), and
- the voltage standing wave ratio (VSWR) which is defined as the ratio of the maximum-to-minimum voltage values in the coaxial line.

In order to determine Γ_o from the values of x_o and the VSWR, first recall that Γ_o is a complex quantity that can be expressed in the following amplitude-phase format:

$$\Gamma_o = |\Gamma_o| e^{-j2\psi} \quad (30)$$

The magnitude, $|\Gamma_o|$, and phase, 2ψ , of Γ_o can then be computed from the values of VSWR and x_o by using the following relationships [13]:

$$\Gamma_o = \frac{\text{VSWR} - 1}{\text{VSWR} + 1}, \text{ and} \quad (31)$$

$$2\psi = 4\pi \left(\frac{1}{4} - \frac{x_o}{\lambda_o} \right) \quad (32)$$

Normally, the sample material is positioned in a specially-designed sample holder (to be described in the following subsection) that is then attached to the slotted-line system. Since this sample holder is usually several wavelengths long, it is not possible to directly measure the position of the minimum point, x_{s1} , that determines the value of x_o (see Figure 9). However, this problem is easily solved by using the following procedure. First, the position of a minimum point in the slotted-line portion of the system is measured with the sample holder empty. This position is denoted as x_e in Figure 9a. The sample is then placed in the sample holder and again, the position of a minimum point in the slotted line portion of the system is measured. This position is denoted as x_{s2} in Figure 9b. The value of x_o can then be computed from the following formula [13]:

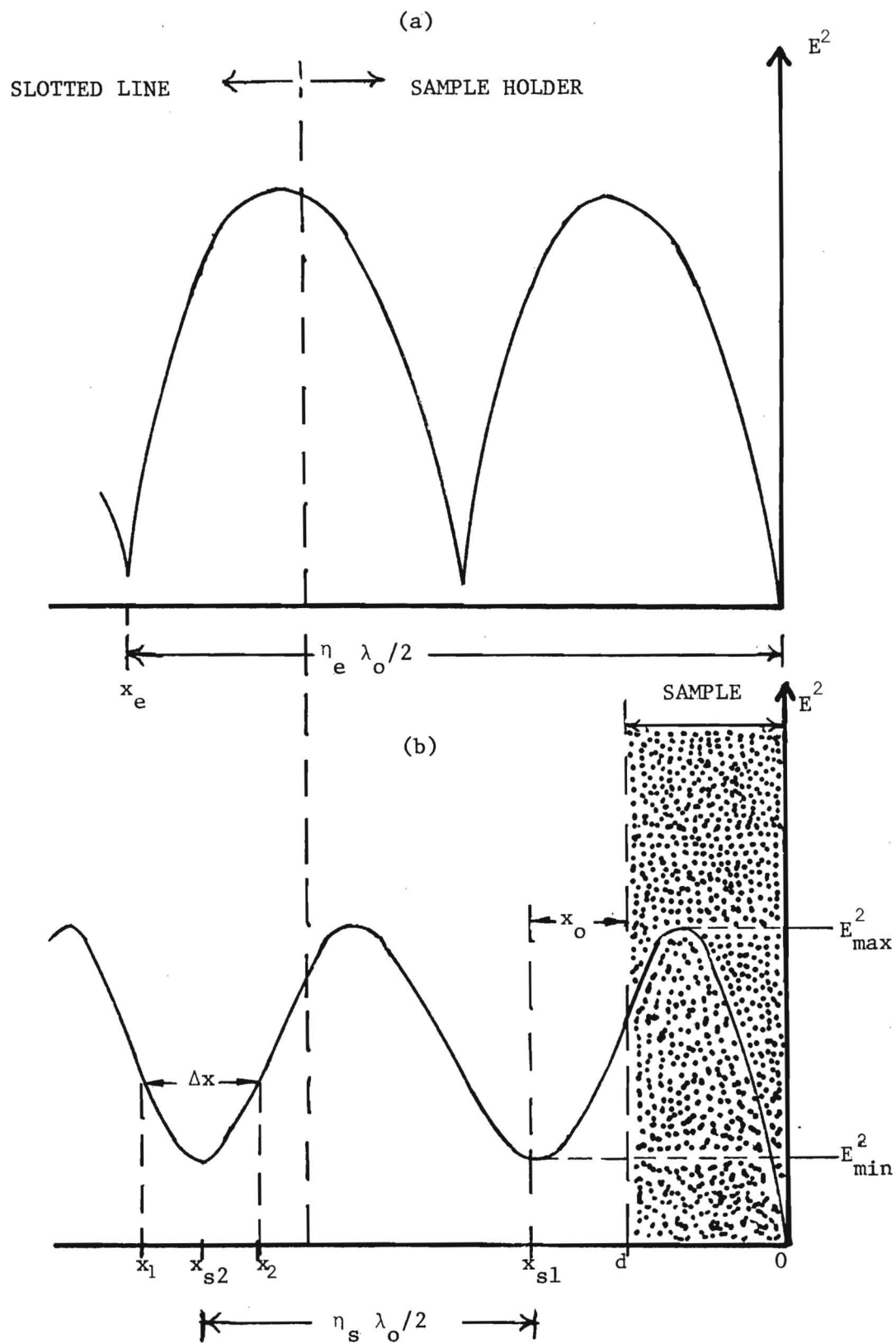


Figure 9. Standing wave pattern inside short-circuited coaxial line (a) coaxial line empty and (b) coaxial line containing sample.

$$x_o = x_e - x_{s2} + \frac{\eta_e \lambda_o}{2} + \frac{\eta_s \lambda_o}{2} - d, \quad (33)$$

where η_e = number of half-wavelengths between x_e and the short circuit, and

η_s = number of half-wavelengths between x_{s2} and x_{s1} .

Often, the VSWR in the short-circuited coaxial line will be extremely high. Therefore, to avoid probe interference effects and prevent saturation of the crystal detector, the travelling probe is usually operated only in low-power regions of the standing wave pattern (i.e., near the minimum points in the standing wave pattern). This means that the value of E_{\max} can not be measured directly and, hence, the VSWR must also be determined indirectly.

The procedure for indirectly measuring the VSWR makes use of the fact that the equation describing E^2 at any point x in a lossless coaxial line can be expressed as follows [13]:

$$E^2(x) = \left[E_{\max} \sin \frac{\pi \Delta x}{\lambda_o} \right]^2 + \left[E_{\min} \cos \frac{\pi \Delta x}{\lambda_o} \right]^2, \quad (34)$$

where $\Delta x = x_1 - x_2$ is the distance between equal power points as shown in Figure 9b. If Equation (34) is solved for the ratio E_{\max}/E_{\min} , the following result is obtained:

$$\text{VSWR} = \frac{E_{\max}}{E_{\min}} = \frac{\left[\left(\frac{E(x)}{E_{\min}} \right)^2 - \cos^2 \left(\frac{\pi \Delta x}{\lambda_o} \right) \right]^{1/2}}{\sin \left(\frac{\pi \Delta x}{\lambda_o} \right)}. \quad (35)$$

The position x is usually selected so that $E^2(x)$ is either 3 dB or 10 dB above E_{\min}^2 . For these two cases, the square of the ratio $E(x)/E_{\min}$ will simply be equal to either 2 or 10, respectively. (Hence, this procedure is often referred to as the "twice-minimum" or "ten-times minimum" measurement procedure.) Therefore, by measuring the positions (x_1 and x_2 in Figure 9b) where $E^2(x)$ is some selected value higher than

E_{\min}^2 , the VSWR can be computed. Also, it is noted that, since the standing wave pattern is symmetrical about the position x_{s2} , x_{s2} can also be computed from the measured values of x_1 and x_2 as the following equation shows:

$$x_{s2} = \frac{x_1 + x_2}{2} \quad (36)$$

A similar procedure can be used to measure the minimum position x_e for the empty short-circuited line.

An equipment configuration involving a slotted line was used to make the measurements necessary for determining tissue electrical properties. With the exception of a specially-designed tissue holder, all components of this measurement system were commercially-available devices. A block diagram and photograph of the measurement system are shown in Figures 10 and 11. Referring to Figure 10, it is seen that the basic signal for the system was provided by a signal generator. This generator was tuned to the frequency at which electrical property values were to be determined (either 918 MHz or 2450 MHz), and its output was square-wave, amplitude modulated at 1 kHz. This modulation was necessary because it corresponded with the center frequency of the narrowband SWR meter. The output signal of the generator was first routed through an isolator that prevented reflected signals from damaging the generator's output circuitry. From the isolator, the signal was filtered by a low-pass microwave filter to remove any spurious or harmonic components from the system. The filtered signal was then coupled to a three-port directional coupler. The largest majority of the signal passed directly through the directional coupler and on to other components in the measurement system; however, a small portion was extracted and used with a frequency meter and power meter to indicate the signal frequency. When the frequency meter was off-tuned, the power meter could be used to indicate the signal level in the system. The straight-through signal out of the directional coupler was routed next to a precision step attenuator adjustable in 1-dB steps. This attenuator was used to (1) adjust the signal magnitude to a level

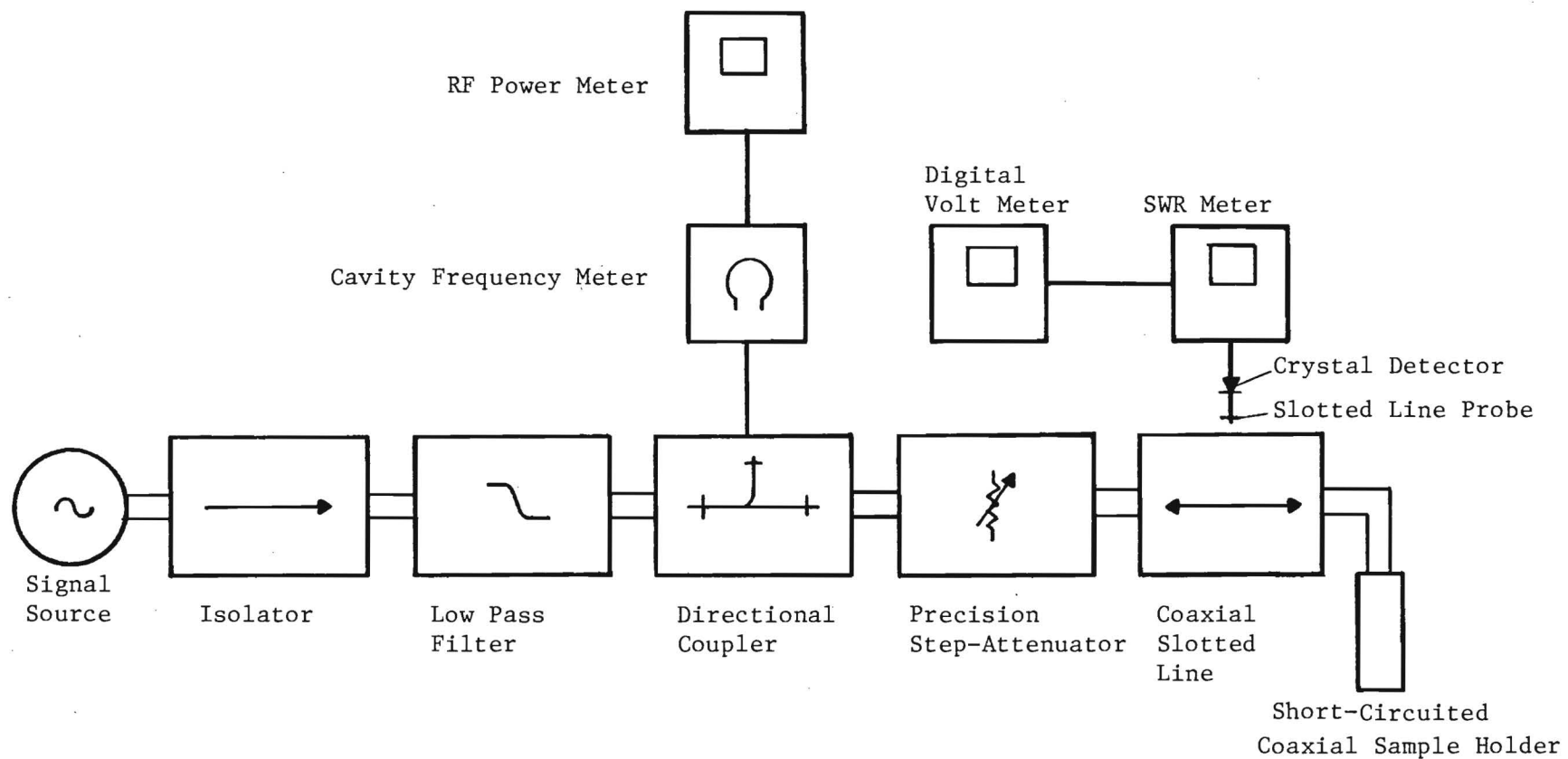


Figure 10. Block diagram of the short-circuited coaxial line measurement system.

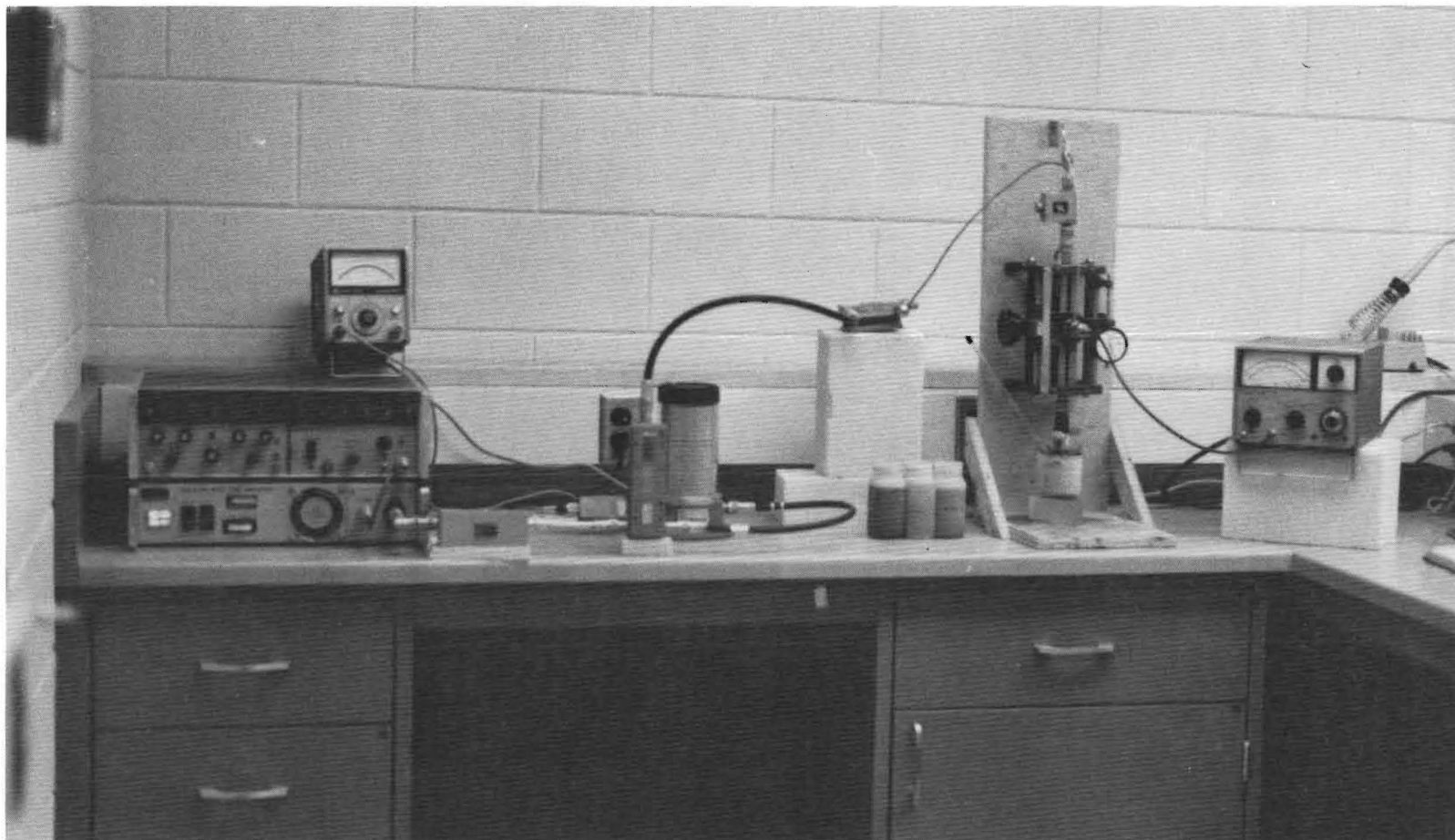


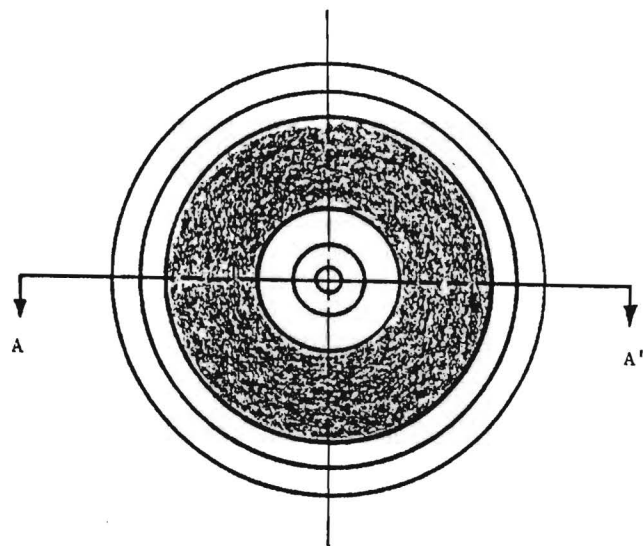
Figure 11. Photograph of the short-circuited coaxial line measurement system.

suitable for the voltage measurements in the slotted line, (2) set the 3 dB and 10-dB levels for the "twice-minimum" and "ten-times-minimum" measurements, and (3) reduce the amplitude of any undesired signals that might be reflected back toward the signal source.

Beyond the attenuator, the signal was routed to a coaxial slotted line that provided a carriage upon which a movable probe was mounted. This probe could be inserted into the coaxial line and positioned at a point near the center conductor of the line. From the slotted-line, the signal was fed to the short-circuited sample holder. The cross-sectional dimensions of the main body of the sample holder conformed to the dimensions of standard 0.875-inch rigid coaxial line. A special adapter was used to mate the sample holder with connectors on the slotted line. A sectional view of the sample holder's main body is shown in Figure 12. As is evident in the figure, a ring-shaped tissue sample was positioned at the bottom of the holder adjacent to the short-circuiting plate. A photograph of the sample holder was shown in Figure 3. The signal travelled through the sample holder, interacted with the tissue sample and the short-circuiting plate, and caused a composite reflected signal to be generated. The superposition of this reflected signal and the original signal resulted in a voltage standing wave on the coaxial line. The slotted line probe measured the relative strength of this standing wave as a function of position, and provided a signal for detection and demodulation by a square-law crystal detector. The demodulated signal from the detector was coupled to a SWR meter whose scale readings provided the desired measurement data.

The data obtained using the slotted line measurement system represented an important part of the overall procedure that was used during experimental efforts to determine the electrical properties of tissue. This overall procedure, including the slotted-line measurement system, is summarized as follows:

- Energize equipment, allow a 30-minute warm-up, and adjust the frequency and power level to desired values. Adjust the probe depth in the slotted line for the minimum depth that permits steady indications of the standing wave pattern on the SWR meter.



SCALE: 3:1

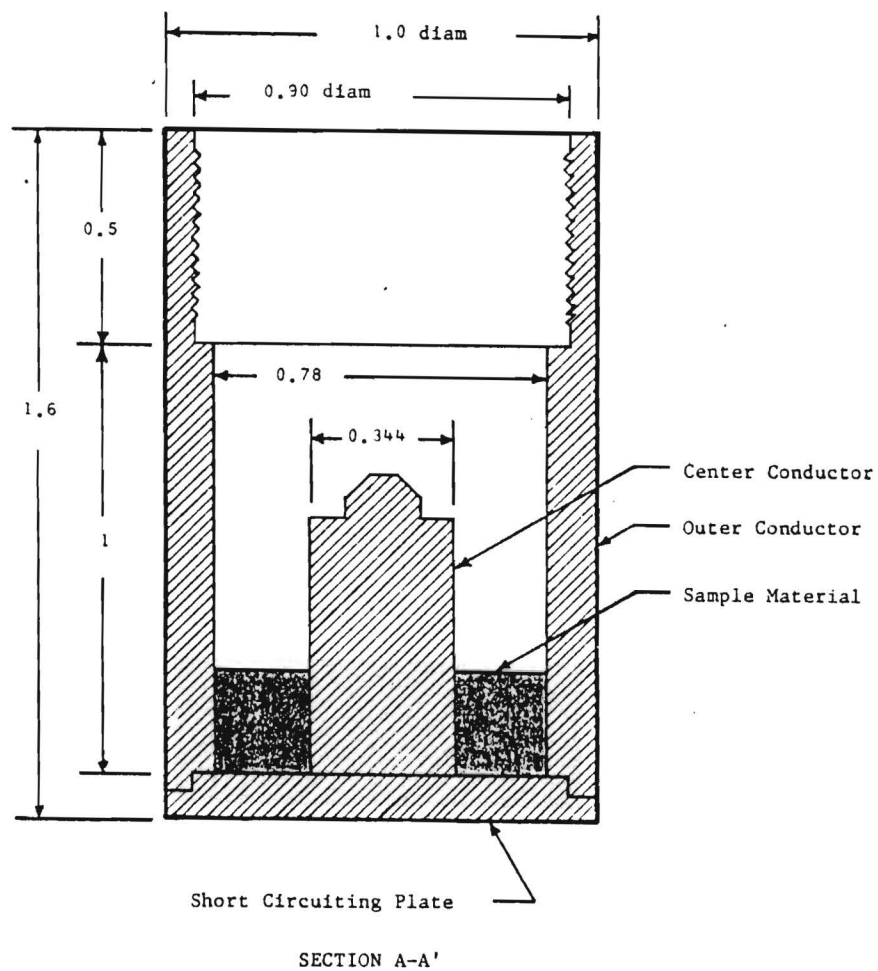


Figure 12. Cross-sectional view of sample holder main body.

- Attach an empty sample holder to the slotted line output and make reference measurements using either the "twice minimum" or "ten-times-minimum" method described earlier.
- Remove sample holder from slotted line, insert sample, and measure sample thickness.
- Attach sample holder to the slotted line and immerse it in a solution of the desired temperature. After approximately 30 minutes, measure the standing wave pattern using either the "twice minimum" or "ten-times-minimum" method described earlier. Repeat the measurement several times to assure valid readings.
- Remove the sample holder from the temperature bath and slotted line, and immediately measure the sample thickness. Note any measurable increase in thickness caused by low-temperature expansion.
- Attach the sample holder to the slotted line and immerse it in a solution whose freezing point occurs at the next desired temperature. (The first measurements were usually made at room temperature, with subsequent measurements made at progressively lower temperatures.)
- The above steps were continued until measurements were made at the two frequencies, for the two different tissue types, over the -68°C to $+20^{\circ}\text{C}$ temperature range, and for the 0, 5, and 10 percent concentrations of dimethyl sulfoxide.

It is noted that every step of this measurement process had to be performed with extreme precision and accuracy. Cable connections, sample thickness, bath temperature, signal frequency and power level, probe depth, etc., were constantly checked during the measurement process to assure valid data.

When the measurement process was completed, the data and appropriate housekeeping information were entered into the computer program. This program solved the transcendental equation for $\gamma_s d$ (see Equation (28)). Once $\gamma_s d$ was determined, components of ϵ_s^* could be readily computed using Equation (29). From these components, the electrical properties of dielectric constant, conductivity, and loss tangent were determined according to Equations (8a), (7c), and (8c).

E. Assessment of Measurement Accuracy

Associated with the short-circuited coaxial line measurement system were the following two primary sources of measurement error:

- errors in sample thickness measurement, and
- errors in standing wave pattern measurements.

The significance of these errors is dependent on the sample thickness being used. For example, if the sample thickness is approximately one-half wavelength (within the sample material), accuracy of the measured electrical properties will be significantly influenced by small errors in the standing wave patterns, but not significantly influenced by small errors in sample thickness measurements. Conversely, if the sample thickness is approximately one-quarter or three-quarters wavelength (within the sample material), the opposite effects will exist. The basis for these wavelength-dependent effects is presented by von Hippel [12].

Repeated measurements with the device for measuring sample thickness (see Figure 6) revealed that repeatable measurements could be made within approximately ± 0.2 millimeter. However, there was no satisfactory method for determining the accuracy of the standing wave pattern measurements. Consequently, in order to make possible a determination of the accuracy of electrical property data, measurements during this study were made with sample thickness of either one-fourth or three-fourths wavelength (within the tissue).

In addition to errors associated with sample thickness and standing wave pattern measurements, a number of more subtle error sources were encountered. These included irregularities in the sample geometry resulting from either non-perfect fit of the sample in the holder, non-uniform sample thickness, condensation and/or frost on the interior walls of the sample holder, physical changes in sample holder dimensions due to thermal expansions and contractions, and errors in measuring the temperature of the sample in the sample holder. This last error source was particularly troublesome when measurements were being made near the phase transition temperature of the kidney tissue. Within a relatively narrow range of temperatures around the phase transition temperature, electrical property values change very rapidly and, for this reason, accurate knowledge of temperature was important. It is estimated that temperature could be determined within an accuracy of $\pm 3^{\circ}\text{C}$ over the -68°C to $+20^{\circ}\text{C}$ range.

In an effort to quantitate the effects of error sources, a series of measurements was performed using deionized water as the sample material. Deionized water was selected as the sample material for these measurements because its electrical properties had been thoroughly characterized by an alternate measurement system [14]. Water samples with a thickness corresponding to either one-half or three-fourths wavelength (within the water) were used. Results of the measurements are presented in Table I. The dielectric constant, loss tangent, and conductivity values in the table were determined assuming that a ± 0.2 millimeter error existed in measuring the sample thickness. From electrical property values shown in the table, it is seen that, when a three-fourths wavelength sample thickness is used, measurement accuracies within ± 5 percent were obtained. However, difficulties with an irregular-shaped sample such as kidney tissue resulted in thickness measurements being accurate only within ± 0.3 millimeters. Therefore, it was estimated that the accuracy of electrical property values determined during this study is ± 10 percent.

Where possible, remedial measures were incorporated to reduce error sources to the minimum possible; however, errors still remained and are reflected in some of the electrical property values as large standard deviations.

TABLE I
ELECTRICAL PROPERTIES OF DEIONIZED WATER

	Dielectric Constant	Loss Tangent	Conductivity (mmho/cm)
Reference Values [14]	77	0.14	14.7
Measured using half wavelength thick sample	69.2 \pm 0.1	0.11 \pm 0.003	10.2 \pm 0.3
Measured using three-quarter wavelength thick sample	77.7 \pm 3	0.14 \pm 0.003	14.8 \pm 0.3

SECTION IX

THERMOMETRY DEVICE INVESTIGATIONS

Thermometry devices capable of accurately measuring cryogenic temperatures in the presence of electromagnetic waves and over a wide dynamic range were not available at the time of this study. Yet such devices are essential in studies concerned with the electromagnetic recovery of large, cryogenically-preserved organs. In view of this situation, a limited investigation was conducted to define a thermometry device capable of accurately measuring temperature over a range of approximately -80°C to $+20^{\circ}\text{C}$, and in the presence of electromagnetic waves with field strengths comparable to those necessary for organ thawing.

Ideally, the desired thermometry device would consist of a small, implantable temperature sensor that was electromagnetically-transparent and which could be connected to control/monitoring circuitry via electromagnetically-transparent leads. Conventional thermometry devices such as thermistors and thermocouples are relatively large in size and made of conductive materials. Consequently, there is typically significant interaction with the electromagnetic waves. This interaction causes distortion of the wave and localized heating of the thermometry device. Recently-developed liquid-crystal probes are operational only over narrow temperature ranges and are too large for convenient implantation in tissue. Several new and somewhat exotic devices are under development, but none had reached the point of widespread commercial availability at the time of need during this study. Therefore, an investigation was undertaken to determine whether recently-introduced, ultra-small thermistors could be used as the temperature sensor in thermometry devices designed to operate in the presence of electromagnetic waves and over cryogenic temperature ranges. Four thermistors with two different sets of physical and electrical characteristics were purchased for evaluation. Characteristics of these thermistors were as follows:

	<u>Type 1</u>	<u>Type 2</u>
Diameter (inches)	0.005	0.01
Dissipation Constant (mW/°C)	0.045	0.09
Time Constant (seconds)	0.12	0.5
Zero-Power Resistance (ohms at 25°C)	5000	3000

The size of one of these thermistors is shown in relation to a pinhead in Figure 13. Upon receipt, arrangements were made with a microcircuitry laboratory to attach No. 38 Gauge wire to the thermistor leads. The resulting temperature sensors were then connected to balanced bridge circuits of the type commonly used for temperature monitoring. When measurements were made over the cryogenic temperature range, considerable inaccuracy was noted. Investigations revealed this inaccuracy to be due to the current provided to the thermistor by the bridge circuit. This current both induced self-heating in the thermistor and varied as the thermistor resistance changed with temperature. This led to design efforts aimed at providing improved monitoring and control circuitry. The result was a breadboarded circuit that used operational amplifiers and feedback paths to provide a substantially lower current to the thermistor. This circuit also maintained the magnitude of this current at a constant level even when the thermistor's resistance was changing in response to temperature. These two features of the circuit eliminated the previously-observed data inaccuracies caused by thermistor self-heating and variable current magnitude.

Using this thermometry device configuration (ultra-small thermistors connected to improved control/monitoring circuits via straight wire leads), temperature measuring capabilities were again evaluated, this time during exposure to a variety of electromagnetic waves. These evaluations revealed temperature errors of 8.8°C when this configuration was used in organ thawing applications. The wire leads connecting the control/monitoring circuit to the thermistor were then twisted, and the evaluations were repeated. Under these conditions, temperature errors less than 1°C resulted. Errors of this magnitude were acceptable to

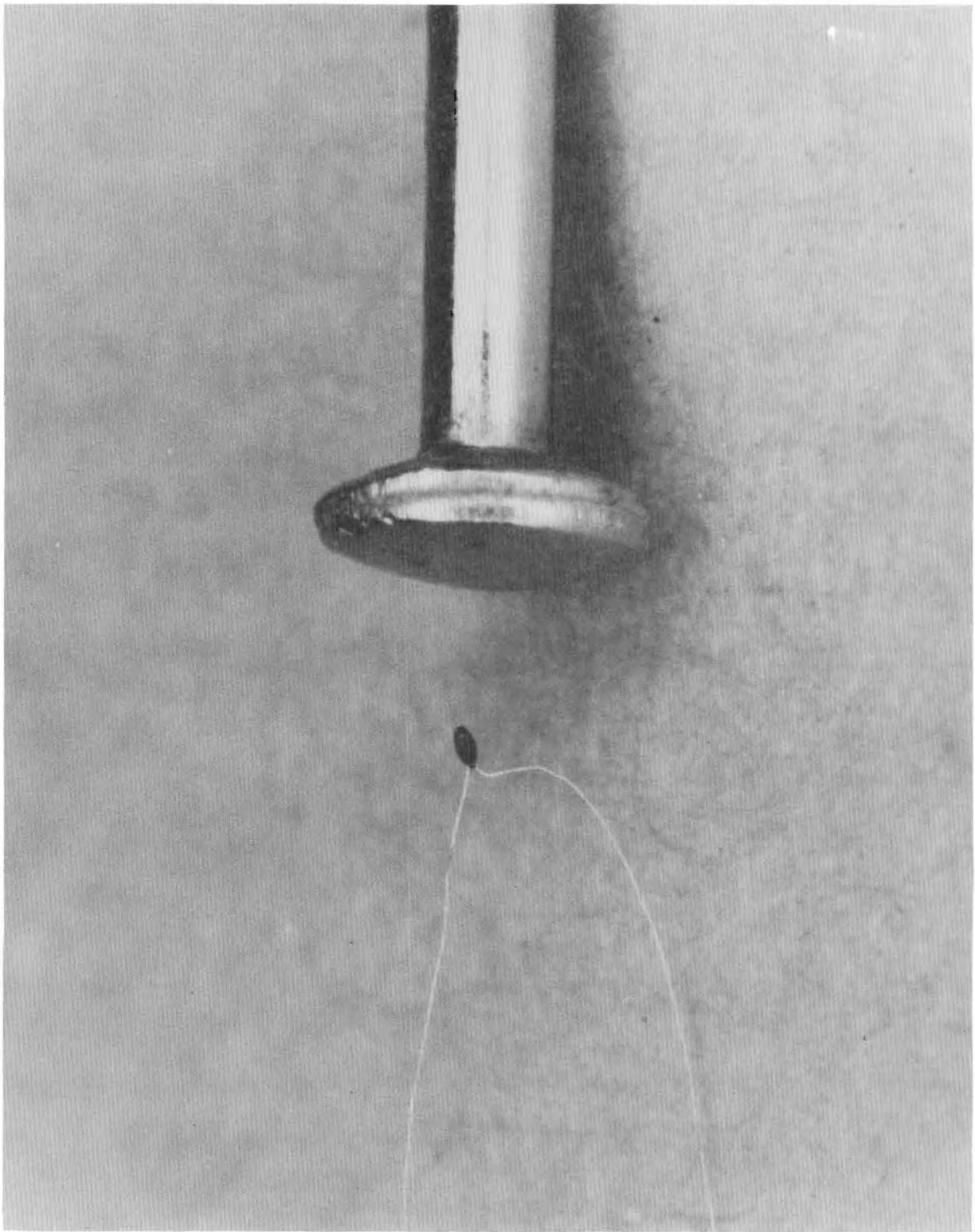


Figure 13. Thermistor size in relation to pin head.

this study concerned with electromagnetic recovery of cryogenically-preserved organs; further, they are generally acceptable in many of the research studies concerned with electrohyperthermia as a cancer treatment modality.

Once efforts to reduce temperature measurement errors to tolerable levels were successful, the thermometry investigation was directed to identifying techniques by which the thermistor could be implanted. This resulted in a procedure for inserting the thermistor beads and their twisted leads in a sheath of small-diameter, Teflon tubing. Epoxy cement was used to secure the thermistor bead in a position such that it barely extended beyond the distal end of the tubing. The Teflon tubing could then be positioned in a hypodermic needle and inserted into either phantom modeling materials or living tissue. A length of Teflon tubing, with a thermistor positioned in the distal end, is shown in a hypodermic needle in Figure 14. When the hypodermic needle was metallic, it was removed from the tissue volume by withdrawing it back over the tubing. Hypodermic needles made of nonconductive materials were either withdrawn or left in place during heating.

The concept of a thermometry device consisting of a small-diameter thermistor with twisted leads inserted in a sheath of Teflon tubing was extended because of the need to measure temperature at multiple locations in an organ during thawing. In this extension of the concept, several thermistors were positioned in-line in a common sheath of Teflon tubing. A small slot was cut in the tubing at the location of each thermistor to assure adequate contact with the material whose temperature was being measured. Leads for the thermistors were routed out the proximal end of the tubing and connected to appropriate circuitry. Hypodermic needles were again used to insert the tubing and thermistors in modeling materials or tissue. Five thermistors positioned 0.375 inch apart in a Teflon sheath are shown in Figure 15. This configuration provided a satisfactory way to monitor temperature profiles in organs during exposure to electromagnetic waves and over cryogenic temperature ranges.

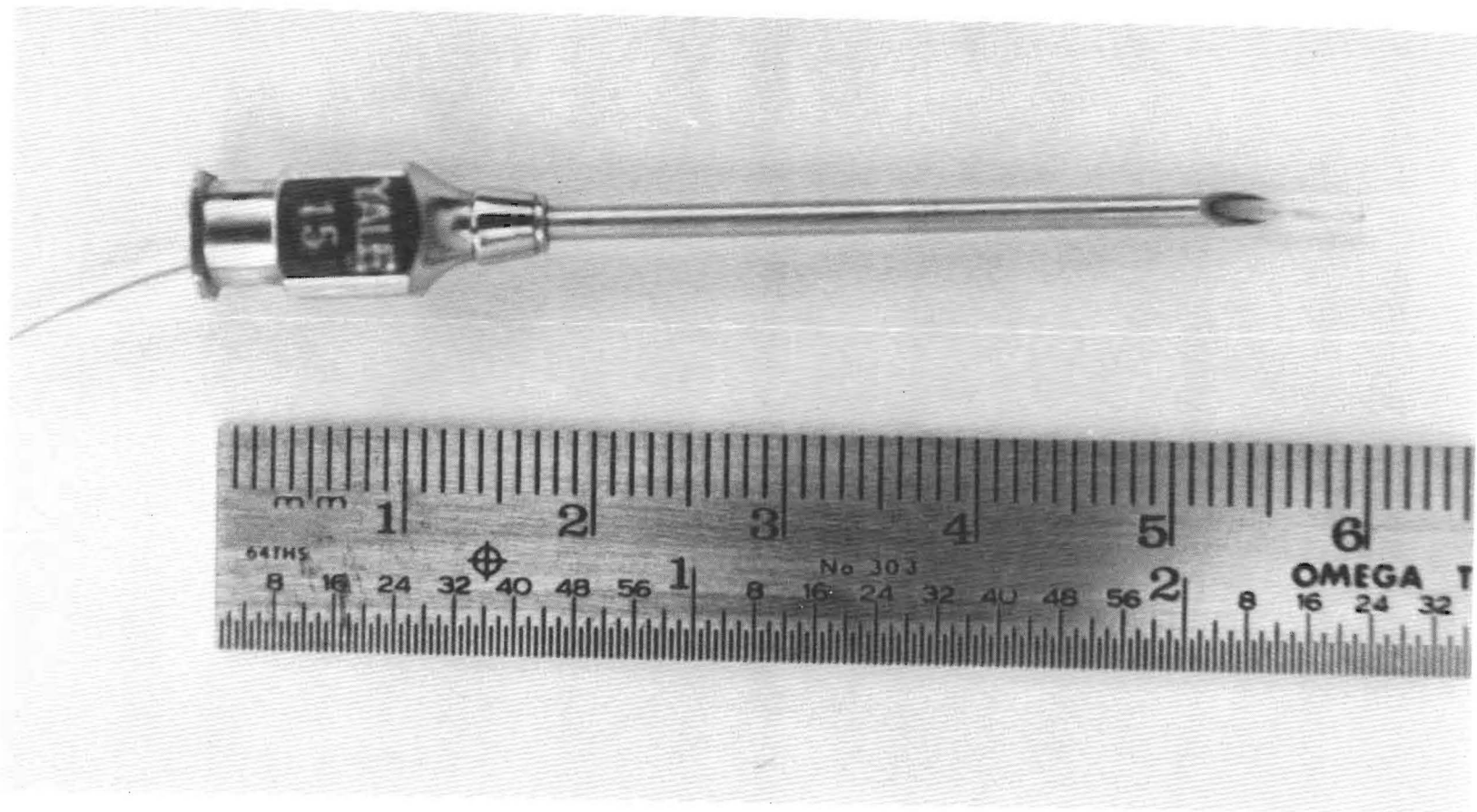


Figure 14. Thermistor temperature sensor mounted in teflon tubing and inserted in hypodermic needle.

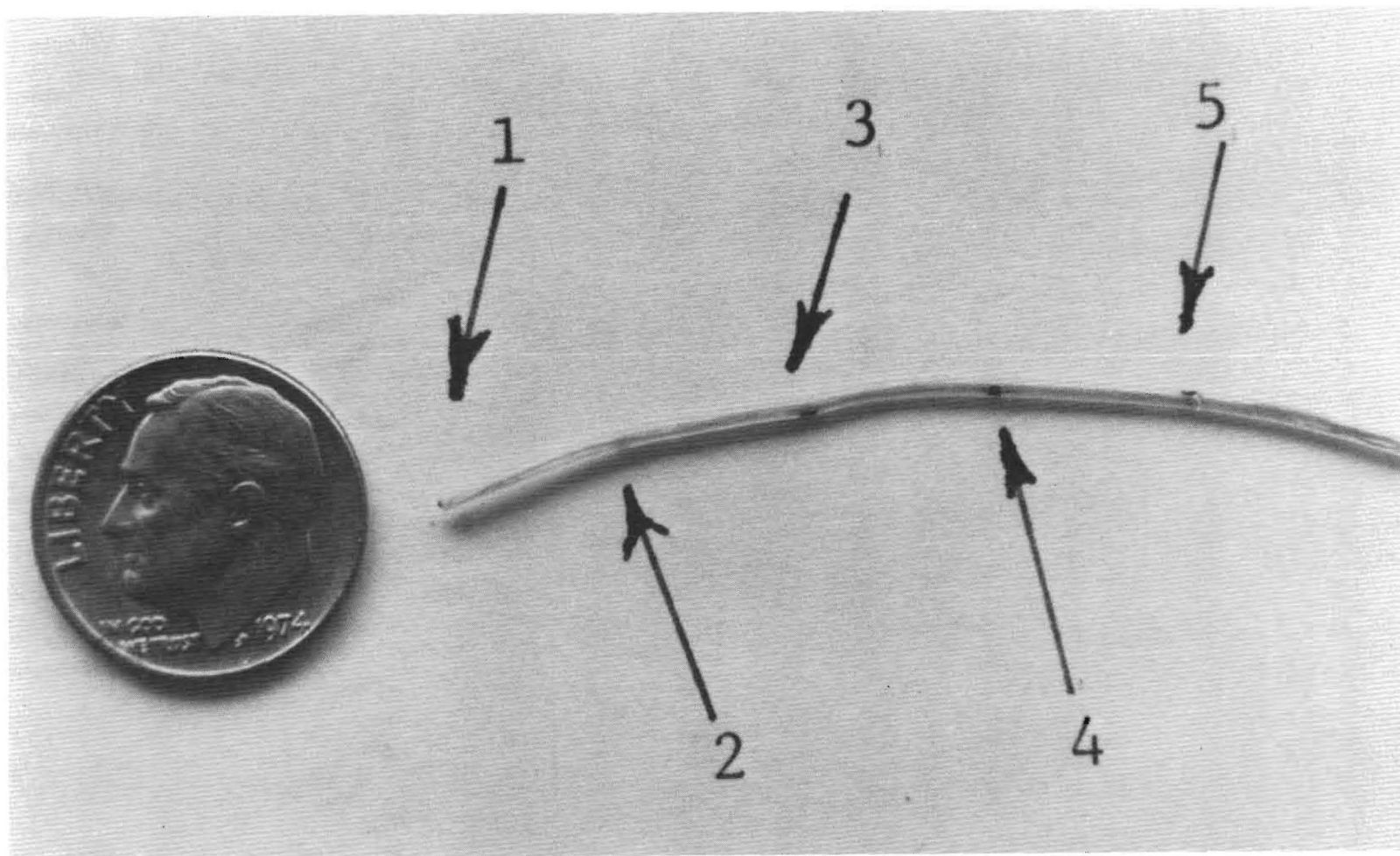


Figure 15. Five thermistors mounted in-line in Teflon tubing sheath.

SECTION X

ELECTRICAL PROPERTY VALUES

In this section, electrical property values determined from the kidney measurements are presented for the various measurement conditions. The measurement conditions involved frequency, perfusate concentration, temperature, and tissue type. As noted earlier, the accessibility of cortex tissue made it possible to determine electrical properties under a wide range of measurement conditions; however, the lack of accessibility of medulla tissue made it impossible to determine electrical properties under anything other than a minimum number of measurement conditions. A summary of the measurements that were made and the applicable conditions are presented in Table II.

The electrical properties of interest during this study were relative dielectric constant, K , electrical conductivity, σ , and loss tangent, $\tan \delta$. These properties were determined as a result of measurements on 50 canine kidneys, and their values are presented as a function of the measurement conditions in Tables III through X. The numerical values in these tables represent measurements on several different tissue samples; therefore, the data are shown as a mean value plus a standard deviation (S.D.). As noted earlier, many subtle and difficult-to-control factors influenced the repeatability of measured data; consequently, electrical property values in the tables have standard deviations that are typically as large as 10 percent of the mean value. Despite these standard deviations, however, these data are extremely useful in evaluating the effect of temperature, frequency, perfusate concentration, and tissue type on electrical property values. These effects are seen more easily when the data are presented in graphical form, as in Figures 16 through 21. These figures show either K , σ , or $\tan \delta$ for cortex tissue and for either 918 MHz or 2450 MHz. The three curves on each figure correspond to the different dimethyl sulfoxide (DMSO) concentrations.

TABLE II
SUMMARY OF TEST CONDITIONS

Code	Tissue Type	Frequency (MHz)	DMSO* Concentration	Temperature Range (°C)
1	Cortex	2450	0%	-68 to +20
2	Cortex	2450	5%	-68 to +20
3	Cortex	2450	10%	-68 to +20
4	Cortex	918	0%	-68 to +20
5	Cortex	918	5%	-68 to +20
6	Cortex	918	10%	-68 to +20
7	Medulla	2450	5%	-68 to +20
8	Medulla	2450	10%	-68 to +20

*DMSO - dimethyl sulfoxide

TABLE III

ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 2450 MHz
AND WITH A 0 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S. D.	Tan δ Mean/S. D.	σ (mmho/cm) Mean/S. D.
20°C	50.1/3.3	0.26/0.03	17.69/1.92
-10°C	49.2/2.3	0.35/0.03	23.42/2.10
-15°C	3.75/0.36	0.19/0.04	0.99/0.22
-20°C	3.33/0.27	0.15/0.03	0.67/0.15
-25°C	3.49/0.41	0.10/0.04	0.49/0.15
-68°C	3.39/0.94	0.08/0.08	0.40/0.43

TABLE IV

ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 2450 MHz
AND WITH A 5 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S. D.	Tan δ Mean/S. D.	σ (mmho/cm) Mean/S. D.
20°C	53.0/4.1	0.29/0.03	20.68/2.20
-10°C	53.6/2.3	0.40/0.04	28.85/2.32
-15°C	51.6/4.4	0.47/0.06	33.05/2.02
-20°C	5.6/0.5	0.42/0.08	3.16/0.66
-25°C	5.1/0.02	0.36/0.08	2.48/0.53
-33°C	3.07/0.69	0.28/0.07	1.48/0.38
-68°C	2.87/0.51	0.23/0.11	0.31/0.30

TABLE V
ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 2450 MHz
AND WITH A 10 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S.D.	Tan δ Mean/S.D.	σ (mmho/cm) Mean/S.D.
20°C	50.8/5.2	0.28/0.02	19.44/1.65
-10°C	50.6/4.6	0.42/0.03	28.96/1.16
-15°C	49.3/6.0	0.48/0.04	32.21/3.22
-20°C	7.3/1.6	0.54/0.06	5.71/1.23
-25°C	6.35/1.53	0.54/0.04	4.63/0.93
-33°C	4.97/0.56	0.51/0.18	3.53/1.50
-68°C	3.2/0.3	0.11/0.05	0.48/0.20

TABLE VI
ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 918 MHz
AND WITH A 0 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S.D.	Tan δ Mean/S.D.	σ (mmho/cm) Mean/S.D.
20°C	52.7/1.53	0.45/0.02	12.00/1.00
-10°C	56.0/1.73	0.31/0.01	8.80/0.36
-15°C	58.0/0.00	0.30/0.01	8.90/0.28
-20°C	6.40/3.05	0.27/0.10	0.97/0.81
-25°C	5.70/3.42	0.15/0.03	0.30/0.01
-68°C	3.30/0.26	0.10/0.09	0.18/0.16

TABLE VII
ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 918 MHz
AND WITH A 5 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S.D.	Tan δ Mean/S.D.	σ (mmho/cm) Mean/S.D.
20°C	53.2/1.5	0.45/0.03	12.28/0.51
-10°C	55.6/1.6	0.34/0.03	9.62/0.85
-15°C	55.6/2.1	0.33/0.03	9.37/0.29
-20°C	5.6/4.4	0.30/0.01	1.37/0.13
-25°C	6.9/0.9	0.24/0.12	0.80/0.31
-68°C	4.5/5.0	0.12/0.01	0.27/0.29

TABLE VIII

ELECTRICAL PROPERTIES OF CORTEX TISSUE AT 918 MHz
AND WITH A 10 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S.D.	Tan δ Mean/S.D.	σ (mmho/cm) Mean/S.D.
20°C	50.9/3.7	0.40/0.04	10.3/0.3
-10°C	54.4/0.5	0.31/0.01	8.7/0.2
-15°C	54.1/0.6	0.32/0.01	8.8/0.2
-22°C	14.1/2.0	0.31/0.06	2.2/0.1
-27°C	10.2/3.2	0.50/0.19	2.38/0.4
-68°C	4.8/2.2	0.02/0.01	0.04/0.0

TABLE IX
ELECTRICAL PROPERTIES OF MEDULLA TISSUE AT 2450 MHz
AND WITH A 5 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S.D.	Tan δ Mean/S.D.	σ (mmho/cm) Mean/S.D.
20°C	61.0/1.0	0.32/0.02	26.1/1.5
-10°C	60.3/0.17	0.42/0.01	34.5/0.7
-15°C	28.4/27.6	0.29/0.20	14.6/20.8
-20°C	4.4/2.9	0.57/0.40	2.7/0.3
-30°C	4.8/*	0.15/*	0.95/*

*Single Data Point

TABLE X

ELECTRICAL PROPERTIES OF MEDULLA TISSUE AT 2450 MHz
AND WITH 10 PERCENT PERFUSATE CONCENTRATION

Temperature (°C)	K Mean/S.D.	Tan δ Mean/S.D.	σ (mmho/cm) Mean/S.D.
20°C	73.0/1.4	0.32/0.04	30.5/3.5
-10°C	71.5/3.5	0.39/0.06	37.5/4.9
-15°C	68.5/3.5	0.46/0.07	43.0/4.2
-20°C	10.2/4.0	0.55/0.04	7.5/2.2
-30°C	5.6/1.6	0.49/0.01	3.7/1.1
-68°C	3.9/2.7	0.05/0.04	0.26/0.32

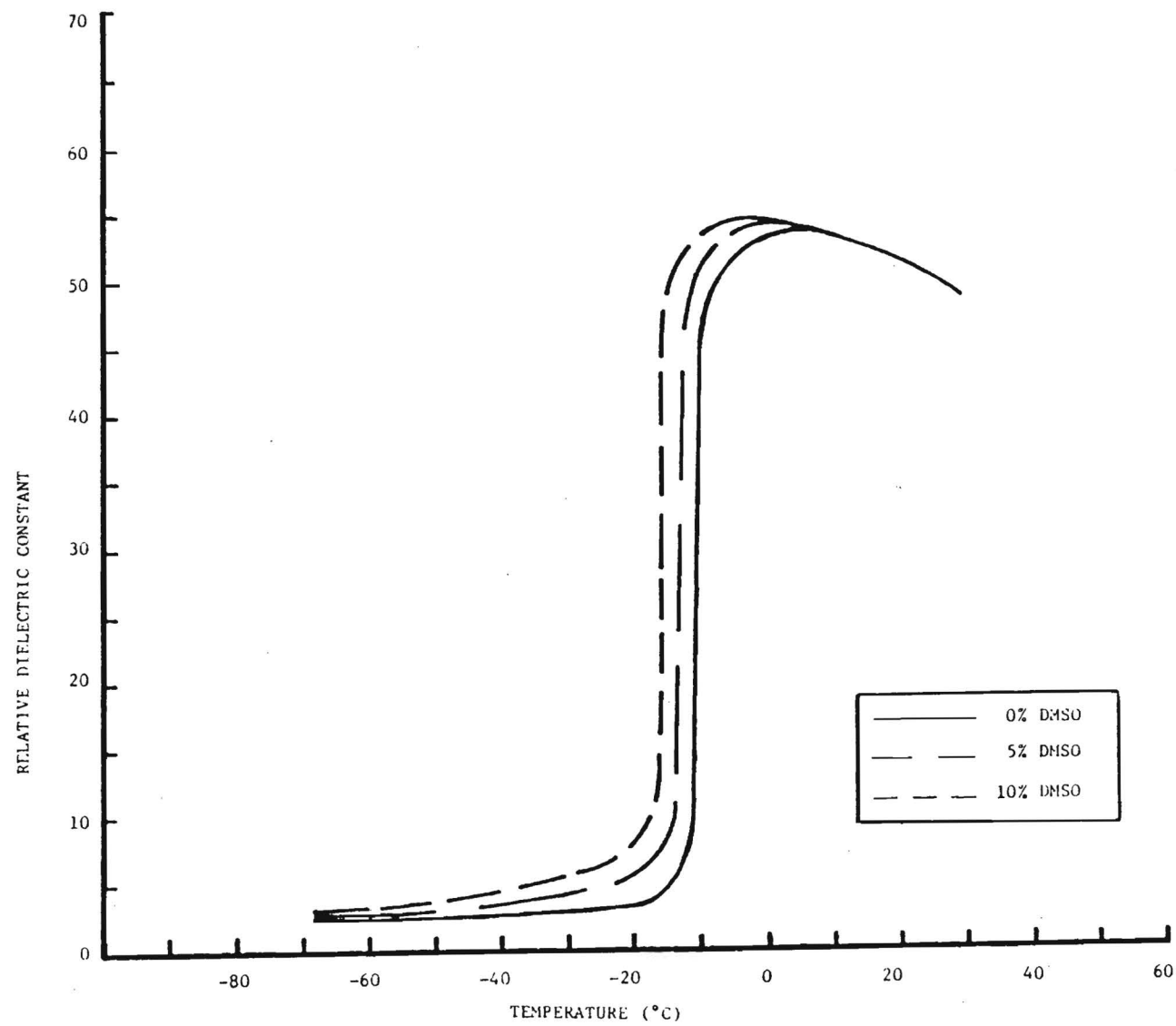


Figure 16. Relative dielectric constant of cortex tissue at 2450 MHz.

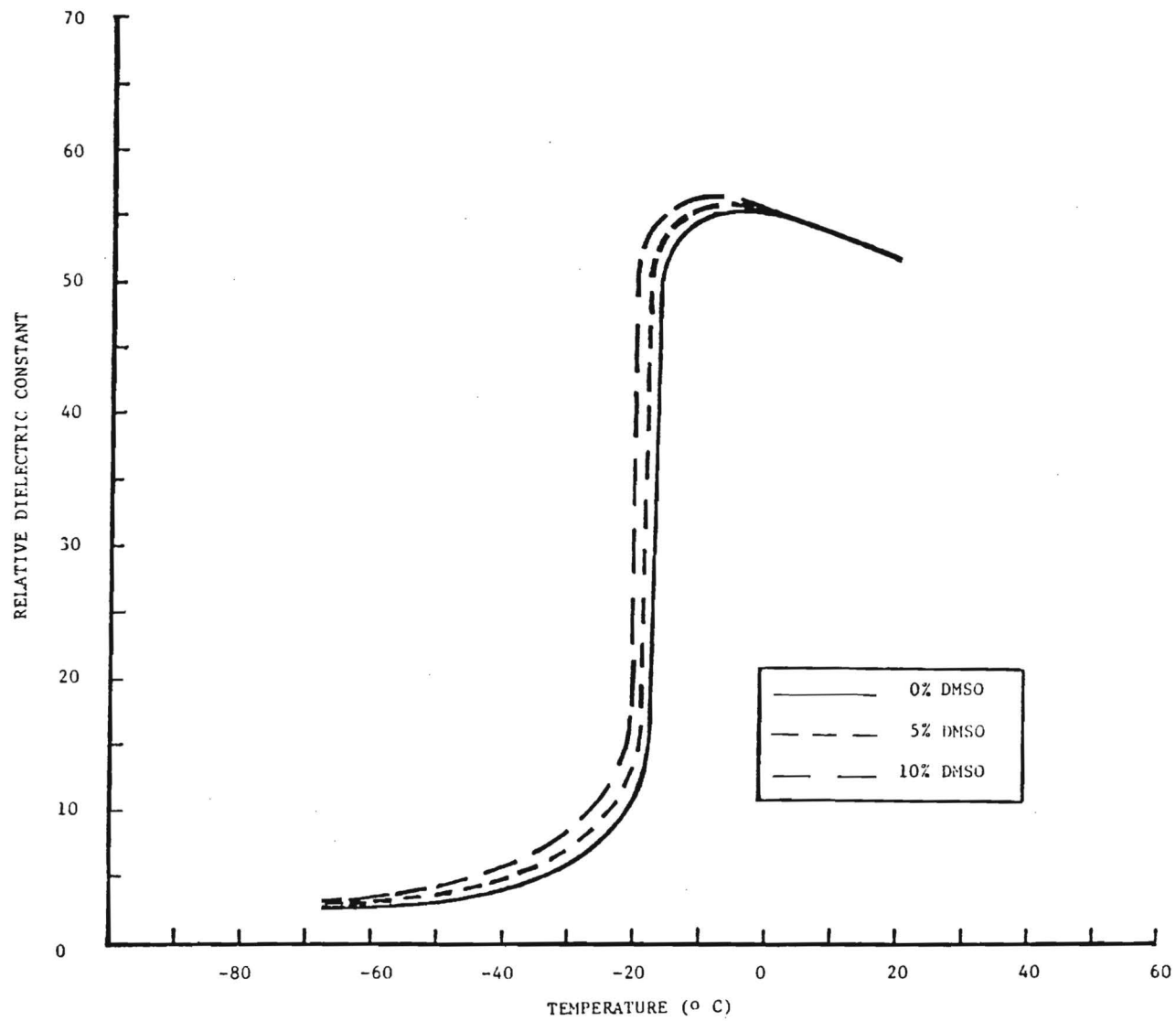


Figure 17. Relative dielectric constant of cortex tissue at 918 MHz.

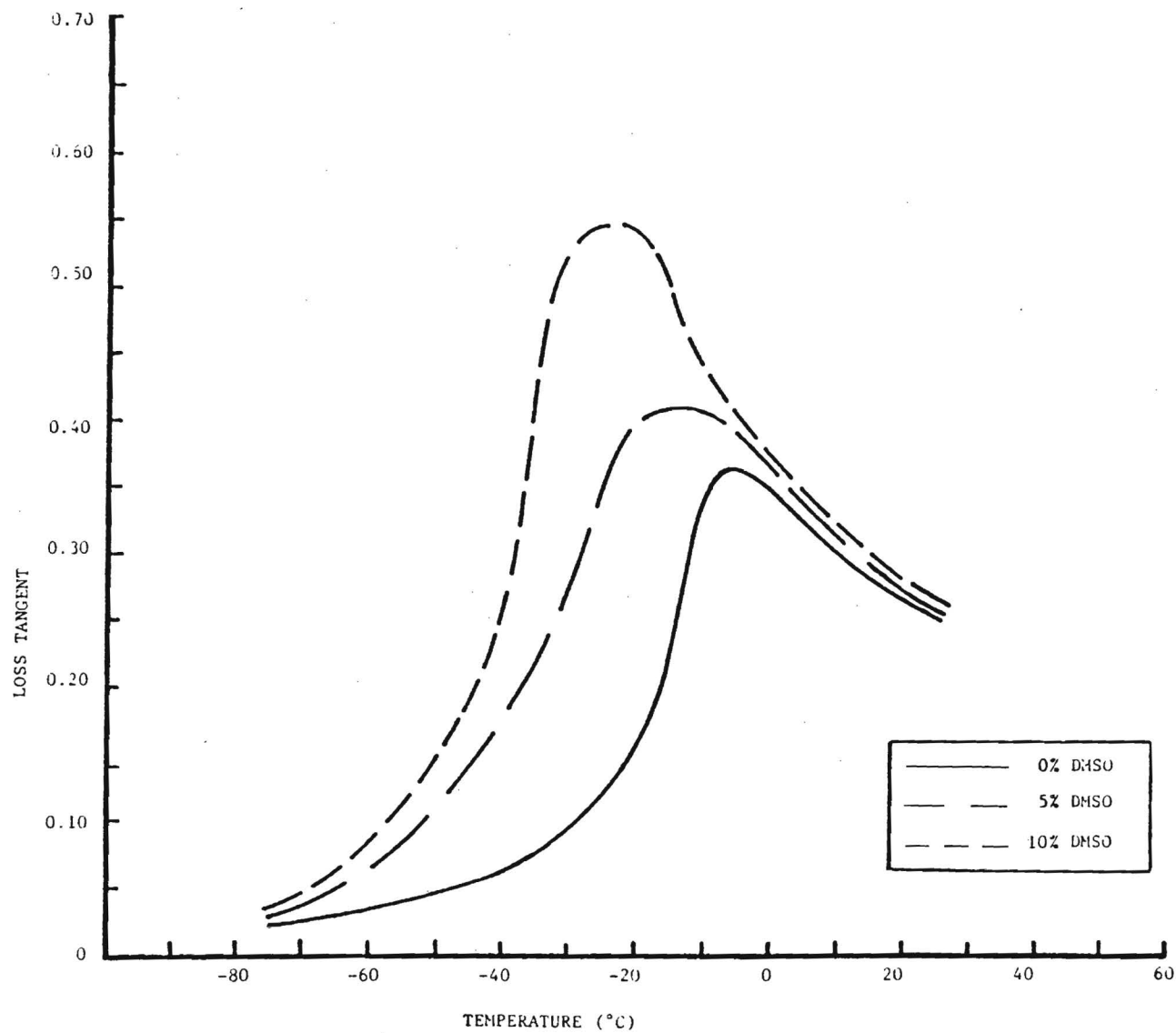


Figure 18. Loss tangent of cortex tissue at 2450 MHz.

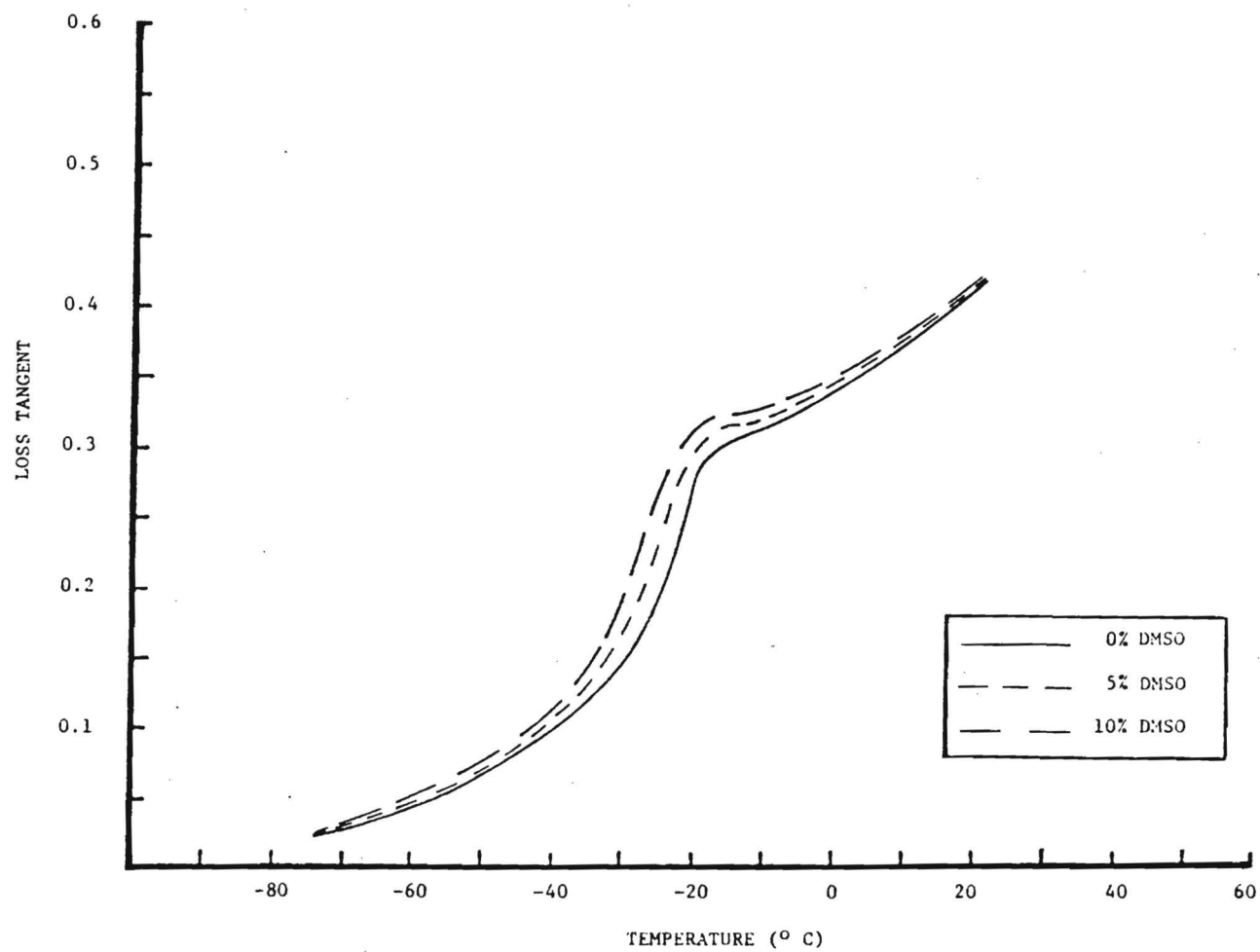


Figure 19. Loss tangent of cortex tissue at 918 MHz.

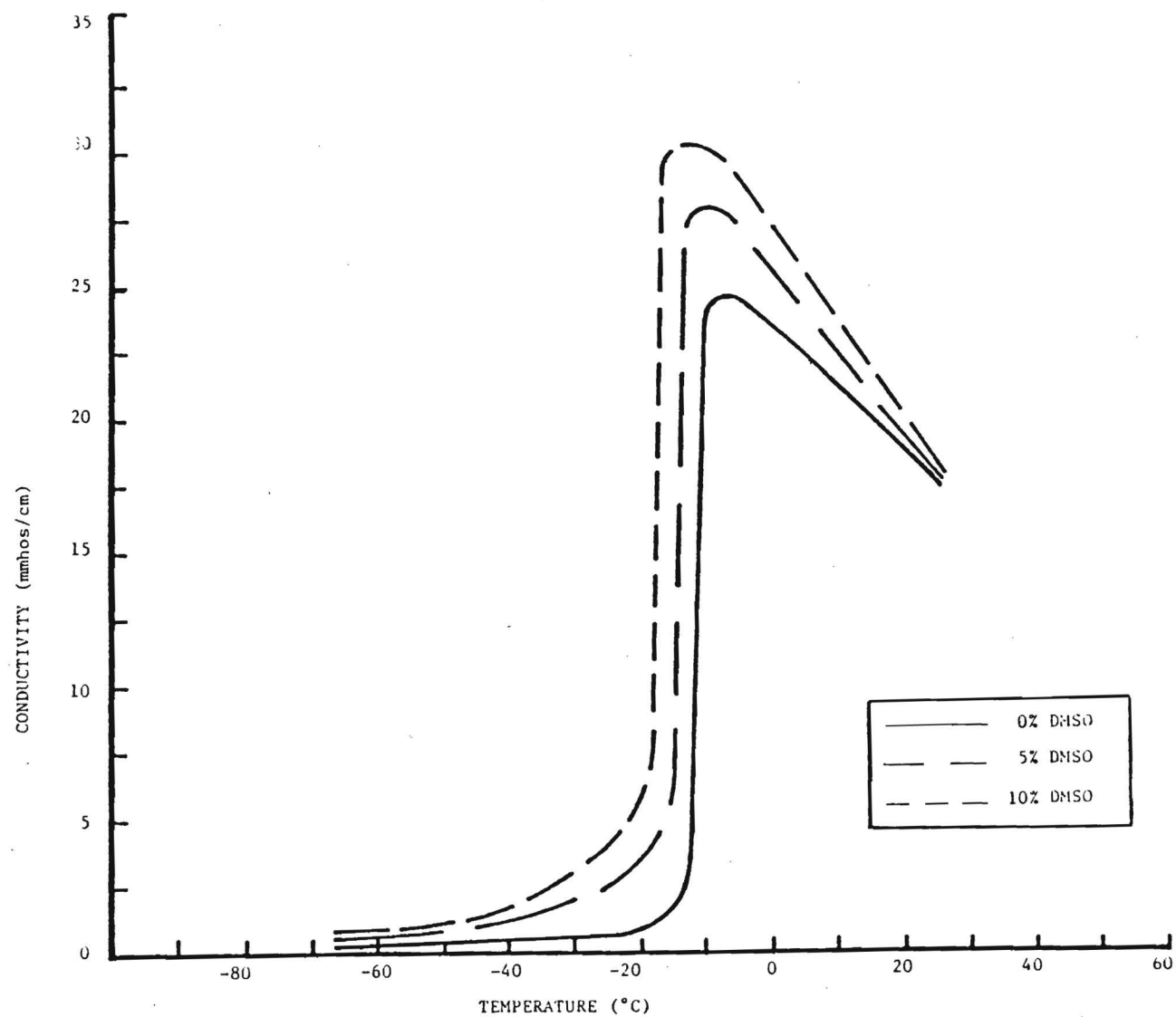


Figure 20. Electrical conductivity of cortex tissue at 2450 MHz.

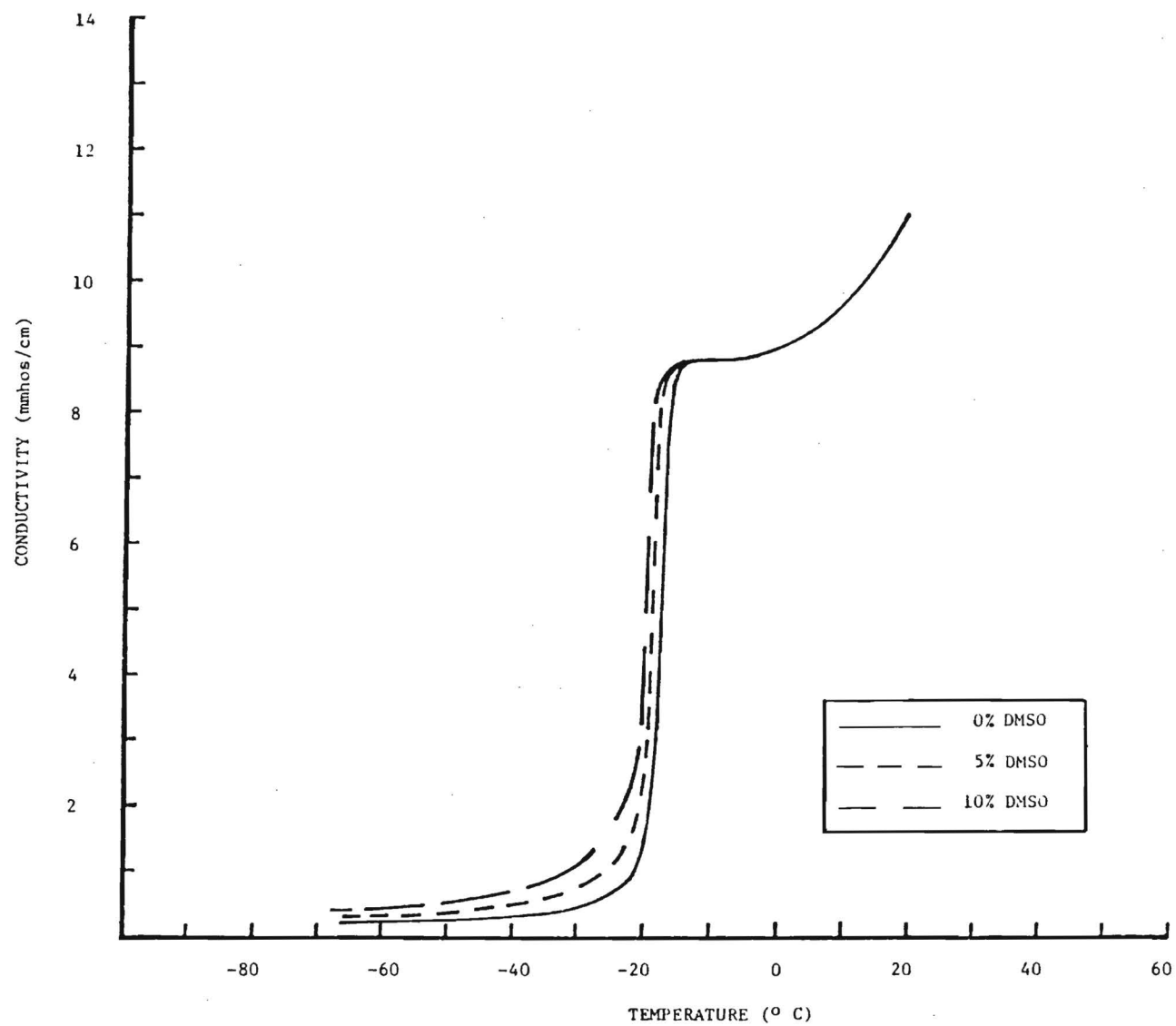


Figure 21. Electrical conductivity of cortex tissue at 918 MHz.

SECTION XI

CONCLUSIONS AND RECOMMENDATIONS

The electrical property values presented in Tables III through X and Figures 16 through 21 of Section X were obtained as a result of measurements made on 50 canine kidneys. These measurements were made as a function of frequency (918 MHz and 2450 MHz), temperature (-68°C to $+20^{\circ}\text{C}$), cryoprotectant concentration (0, 5, and 10 percent DMSO), and tissue type (cortex and medulla). Conclusions that can be drawn from the property values and measurement conditions are presented in this section. These conclusions are followed by recommendations regarding how knowledge of electrical property values should be used.

In Figures 16 and 17, the relative dielectric constant K of cortex tissue is shown as a function of frequency, temperature, and DMSO concentration. In both figures, the dramatic change in K over the temperature range where phase transition occurs is particularly conspicuous, and it can be concluded that temperature has a pronounced effect on relative dielectric constant. Below the phase transition temperature, the value of K is less than 10, while above this temperature, K exceeds a value of 50. The phase transition is seen to occur over a temperature range of approximately 6°C from -14°C to -20°C . It must be noted that the data in Figures 16 and 17 show the DMSO concentration shifting the temperature at which the phase transition occurs. However, it is recalled that there was an uncertainty of approximately $\pm 3^{\circ}\text{C}$ in determining tissue sample temperatures; therefore, the shifts in phase-transition temperature may be less pronounced than shown. Except for the possibility of shifting the phase-transition temperature, the DMSO concentration appears to have no conclusive effect on relative dielectric constant. Also, any effects due to frequency are minimal and inconclusive.

In Figures 18 and 19, loss tangent values for cortex tissue are presented as a function of frequency, temperature, and DMSO concentration. From Figure 18, it can be concluded that DMSO affects

both the magnitude and temperature dependence of cortex tissue loss tangent at 2450 MHz. The nature of this effect is such that increasing concentrations of DMSO cause a downward shift in phase transition temperature and an upward shift in loss tangent magnitude. At 918 MHz (see Figure 19), it is conclusively shown that these effects are much less pronounced. Also, at 918 MHz, the loss tangent is continuing to increase at +20°C, regardless of the DMSO concentration, while the opposite effect is seen at 2450 MHz.

Conductivity values for cortex tissue are presented as a function of frequency, temperature, and DMSO concentration in Figures 20 and 21. As was true for the relative dielectric constant, it can be readily concluded that temperature also has a dramatic effect on conductivity. Above the phase transition temperature, it can also be concluded that frequency affects conductivity. In fact, at 918 MHz, the conductivity magnitude is lower and increasing at temperatures above the phase transition, but at 2450 MHz, the opposite effect exists. Based on the figures, it can be concluded that effect of DMSO on electrical conductivity is similar to but less pronounced than the DMSO effect on the loss tangent.

Regarding recommendations, it is noted that an examination of Figures 16 through 21 reveals considerable information regarding the interaction between tissue and electromagnetic waves. This information is of importance to engineering efforts concerned with designing electromagnetic instrumentation for thawing cryogenically-preserved large organs. For example, efficient and uniform thawing requires that the cryogenically-preserved organ be heated with an electromagnetic wave whose penetration depth is two-to-four times greater than the organ thickness. (The optimum ratio of penetration depth to organ thickness is yet to be determined.) By using the data in Tables III through X and Equation (15a), penetration depth can be computed as a function of the measurement conditions. Such a computation yields the graphs shown in Figures 22 and 23 when frequency and DMSO concentration are the variables. From these figures, it is evident that the perfusate significantly affects penetration depth at 2450 MHz, but has little or no effect at 918 MHz. Considering the fact that canine kidneys are

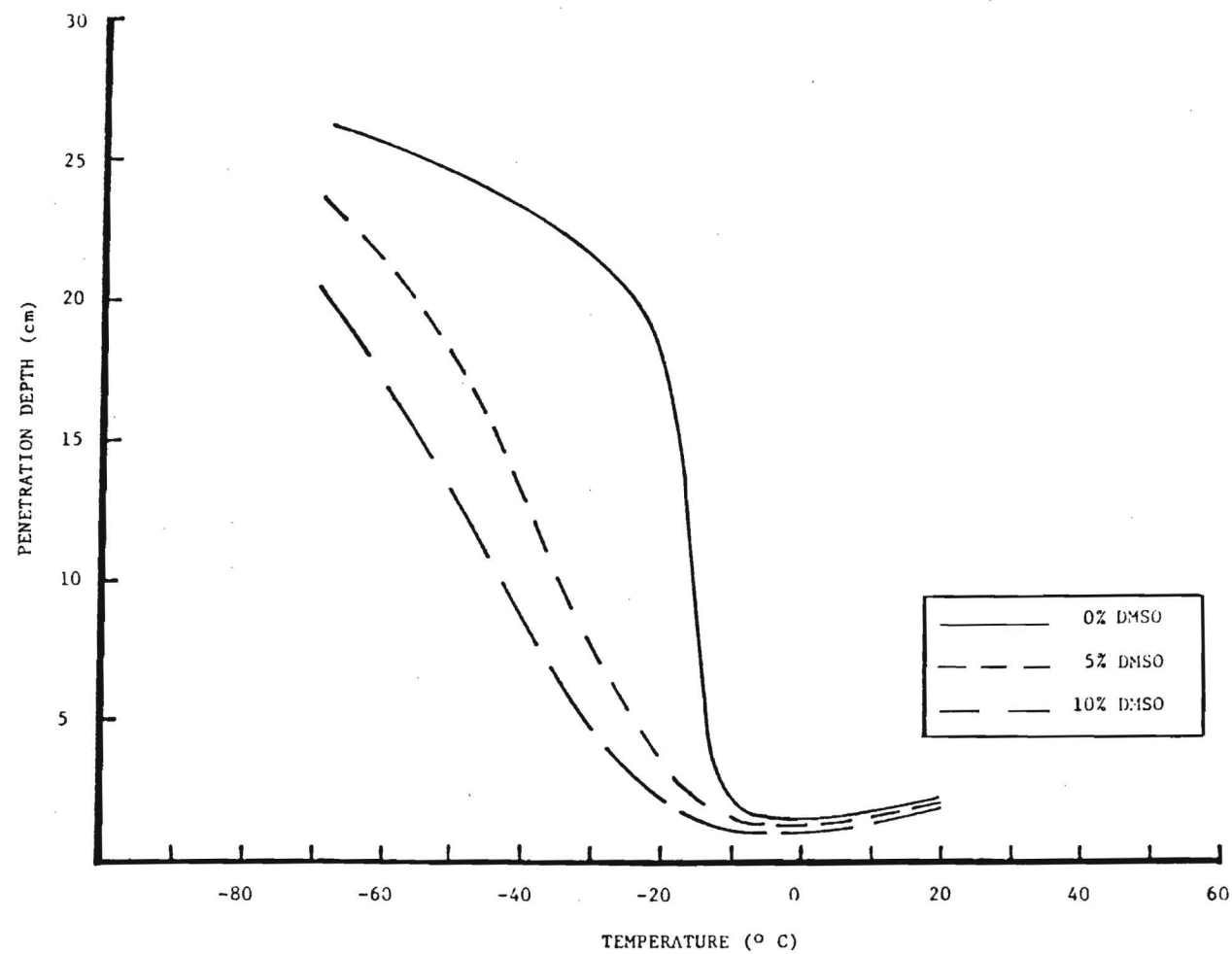


Figure 22. Penetration depth of cortex tissue at 2450 MHz.

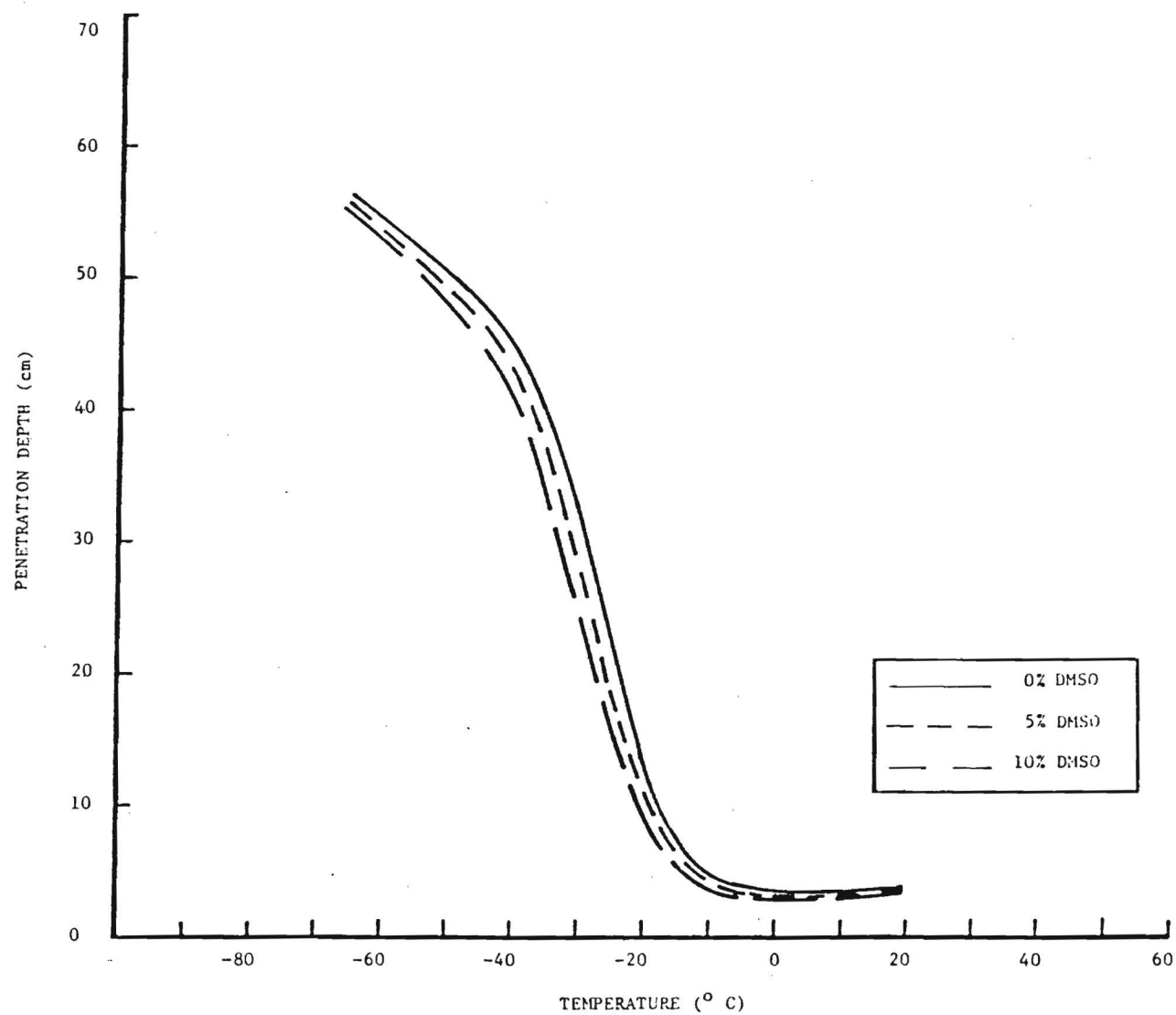


Figure 23. Penetration depth of cortex tissue at 918 MHz.

approximately 4.0 centimeters in thickness, Figure 22 indicates that electromagnetic waves at 2450 MHz are best suitable for thawing over a temperature range of -58°C to -40°C if the organ is perfused with a 10 percent concentration of DMSO. If the perfusate concentration is changed to 5 percent, the 2450 MHz electromagnetic waves are suitable for thawing over a range of -45°C to -30°C . For temperatures greater than these, non-uniform heating is likely to occur because of the small penetration depth. On the other hand, inefficient heating is likely to occur at temperature ranges below these because the penetration depth will be too large. If the organ were perfused with a DMSO-free solution, the penetration depth at 2450 MHz would be significantly greater and the organ could be uniformly and efficiently thawed over a temperature range of only -19°C to -17°C . Further, the rapidly changing penetration depth over this temperature range means that it would be difficult to control thermal runaway in organs perfused with DMSO-free solutions.

Figure 23 shows that, at 918 MHz and at temperatures below the phase-transition region, the penetration depth is greater by an approximate factor of two than at 2450 MHz. From this, it is evident that, at temperatures below approximately -40°C , 918-MHz electromagnetic waves will thaw tissue in a highly uniform manner; however, since the penetration depths are large, the thawing will be somewhat inefficient. Over a temperature range of approximately -40°C to -25°C , the Figure 23 data indicate that electromagnetic waves at 918 MHz are ideally suited for uniform and efficient thawing of cryogenically-preserved kidneys. As the temperature increases above -20°C , there is again a danger of overheating because of small penetration depths.

It is recommended that analyses of the type above for penetration depth be expanded using the electrical property data obtained during this study. Results of these analyses should then be used to custom-design an electromagnetic system that uniformly, rapidly, efficiently, and hygienically thaws cryogenically-preserved kidneys. Studies should then be undertaken, in collaboration with the Medical College of Georgia, in which a kidney is removed from a dog, perfused, frozen, stored, thawed, and implanted back into the dog. The contralateral

kidney should then be removed, thereby forcing the dog to function with the kidney that was cryogenically-preserved and electromagnetically recovered. These studies would concentrate on providing engineering procedures for clinical use during the transplantation of cryogenically-preserved kidneys.

SECTION X

REFERENCES

1. A.M. Karow, G.J. Abouna, and A.L. Humphries, Jr., Organ Preservation for Transplantation, Little & Brown Co., Boston, MA., 1974, p. 435.
2. I. Georgiev and G. Mateeva, "Survival and Growth of Kidney Tissue in Cultures In-Vivo After Freezing and Preservation at Low Temperatures," Comptes Rendus Acad., Bulgar. Sci., 20:621-624, 1967.
3. A.H. Jeske, M.C. Fonteles, and A.M. Karow, Jr., "Functional Preservation of the Mammalian Kidney, II. Ultrastructure with Low Flow Perfusion at Normothermia," J. Surg. Res., 15:4-13, 1973.
4. A.H. Jeske, M.C. Fonteles, and A.M. Karow, Jr., "Functional Preservation of the Mammalian Kidney, II. Ultrastructure Effects of Perfusion with Dimethylsulfoxide (DMSO)," Cryobiology, 11:170-181, 1974.
5. N.A. Halasz, L.N. Seifert, and M.J. Orloff, "Whole Organ Preservation, I. Organ Perfusion Studies," Surgery, 60:368-372, 1966.
6. N.A. Halasz, H.A. Rosenfield, M.J. Orloff, and L.N. Seifert, "Whole Organ Preservation, II. Freezing Studies," Surgery, 61:417-421, 1967.
7. C.P. Burns, E.C. Burdette, and A.M. Karow, Jr., "Thawing of Rabbit Kidneys from -79°C with 2450-MHz Radiation," Cryobiology, 21:577, 1975.
8. S. Kubola and R. Lillehei, "Some Problems Associated with Kidneys Frozen to -50°C or Below," Low Temp. Med., 2:95-105, 1976.
9. W.R. Webb and A.M. Karow, Jr., "Hypothermia Organ Preservation: Comparison of Cooling and Warming Methods," J. Am. Med. Assn., 191:1012-1014, 1965.
10. A.M. Karow, Jr., W.P. Liu, and A.L. Humphries, Jr., "Survival of Dog Kidneys Subjected to High Pressure: Necrosis of Kidney After Freezing," Cryobiology, 7:128, 1970.
11. H.A. Ecker, E.C. Burdette, and F.L. Cain, "Simultaneous Microwave and High Frequency Thawing of Cryogenically-Preserved Canine Kidneys," 1976 IEEE International Symp. on EM Comp., Washington, D.C., 1976.
12. S. Roberts and A. von Hippel, "A New Method for Measuring Dielectric Constant and Loss Tangent in the Range of Centimeter Waves," J. App. Phy., 17:610-1616, 1946.
13. Dielectric Materials and Applications, Edited by A. R. von Hippel, MIT Press, Cambridge, MA., 1954.
14. F. Cain, C. Burdette, and J. Seals, "In-Vivo Determination of Energy Absorption in Biological Tissue," Georgia Tech Annual Technical Report on Project A-1755, Grant No. DAAG29-75-G-0182, July 1977.

FINAL PROJECT REPORT
NSF FORM 98A

PLEASE READ INSTRUCTIONS ON REVERSE BEFORE COMPLETING

PART I-PROJECT IDENTIFICATION INFORMATION

1. Institution and Address Ga. Institute of Technology Biomedical Research Group Atlanta, Georgia 30332	2. NSF Program	3. NSF Award Number ENG-76-10124
	4. Award Period From 9/1/76 To 9/1/78	5. Cumulative Award Amount \$68,500
6. Project Title		

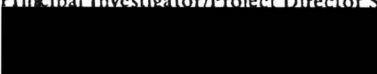
PART II-SUMMARY OF COMPLETED PROJECT (FOR PUBLIC USE)

Research and engineering studies were undertaken in two technical areas of crucial importance in the long-range goal of providing an electromagnetic system for rapidly and uniformly thawing cryogenically-preserved large organs. The two areas were (1) establishing a base of tissue electrical property data that can be used to indicate design parameters for the electromagnetic thawing system and (2) investigating temperature measurement techniques that can be used under conditions which simultaneously involve cryogenic temperatures and electromagnetic waves. Engineering progress made in these two areas is presented in this report.

An a priori knowledge of tissue electrical properties is essential because these properties govern the interaction between the electromagnetic wave and the cryogenically-preserved organ. Engineering efforts during this study clarified the theoretical relationship between tissue electrical properties and electromagnetic waves, and then provided instrumentation with which electrical properties could be measured as a function of frequency (918 MHz and 2450 MHz), tissue type (kidney medulla and cortex), cryoprotectant concentration (0, 5, and 10 percent dimethyl sulfoxide), and temperature (-68°C to +20°C). Results of these measurements, which were made using tissue samples from 50 individual canine kidneys, are presented.

Satisfactory temperature measurement techniques for use under simultaneous conditions of cryogenic temperature and electromagnetic waves have not been available. Engineering efforts during this study resulted in the assembly and evaluation of a thermistor-based thermometry system with improved electronic control circuitry. This system yielded temperature values accurate to within 1°C in the presence of electromagnetic waves and at cryogenic temperatures. The electromagnetic waves were comparable in magnitude to those used for organ thawing. Operation and performance of this thermometry system are described.

PART III-TECHNICAL INFORMATION (FOR PROGRAM MANAGEMENT USES)

1. ITEM (Check appropriate blocks)	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM	
				Check (✓)	Approx. Date
a. Abstracts of Theses					
b. Publication Citations					
c. Data on Scientific Collaborators					
d. Information on Inventions					
e. Technical Description of Project and Results					
f. Other (specify)					
2. Principal Investigator/Project Director Name (Typed) James C. Toler		3. Principal Investigator/Project Director Signature 		4. Date 3-21-79	

FINAL PROJECT REPORT
NSF FORM 98A

PLEASE READ INSTRUCTIONS ON REVERSE BEFORE COMPLETING

PART I-PROJECT IDENTIFICATION INFORMATION


1. Institution and Address Georgia Institute of Technology Atlanta, GA 30332	2. NSF Program Automation, Bioengineering & Sensing System	3. NSF Award Number ENG-7610124
	4. Award Period From 1 Nov '76 To 31 Aug '81	5. Cumulative Award Amount \$150,477
6. Project Title Engineering Study of Electromagnetic Field Distributions in Large Organs		

PART II-SUMMARY OF COMPLETED PROJECT (FOR PUBLIC USE)

Research and engineering studies were conducted in six technical areas of crucial importance to the long-range goal of providing an electromagnetic system for rapidly and uniformly thawing cryogenically-preserved large organs. These areas were (1) measurement of canine kidney dielectric properties, (2) definition of tissue-equivalent modelling materials that simulate the dielectric properties of cryogenically-preserved canine kidneys, (3) design, construction, and evaluation of a 12-channel, computer-controlled, thermistor-based thermometry system, (4) implementation of an increased power capability for the 918 MHz thawing system, (5) preliminary heating studies on kidney models, and (6) an analysis of the feasibility of an automated thawing system.

The dielectric properties of 50 canine kidneys were measured as a function of temperature (-80 to +20°C), cryoprotectant concentration (0, 5, and 10 percent dimethylsulfoxide), tissue type (cortex and medulla), and frequency (918 and 2450 MHz). Knowledge of these properties was used to define a modelling material recipe suitable for simulating the electrical properties of canine kidneys from -80 to +20°C and at 918 MHz. A 12-channel, computer-controlled thermometry system using ultrasmall thermistors as temperature sensors was then designed, constructed, and evaluated under conditions simulating kidney thawing. After increasing the output power of the 918-MHz source, phantom models of canine kidneys were instrumented with the temperature sensors and a series of thawing experiments were initiated. These experiments showed that the heating uniformity at 918 MHz was not sufficient to assure a functioning kidney post-thaw. Analyses indicated that a dual-frequency electromagnetic system will be necessary to achieve the required heating uniformity.

PART III-TECHNICAL INFORMATION (FOR PROGRAM MANAGEMENT USES)

1. ITEM (Check appropriate blocks)	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM	
				Check (✓)	Approx. Date
a. Abstracts of Theses	X				
b. Publication Citations		X		X	1 July 1982
c. Data on Scientific Collaborators		X			
d. Information on Inventions	X				
e. Technical Description of Project and Results			X		
f. Other (specify)					
2. Principal Investigator/Project Director Name (Typed) James C. Toler	3. Principal Investigator/Project Director Signature 			4. Date 2.10.82	

ATTACHMENT TO NSF FORM 98A

Part III.1.b

Efforts are underway to obtain approval for the publication of a text titled Dielectric Properties of Biological Materials and published by the IEEE Press. A decision on the approval should be known by 1 July 1982.

Part III.1.c

Joseph Seals, Investigator, Research Engineer II
Walter Barry, Graduate Student, Electrical Engineering