

In-Vivo Measurement of Swine Myocardial Resistivity

Jang-Zern Tsai, James A. Will, Scott Hubbard-Van Stelle, Hong Cao, *Student Member, IEEE*,
Supan Tungjitikusolmun, *Member, IEEE*, Young Bin Choy, *Student Member, IEEE*,
Dieter Haemmerich, *Student Member, IEEE*, Vicken R. Vorperian, and John G. Webster*, *Life Fellow, IEEE*

Abstract—We used a four-terminal plunge probe to measure myocardial resistivity in two directions at three sites from the epicardial surface of eight open-chest pigs *in-vivo* at eight frequencies ranging from 1 Hz to 1 MHz. We calibrated the plunge probe to minimize the error due to stray capacitance between the measured subject and ground. We calibrated the probe in saline solutions contained in a metal cup situated near the heart that had an electrical connection to the pig's heart. The mean of the measured myocardial resistivity was $319 \Omega \cdot \text{cm}$ at 1 Hz down to $166 \Omega \cdot \text{cm}$ at 1 MHz. Statistical analysis showed the measured myocardial resistivity of two out of eight pigs was significantly different from that of other pigs. The myocardial resistivity measured with the resistivity probe oriented along and across the epicardial fiber direction was significantly different at only one out of the eight frequencies. There was no significant difference in the myocardial resistivity measured at different sites.

Index Terms—Calibration, four-terminal, heart, *in-vivo*, leakage current, myocardium, pig, plunge probe, probe constant, resistivity, stray capacitance.

I. INTRODUCTION

RESEARCHERS have measured myocardial resistivity for various purposes. The four-terminal method is a popular method for biological resistivity measurement because it minimizes the error caused by polarization impedance at low frequencies. In the four-terminal configuration, the two electrodes used to sense the voltage difference are separate from the two for current injection. They are connected to an amplifier with high input impedance so that voltage across the polarization impedance on the voltage electrodes will be very small. Due to

change in blood perfusion and postmortem autolysis, myocardial resistivity may change after the animal's heart stops beating or after the myocardium is excised from the heart. Hence, it is desirable to measure myocardial resistivity while the heart is alive and beating. There are several difficulties in measuring myocardial resistivity *in-vivo*. It is difficult to apply a closed tube, such as the one used by Zheng *et al.* [1], in an *in-vivo* measurement. An open probe, such as a plunge probe, for which the injected current flows through a presumably semi-infinite space, must be used. The measured object actually is a multiple-layer structure including the heart walls, in-chamber blood, and other body parts. The different resistivity values of the deeper layers cause error in the measured myocardial resistivity if the measured heart wall is not thick enough compared with the inter-electrode spacing or the electrode insertion depth [2]. Unlike the electric field lines in a closed tube, which can be easily made straight, the electric field lines between the two voltage electrodes of an open probe in the tissue are not straight. It is, therefore, not possible to measure the tissue resistivity along a single direction, such as along (longitudinal) or across (transverse) the fiber direction. Furthermore, myocardial fiber direction changes transmurally about 160° from epicardium to endocardium [3]. Depending on the thickness of the measured ventricular wall, the interelectrode spacing, and the electrode insertion depth, the measured apparent resistance has different contributions from the myocardial resistivity in different directions with respect to the fiber direction. If the fibers of the measured tissue all go in the same direction, there are analytical formulas for extracting the tissue resistivity longitudinal or transverse to the fiber direction from the measurements in the two directions with point electrodes applied on the tissue surface [4], [5]. Nevertheless, the accuracy of extracting these data is questionable when considering the transmural change of the myocardial fiber direction and the applicability of the formula with finite electrode diameter.

For measurements near 1 MHz, the stray capacitance causes error. The stray capacitance between a 15 kg pig situated on a surgical table and the ground is about 150 pF. At frequencies near 1 MHz, leakage current flows through the pig to ground from the open resistivity probe attached to the pig's heart. Scharfetter *et al.* [6] modeled the effect of stray capacitance during bioimpedance spectroscopy. However, the stray capacitance problem in measuring tissue resistivity *in-vivo* has been commonly ignored by other researchers.

It is difficult to fix an open probe on a beating heart. Steendijk *et al.* [5] used a suction cup to hold their surface point probe

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J.-Z. Tsai, H. Cao, and Y. B. Choy are with the Department of Electrical and Computer Engineering, University of Wisconsin, Madison, WI 53706 USA.

J. A. Will is with the Department of Animal Health and Biomedical Sciences, University of Wisconsin, Madison, WI 53706 USA.

S. Hubbard-Van Stelle is with the Research Animal Resources Center, University of Wisconsin, Madison, WI 53705 USA.

S. Tungjitikusolmun is with the Department of Electronics Engineering, Faculty of Engineering, and the Research Center for Communications and Information Technology, King Mongkut's Institute of Technology Ladkrabang, Ladkrabang, Bangkok 10520, Thailand.

D. Haemmerich is with the Department of Biomedical Engineering, University of Wisconsin, Madison, WI 53706 USA.

V. R. Vorperian is with the University of Wisconsin Hospital and Clinics, Madison, WI 53792 USA.

*J. G. Webster is with the Department of Biomedical Engineering, University of Wisconsin, 1410 Engineering Drive, Madison, WI 53706 USA (e-mail: webster@engr.wisc.edu).

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on epicardium. This method can also be used to hold a plunge probe. One problem of this method is that, if the suction is too strong, there will be a bruise under the suction cup; this has unknown effect on the measured resistivity. In a measurement with a plunge probe, if we just insert the electrodes into the heart wall and let go without assisting to help them stay at a constant depth in the myocardium, the insertion depth varies with the heart beat, which causes measurement error, and the electrodes come out in most cases.

Radio-frequency cardiac catheter ablation is a technique that applies power up to 50 W at 500 kHz to destroy the excitability of abnormal myocardium in order to cure cardiac arrhythmia. We measure myocardial resistivity in order to create finite-element models of ablation. Pigs are convenient experimental animals for measuring myocardial resistivity. There are measurement results of *in-vivo* myocardial resistivity of various other animals, such as dogs [5], [7], [8], sheep [9], and frogs [10]. There are previous studies of *in-vivo* swine myocardial resistivity [11]–[14]. This study adds more accurate results of swine myocardial resistivity in the frequency range from 1 Hz to 1 MHz. We also show how to correct for stray capacitance in order to obtain accurate measurement of tissue resistivity *in-vivo*.

II. METHOD

A. Pig Preparation

Pigs were obtained from the Department of Animal Science, University of Wisconsin. The protocol for these studies was approved by the Animal Care and Use Committee and was in compliance with all NIH guidelines for the humane use of animals in research. Male and female pigs weighed between 15 and 22 kg. They were injected intramuscularly with Telazol, a narcotic pre-anesthetic at a dose of ~ 4 mg/kg. When the animals were sedated, they were masked to a surgical plane of anesthesia with halothane at a 5% level. The anesthetic was reduced to 3%–4% and an electrosurgical unit was used to make a cut-down through the skin and underlying tissue to expose the trachea and the sternum. The trachea was isolated by blunt dissection, and the animal intubated via a tracheostomy. The animal was placed on a ventilator and the animal maintained for the balance of the experiment at a level where the oxygen saturation was near 100% and the heart rate was between 90 and 120. Anesthetic levels were adjusted to maintain these levels. The sternum was split by cutting from the xiphoid process through the most anterior aspect. The chest was opened, any bleeding from the incisions ligated or stopped by electrocautery. The chest was held open by a surgical retractor exposing the intact heart within the pericardium. When measurements were performed, the pericardium was opened, retracted and the epicardium exposed for probe insertion.

B. Resistivity Probes

We measured the myocardial resistivity with a plunge probe consisting of four electrodes made of 27-gauge stainless-steel hypodermic needles, whose outer diameter was 0.41 mm. The

sharp ends of the needles made insertion into the myocardium easy. The four electrodes were deployed in a linear array held to an epoxy base. Each of the four electrodes protruded from the epoxy base by 4.5 mm without insulation and the interelectrode spacing was 1.5 mm. Using epoxy resin, we attached the shaft of a disposable spoon to the epoxy base. We held the shaft to maintain the electrodes in the myocardium to make measurements.

The electrode length and the interelectrode spacing were small compared with the myocardial thickness, which ranged from about 1 cm to 2 cm at the measured sites, so that the in-chamber blood would not influence the measurement result [2]. We ensured this by using the plunge probe to measure a piece of excised heart wall with the endocardium in contact with saline solutions whose resistivity ranged from very large to very small and finding that the apparent resistance measured by the probe did not change.

C. Measurement System

Fig. 1 shows the electrical system for measuring myocardial resistivity. An HP 33120A (Hewlett–Packard) function generator injected electric current of various frequencies and magnitudes through a $10\text{ k}\Omega$ resistor into the myocardium through the current electrodes. The tissue resistance-detecting circuit included a current-to-voltage converter to detect the current magnitude I_e flowing through the myocardium and a differential amplifier to detect the voltage difference V_e between the two voltage electrodes. The ratio V_e/I_e was called the apparent resistance. Due to the effect of the signal wires' stray capacitance, the tissue resistance-detecting circuits measured a different value, V_c/I_c , of the apparent resistance. However, the difference between V_c/I_c and V_e/I_e can be limited within 0.1% by using signal wires shorter than 15 cm and its effect in the measured resistivity will be eliminated by calibration. The circuits of the differential amplifier and the current-to-voltage converter have been described [2]. The gain of the current-to-voltage converter and that of the differential amplifier were $10\text{ k}\Omega$ and 50 V/V , respectively, from 1 Hz to 1 MHz. The differential amplifier had a common-mode rejection ratio (CMRR) larger than 60 dB at 1 MHz, and its front end consisted of LM310 (National Semiconductor Corporation) unity-gain buffers, which had an input resistance of $1\text{ T}\Omega$ and input capacitance of 1.5 pF. Channel 1 and channel 2 of an HP54600B (Hewlett–Packard) digital oscilloscope measured the output voltage, V_o , of the differential amplifier and, V_i , of the current-to-voltage converter. A LabVIEW (National Instrument) virtual instrument program in a personal computer controlled the operations of the function generator and the digital oscilloscope, with the addition of a measurement/storage module (Hewlett–Packard, HP54659B), and accessed the measurement output, V_1 and V_2 , of the digital oscilloscope through RS232 serial ports. The virtual instrument program also controlled a data acquisition unit to activate a temperature-measuring circuit to detect the resistance of a thermistor placed in the measured site. The computer accessed the data acquisition unit to determine the resistance of the thermistor in order to calculate the tissue temperature using table lookup.

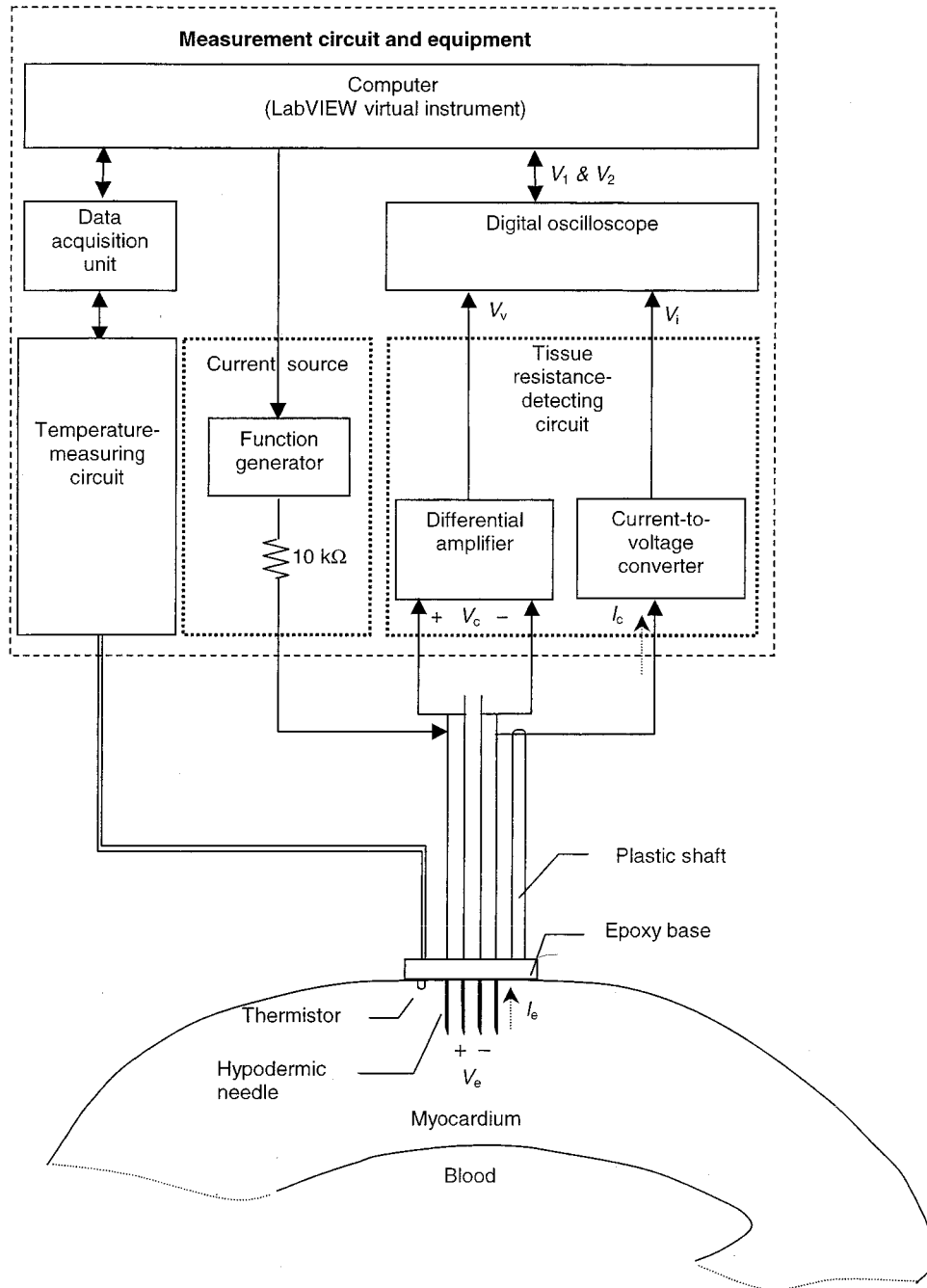


Fig. 1. The four-terminal tissue resistivity measurement system.

D. Calibration and Measurement Procedure

We calibrated the resistivity probe and measured the tissue resistivity by the following four steps.

Step 1) Measuring the oscilloscope-circuit constant.

The oscilloscope-circuit constant K_{o-c} is defined as the ratio of the measured apparent resistance V_c/I_c of the measured subject divided by the output voltage ratio V_1/V_2 of the differential amplifier and the current-to-voltage converter. The oscilloscope-circuit constant K_{o-c} is the multiplication of the oscilloscope constant K_o , defined as

$(V_v/V_i)/(V_1/V_2)$, which accounted for the disparity of the two channels of the oscilloscope, and the circuit constant K_c , defined as $(V_c/I_c)/(V_v/V_i)$, which was the inverse response of the tissue resistance-detecting circuit.

We first measured the resistance R_f of a reference resistor with a multimeter and then added two other resistors and connected them to the four terminals of the measurement circuit as shown in Fig. 2(a). The resistance ratios within the four terminals were close to those in Step 2 in order that the ratios of the common-mode voltage to the differential voltage

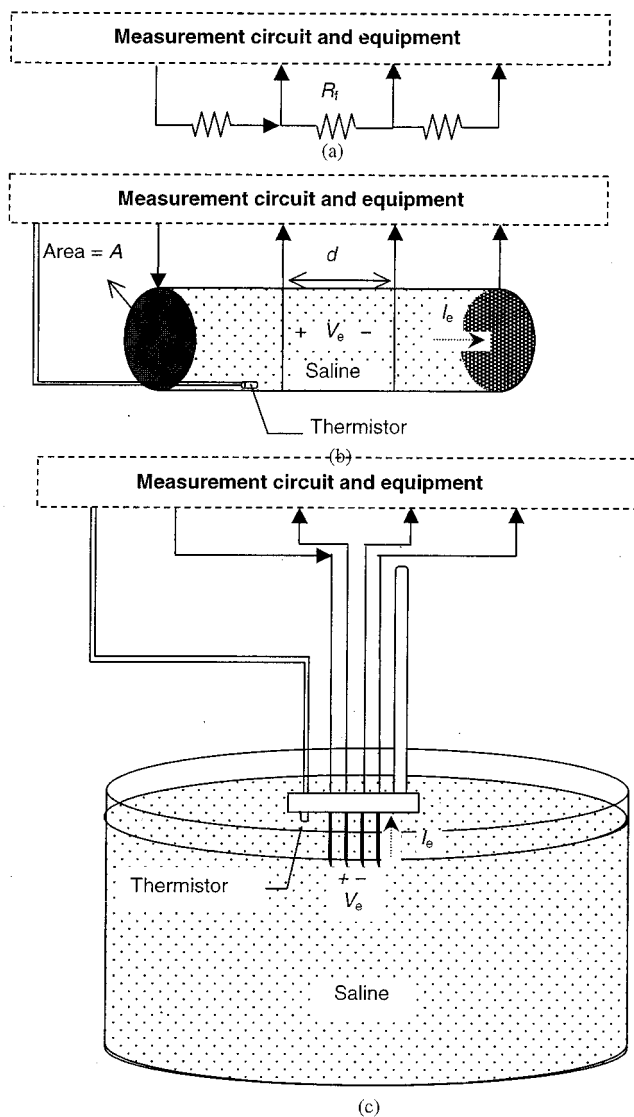


Fig. 2. The configurations used in Step 1–3. Note that the “measurement circuit and equipment” block is identical to that in Fig. 1. (a) The configuration for measuring the oscilloscope-circuit constant K_{o-c} in Step 1. (b) The configuration for measuring the saline resistivity in Step 2. (c) The configuration for measuring the wire-probe constant K_{w-p} in Step 3.

would be close in the two steps. The computer calculated the oscilloscope-circuit constant as

$$(K_{o-c})_1 = \frac{(R_f)_1}{\left(\frac{V_1}{V_2}\right)_1} \tag{1}$$

Note that the subscript next to a parenthesis represents the step number in which the quantity inside the parenthesis was measured or was pertinent to the configuration used.

Step 2) *Measuring the saline resistivity.*

We prepared several saline solutions of various salt concentrations. The saline resistivities encompassed the possible resistivity range of the myocardium. We then measured the resistivity of the saline solutions with a syringe tube with four

silver wires penetrating through the tube, as shown in Fig. 2(b). The measured saline resistivity was

$$(\rho_s)_2 = \left(\frac{V_1}{V_2}\right)_2 (K_{o-c})_1 \left(\frac{A}{d}\right)_2 \tag{2}$$

where $(A/d)_2$ was the value of the wire-probe constant, defined in Step 3, of the syringe tube, where A was the inner cross-sectional area of the syringe tube and d was the voltage electrode distance. The nominal value of A was 1.54 cm^2 and of d was 3 cm. The distance between either of the current electrodes and its adjacent voltage electrode was 1 cm.

In (2), we used the oscilloscope-circuit constant $(K_{o-c})_1$ measured in Step 1 since we used the same circuit and the same oscilloscope in all steps.

Step 3) *Measuring the wire-probe constant.*

The wire-probe constant K_{w-p} is defined as the ratio of the real tissue resistivity ρ_r of the measured subject divided by the measured apparent resistance V_c/I_c seen by the tissue-resistance detecting circuit through the signal wires and the resistivity probe. It was the multiplication of the wire constant K_w , defined as $(V_e/I_e)/(V_c/I_c)$, which accounted for the effect of the signal wires’ stray capacitance, times the probe constant K_p , defined as $\rho_r/(V_e/I_e)$, which was the inverse response of the resistivity probe. To calibrate the plunge probe, we put a cylindrical metal cup with 8 cm diameter and 10 cm height on top of the heart in the opened chest. While the bottom of the cup was in contact with the pig’s heart, we attached the cup to the surgical retractor so that the heart would not be overloaded by the weight of the cup. We poured each of the saline solutions, whose resistivity had been measured in Step 2, in the cup and immersed the electrodes of the plunge probe in the solution to measure the apparent resistance. We obtained wire-probe constants with the saline solutions of various resistivity values. We used a thermistor to measure the saline temperature both in Steps 2 and Step 3 and we corrected the measured saline resistivity with a $-2\%/^{\circ}\text{C}$ temperature coefficient.

Step 4) *Measuring the tissue resistivity.*

We inserted the plunge electrodes into the myocardium of the open-chest pig and measured the myocardial resistivity. With the oscilloscope-circuit constant K_{o-c} measured in Step 1, the wire-probe constant K_{w-p} measured in Step 3, and the output ratio V_1/V_2 of the oscilloscope measured in this step, the computer calculated the myocardial resistivity as

$$(\rho_r)_4 = \left(\frac{V_1}{V_2}\right)_4 (K_{o-c})_1 (K_{w-p})_3 \tag{3}$$

At three sites in the left ventricles, we measured the resistivity by placing the electrode array in two directions, one along the epicardial fiber direction and

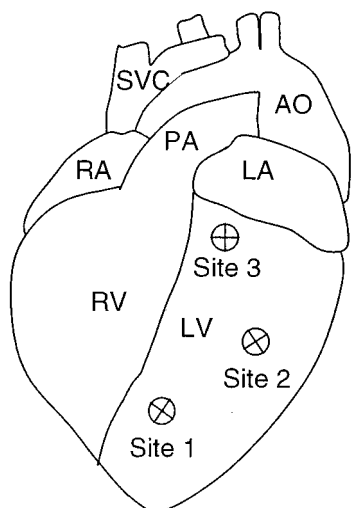


Fig. 3. The three measurement sites on left ventricular surface. LV = left ventricle; RV = right ventricle; LA = left atrium; RA = right atrium; AO = aorta; PA = pulmonary artery; SVC = superior vena cava.

the other across. We determined the fiber direction by visual inspection and from previous *in-vitro* study of the fiber direction of excised pig hearts. Fig. 3 shows the three sites of measurement. We measured at 1 Hz, 10 Hz, 100 Hz, 1 kHz, 10 kHz, 100 kHz, 500 kHz, and 1 MHz. During the injection of current, we fixed the output voltage of the function generator at 4 V for every frequency except 10 and 100 Hz, for which we fixed it at 0.8 and 2 V, respectively. During this step, we also measured the temperature of the myocardium and corrected the myocardial resistivities with a $-2\%/^{\circ}\text{C}$ temperature coefficient.

Step 4a. Subtracting the system error. (optional)

In another paper [15], we introduce a method for analyzing and measuring the errors accompanying the measurement of tissue resistivity. The overall measurement error comprises random error and systematic error. At this optional step, we subtract the systematic error from the measured myocardial resistivity, if it is available.

E. Practical Measurements

We measured eight pigs *in-vivo*. For each pig, we repeated Step 2 and Step 3 to obtain a new set of wire-probe constants. For each calculation with (3), the computer interpolated the wire-probe constant set to obtain a value of K_{w-p} specifically for the measured voltage ratio $(V_1/V_2)_4$. We used the SPLINE (Cubic spline interpolation) function in MATLAB (The MathWorks, Inc., Natick, MA) for interpolation.

In addition to the *in-vivo* measurement, we also measured the postmortem change of myocardial resistivity. We first inserted the plunge probe and made *in-vivo* baseline measurements when the pig was still alive, and then we injected a large current magnitude at 10 Hz for several seconds to cause ventricular fibrillation and sacrifice the pig. Within 1 min after we injected the large current, the pig's heart stopped beating, and then, we made a measurement from 1 Hz to 1 MHz every few minutes.

With an averaging function in the LabVIEW program, We took 101-time averages in Step 1 and 10-time averages in Steps 2 and 3 in order to decrease the quantization error of the digital oscilloscope [15].

III. RESULTS AND DISCUSSION

A. In-Vivo Calibration

Fig. 4(a) shows an example of the wire-probe constant measured in Step 3, where the calibrating saline solution was contained in a stainless-steel cup, which was in contact with the pig's heart. The stray capacitance between the saline solution and the ground measured with a simple resistance-capacitance configuration was about 250 pF. Connection or disconnection of the metal cup to the pig did not affect the measured value of the stray capacitance. The dependence of the wire-probe constant on the saline resistivity increased drastically at frequencies higher than 100 kHz due to the variation of the leakage current through the stray capacitance.

Fig. 4(b) shows the wire-probe constant measured with the same pig in the same conditions except that we disconnected the metal cup from the pig's heart by placing a plastic layer in between. In this situation, at high frequencies, the wire-probe constant was very different from that measured with contact between the metal cup and the pig's heart. It was less sensitive to the change of saline resistivity because of smaller stray capacitance, which was about 50 pF, between the saline solution and the ground.

A comparison of Fig. 4(a) and (b) shows that it is important to calibrate the resistivity probe with various saline resistivity values and with a connection between the saline and the pig in order to minimize the error caused by the leakage current flowing through the stray capacitance between the pig and the ground. Our *in-vivo* measurement result showed that the myocardial resistivity at 1 MHz was about $166 \Omega \cdot \text{cm}$ (shown below). If we had used the calibration result of Fig. 4(b) to calculate the myocardial resistivity, the error would have been about 5% at 1 MHz.

To ensure accurate calibration, we suggest repeating Step 2 and Step 3 for every pig experiment. However, the calibration steps take hours and sometimes it may not be convenient to carry out these steps when the pig is still alive. Instead of *in-vivo* calibration, it is appropriate to do it *in situ* after finishing the *in-vivo* measurement of myocardial resistivity.

B. Measurement Results

Fig. 5 shows all the measured myocardial resistivities in the two directions at the three sites on the left ventricles of the eight pigs. The measured myocardial temperature during *in-vivo* measurements was within $(38 \pm 1)^{\circ}\text{C}$. The results shown here represent the myocardial resistivity at 38°C . We have subtracted from the measured resistivity shown here the systematic error that we obtained from analyzing and measuring the error of the resistivity measurement [15]. The systematic error was -0.3412 , 0.1184 , 0.1370 , 0.1950 , 0.0346 , -0.2180 , -0.4837 , and -0.3584 in percentage at the eight frequencies of measurement from 1 Hz to 1 MHz. It is apparent that the measured myocardial resistivity had larger variation

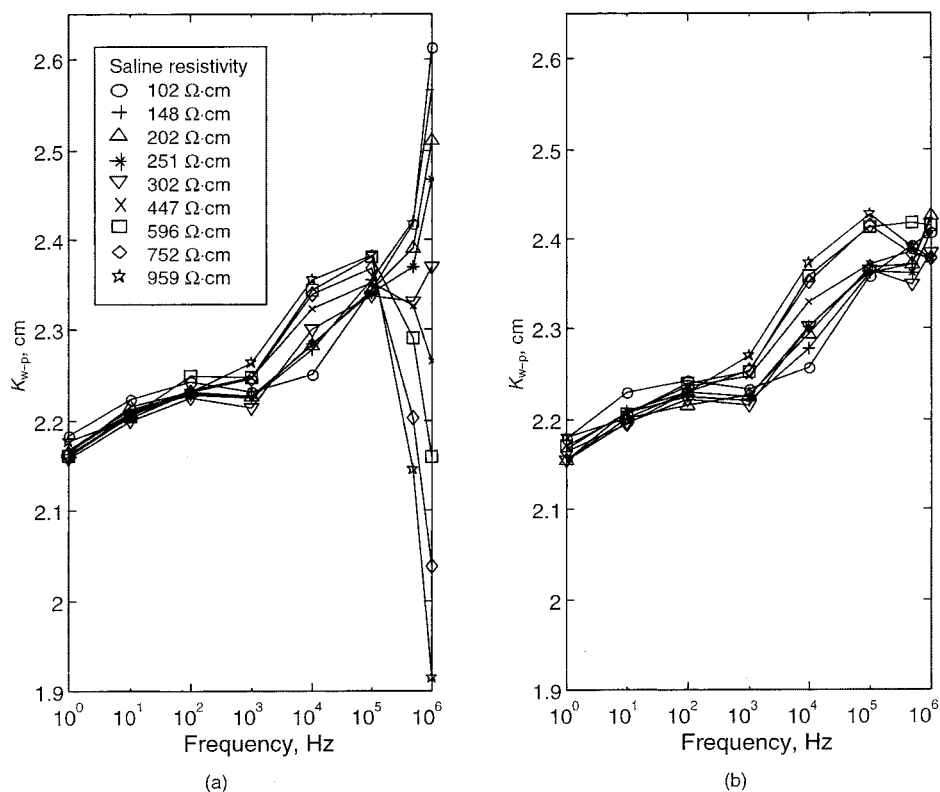


Fig. 4. An example of the wire-probe constant of the four-electrode stainless-steel plunge probe calibrated with various saline resistivities. The saline solution was contained in a metal cup which was placed on the top of the heart. (a) With contact between the metal cup and the pig's heart. (b) Without contact between the metal cup and the pig's heart.

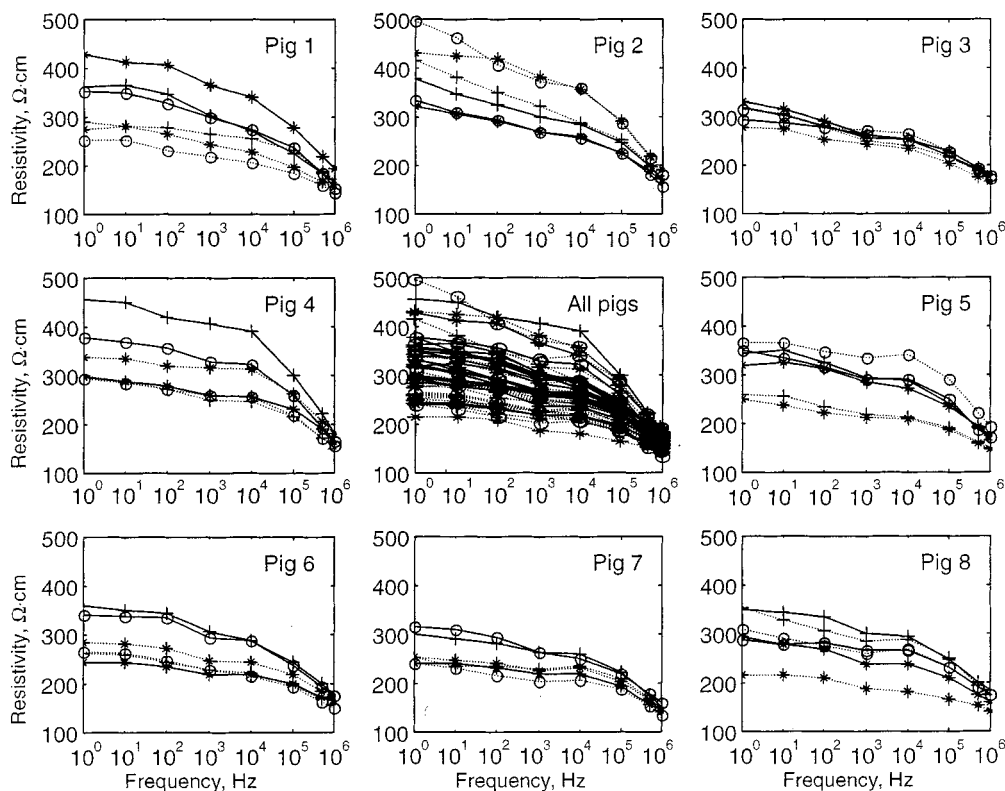


Fig. 5. All the measured *in-vivo* myocardial resistivity results in the two directions at the three sites on the left ventricles of the eight pigs. The results shown here are the original measured myocardial resistivities subtracting the systematic error measured with the method described in [14]. —: Longitudinal;: transverse; o: site 1; +: site 2; and *: site 3.

TABLE I
THE MEAN AND STANDARD DEVIATION OF ALL THE RESULTS OF MEASURED MYOCARDIAL RESISTIVITY
IN TWO DIRECTIONS AT THREE SITES OF THE LEFT VENTRICLES IN EIGHT PIGS

Frequency	1 Hz	10 Hz	100 Hz	1 kHz	10 kHz	100 kHz	500 kHz	1 MHz
Mean ($\Omega\cdot\text{cm}$)	319	310	294	272	264	228	185	166
Std ($\Omega\cdot\text{cm}$)	60	57	53	47	44	30	18	15

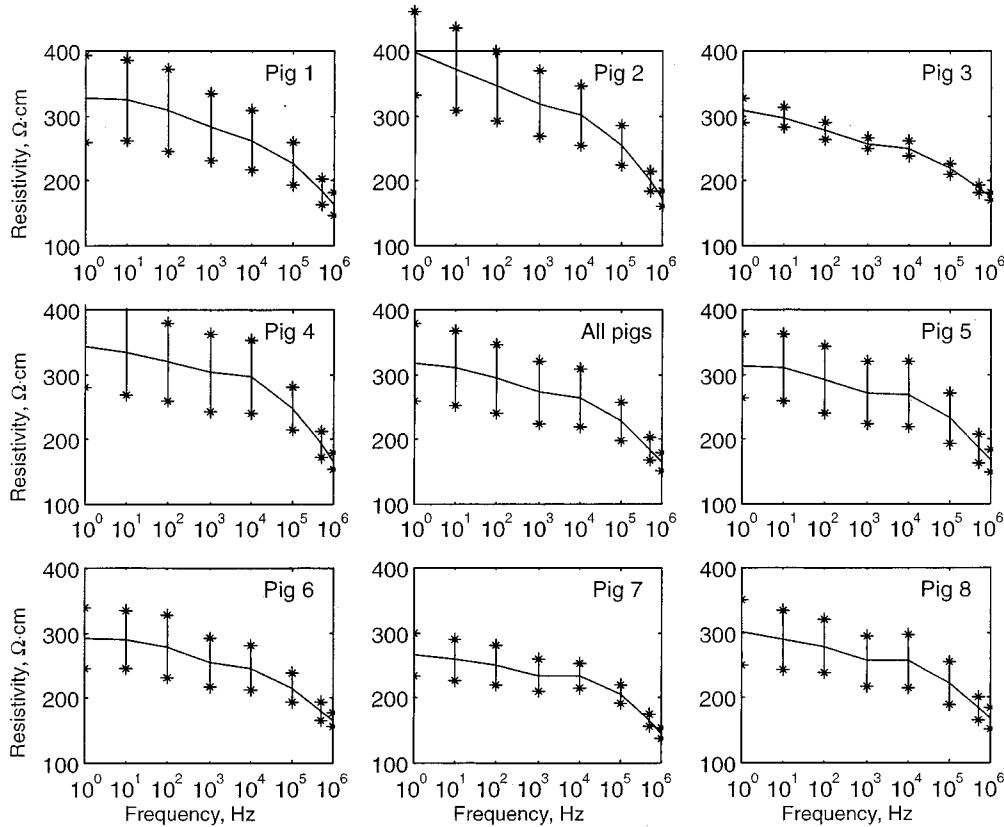


Fig. 6. The mean of the measured myocardial resistivity eight pigs. Mean \pm standard deviation (asterisks) is shown at each measurement frequency.

at low frequencies in each of the eight pigs. This was due to the variation of the fiber direction around the electrodes. At low-frequency, the resistivity had larger differences in the longitudinal and the transverse directions. At high-frequency, the capacitive cell membranes of myocardium become nearly short-circuited and the fiber direction has a smaller effect on the measured resistivity. Table I shows the mean of the 48 samples of myocardial resistivity measured from the eight pigs at the three sites in the two directions.

Fig. 6 shows the mean for all directions and sites, of the measured myocardial resistivity of each of the eight pigs. We used ANOVA to compare the measured results of the eight pigs and found that there was no significant difference at frequencies 10, 100, and 500 kHz ($p > 0.067$). We then used the t -test to compare the means of myocardial resistivity at the other frequencies in every pair of the eight pigs. The t -test shows that the myocardial resistivity of pig 7 was significantly different from that of all the other seven pigs at certain frequencies and that of pig 2 was significantly different from that of five of the other pigs at certain frequencies. Table II shows the result of statistical analysis.

Fig. 7 shows the mean for all directions and pigs, of the measured myocardial resistivity at each of the three sites. We used ANOVA to compare the means at the three sites and found there was no significant difference between any two sites ($p > 0.285$ for all frequencies).

Fig. 8 shows the mean for all sites and pigs, of the measured myocardial resistivity in each of the two directions. The t -test shows that there was significant difference at 100 Hz ($p = 0.030$) and no significant difference at other frequencies ($p > 0.076$). We expected that the tissue resistivity measured with a plunge probe in a direction across the tissue fibers would be higher than that measured along the fibers. Our results showed that the measurement with a plunge probe could not distinguish the two directions. The resistivity measured in the transverse direction could be higher than, equal to, or lower than that in the transverse direction at the same site. We assume this is due to the rapid transmural change of the myocardial fiber orientation. The fiber direction beneath the epicardium is different from that on the epicardium. With a 4.5-mm length, the electrodes passed through myocardial fibers of different directions. With 1–2 cm ventricular wall thickness, the measured myocardial resistivity

TABLE II
THE PIG PAIRS THAT HAD SIGNIFICANT DIFFERENCES IN MYOCARDIAL RESISTIVITY AT FREQUENCIES BETWEEN 1 HZ TO 1 MHZ. EACH DIGIT OF THE EIGHT DIGITS IN TABLE CELLS REPRESENTS ONE FREQUENCY. STARTING FROM THE LEFTMOST DIGIT, THEY ARE 1 HZ, 10 HZ, 100 HZ, 1 KHZ, 10 KHZ, 100 KHZ, 500 KHZ, AND 1 MHZ. "1" MEANS SIGNIFICANT DIFFERENCE ($p < 0.050$) AT THAT FREQUENCY AND "0" MEANS NO SIGNIFICANT DIFFERENCE

Pig	1	2	3	4	5	6	7	8
1								
2	00000000							
3	00000000	11110000						
4	00000000	00000000	00000000					
5	00000000	10000000	00000000	00000000				
6	00000000	11110000	00000000	00000000	00000000			
7	01000001	11110001	11010001	11110001	00000001	00000001		
8	00000000	11110000	00000000	00000000	00000000	00000000	00000001	00000001

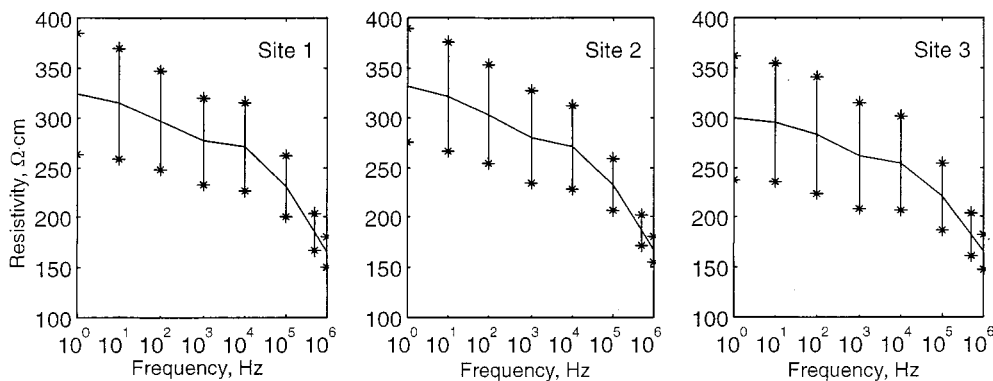


Fig. 7. The mean of the measured myocardial resistivity at the three sites of the left ventricles in eight pigs. Mean \pm standard deviation (asterisks) is shown at each measurement frequency.

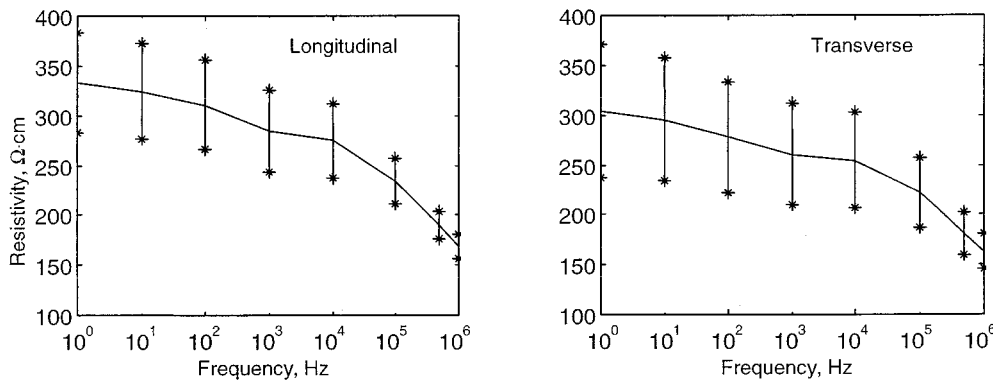


Fig. 8. The mean of the results of measured myocardial resistivity in the two directions from eight pigs. Mean \pm standard deviation (asterisks) is shown at each measurement frequency.

included contributions of the resistivity of myocardial fibers of different directions in about the 45° – 90° range.

Fig. 9 shows the postmortem change in myocardial resistivity measured from one pig. Right after the heart stopped beating, the myocardial resistivity increased rapidly at low frequencies. The values at 1 Hz and 10 Hz reached 150% at 50 min after death. Starting from about the fiftieth min, the resistivity at all frequencies increased even more rapidly, especially at midfrequencies. The low-frequency resistivity reached nearly 250% at 100 min. Between 100 and 150 min, the resistivity changed very slowly, less than 3% at all frequencies. After that, the resistivity at all frequencies increased gradually until 7 h past death, when we stopped the measurement. The myocardial resistivity at 1, 10, and 100 Hz increased to about three times the original

in-vivo value and that at 500 kHz and 1 MHz increased less than 15% 6 h after death.

The time course shown in Fig. 9 is a typical case. However, the result might change depending on how we treated the pig's heart. In this case, during the 6 h of postmortem measurement, we did not cover the epicardial surface around the probe base and we let the heart cool down naturally. The results shown have been corrected with a $-2\%/^\circ\text{C}$ temperature coefficient. We kept the electrodes in the myocardium by fixing the shaft of the probe to the surgical retractor.

C. Comparison With Others' Measurements

Fig. 10 compares our *in-vivo* measurement result of swine myocardial resistivity with that of others. At high frequencies,

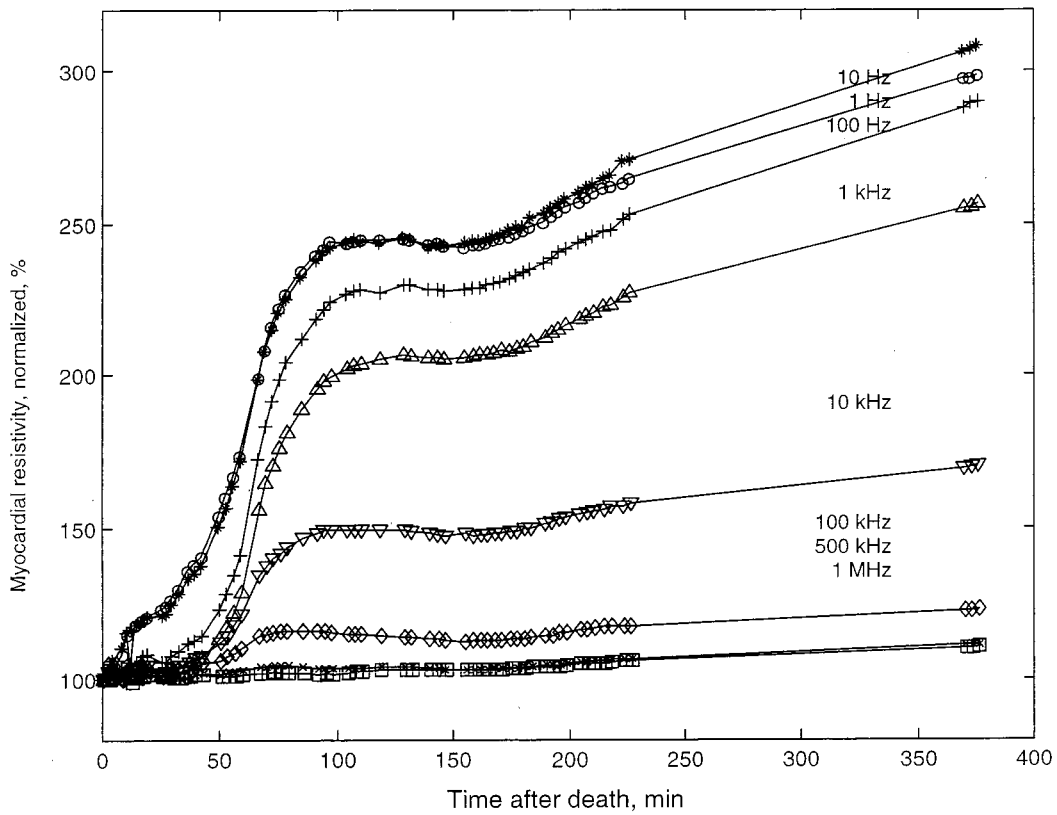


Fig. 9. The postmortem time course of the myocardial resistivity measured at site 1 in transverse direction from one pig.

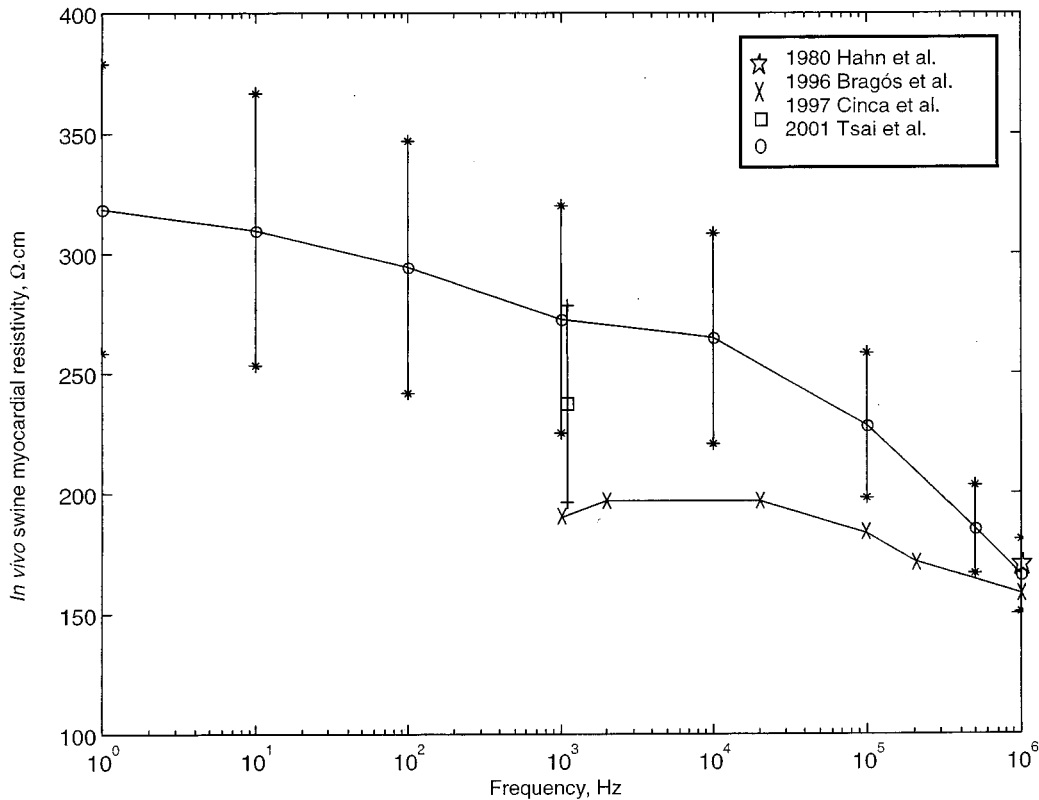


Fig. 10. Comparison of *in-vivo* swine myocardial resistivity measured by different researchers. Not shown in this figure is $(187 \pm 120) \Omega \cdot \text{cm}$ measured by Smith *et al.* [11] with a dc pulse of 20 ms duration.

there was general agreement among research groups. Our result, $(166 \pm 15) \Omega \cdot \text{cm}$, at 1 MHz is close to 170 $\Omega \cdot \text{cm}$

of Hahn *et al.* [11] and 159 $\Omega \cdot \text{cm}$ of Bragós [13], although they did not describe compensation for the problem of stray

capacitance between the pig and ground. Our results in the mid- and low-frequency ranges are higher than others' results. Our result, $(272 \pm 47) \Omega \cdot \text{cm}$, at 1 kHz is higher than $190 \Omega \cdot \text{cm}$ measured by Bragós at 1 kHz and $(237 \pm 41) \Omega \cdot \text{cm}$ measured by Cinca at 1.11 kHz. Our results are also higher than $(187 \pm 120) \Omega \cdot \text{cm}$ measured by Smith *et al.* [12] with a 20 ms dc pulse.

It is noteworthy that each of these measurement results was a combination of the resistivity of myocardial fibers in various directions. However, Rush *et al.* [4] used a four-point probe to measure the myocardium of dogs *in-vivo* in two directions and calculated the transverse and longitudinal resistivity with analytic formulae, which assume uniform fiber direction. They obtained about 2.2 for anisotropy, transverse vs. longitudinal resistivity, at frequencies between 5 Hz and 60 Hz. Steendijk *et al.* [5] used a similar method on dogs. They obtained 1.6 anisotropy at 5 kHz.

D. Ventricular Fibrillation

The cellular excitation of the heart beating caused drifting of the differential voltage sensed by the voltage electrodes. For accuracy's sake, we tried to inject as large a current as possible to increase the signal-to-drifting ratio. However, because the injected current interfered with normal cellular excitation, we could cause ventricular fibrillation by injecting too large a current. We found that the heart was mostly vulnerable to the injected current at 10 Hz and next 100 Hz among the frequencies we used. We tested on several pigs and found that the pig would be free of ventricular fibrillation if the injected current was less than $100 \mu\text{A}$ at 10 Hz and less than $250 \mu\text{A}$ at 100 Hz. We, thus, limited the injected current magnitude accordingly. For all the pigs, we set the output voltage of the function generator to 0.8 V at 10 Hz, 2 V at 100 Hz, and 4 V at other frequencies. This way, we could finish the resistivity measurement *in-vivo* at the three sites in two directions without causing ventricular fibrillation.

E. Electrode Material

In initial studies, we made resistivity probes with silver electrodes and found some undesirable properties. The silver electrodes were too compliant. They bent easily during insertion into myocardium and they could be further bent by the twisting of the heart wall after insertion. Moreover, it was very difficult to insert the silver electrodes into the myocardium, even if we made their tips sharp. The other problem of silver electrodes was that the injected current varied the chloriding and, hence, yielded an unstable probe constant.

The stainless-steel hypodermic needles used to make the plunge electrodes were very stiff and their tips were very sharp. By visual inspection of the electrode surfaces, we found they stayed shiny after every insertion and measurement. Our measurement also showed stable probe constant.

Nevertheless, probably due to small interelectrode spacing, it still was not easy to insert the four-electrode array of hypodermic needles into the myocardium even though they were sharp. Very often the electrodes just went partway into the myocardium and we had to pull them out and re-insert. It was important to inspect the electrodes after insertion to make sure they

all went in entirely. Stabbing quickly instead of driving the electrodes slowly would make insertion easier.

F. Probe Constant

Fig. 4 shows that our probe constant of the plunge probe from 1 Hz to 1 MHz was not constant. The fact that the oscilloscope-circuit constant measured in *Step 1* and the saline solution measurement in *Step 2* are constant over the frequency range suggests that our circuit does not cause the variation of the probe constant. We connected the four terminals to a ladder circuit consisting of three resistors in series. The oscilloscope-circuit constant measured this way was also constant. Furthermore, the probe constant became more constant when we made the electrode distance larger. We speculate that the response variation was caused by the change of the effective center of the electrodes and the change of the electric field around the electrodes when frequency changes. Nevertheless, the variation itself does not cause error in the measured resistivity since it is repeatable.

IV. CONCLUSION

Accurate *in-vivo* measurement of myocardial resistivity is difficult because of the finite-thickness structure of the heart wall, the spatially changing orientation of myocardial fibers, and the movement of the beating heart. The leakage current through stray capacitance between the measured subject and the ground further complicates the problem. We used a plunge probe with electrode length and interelectrode spacing small enough compared with the heart wall thickness to prevent the influence of the in-chamber blood on the measurement result. We added a plastic shaft to the epoxy base of the plunge probe so that we were able to hold the probe with fingers to keep the electrodes in the myocardium with good contact while the pig's heart was beating.

The stray capacitance between a pig on a surgical table and the circuit ground is greater than that between a cup of saline solution and the ground. The difference in the leakage current through the stray capacitance changes the effective probe constant of a plunge probe. It would cause considerable error at frequencies higher than 100 kHz, if we had used the probe constant obtained by calibrating the plunge probe in a cup of saline solution to calculate the tissue resistivity measured *in-vivo* from a pig. Moreover, the leakage current changed with the tissue resistivity and, therefore, the probe constant did also. To deal with the problems caused by stray capacitance, we performed *in-vivo* or *in situ* calibration. We used a metal cup to contain the calibrating saline solution and we made the metal cup in contact with the pig's heart. We calibrated the resistivity probe by measuring a set of probe constants in saline solutions with resistivity that encompassed the possible myocardial resistivity and interpolated them to obtain the probe constant for an apparent resistance value measured from the pig's myocardium. The whole process is time consuming but worthwhile for the applications requiring high accuracy at high frequencies.

We measured the myocardial resistivity at eight frequencies from 1 Hz to 1 MHz at three sites in the left ventricle of each of eight pigs. At each site, we made two separate measurements by

aligning the four-electrode array along and across, respectively, the epicardial fiber direction. The electrodes extended into the myocardium with changing fiber directions, which obscured the distinction in fiber direction between the two measurements. Our measurement results are similar to those of others at high frequencies but higher at mid and low frequencies. We used statistical tests to reveal the difference between pigs, sites, and directions. Some pigs were significantly different from other pigs, but there was little difference in the measured myocardial resistivity between sites and between directions.

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Jang-Zern Tsai was born in Chia-Yi, Taiwan, in 1961. He received the B.S.E.E. degree from National Central University, Chung-Li, Taiwan, in 1984, and the M.S.E.E. degree from National Tsing Hua University, Hsinchu, Taiwan, in 1986. In 2001, he received the Ph.D. degree in electrical and computer engineering from University of Wisconsin at Madison, doing research on myocardial resistivity measurement.

He joined the Industrial Technology Research Institute (ITRI), Hsinchu, Taiwan, as an Integrated-Circuit Applications Engineer and as a Hardware Engineer working on digital recording technology and the Accton Technology Corporation, Hsinchu, Taiwan, as a Software Engineer. He is presently a Postdoctoral Fellow at the University of California-Berkeley developing hardware for electrical impedance tomography.



James A. Will received the B.S. degree in agriculture in 1952, the M.S. degree in animal science in 1953 and the Ph.D. degree in veterinary science in 1967 from the University of Wisconsin-Madison. He received the D.V.M. degree from Kansas State University, Manhattan, in 1960.

Since 1967, he has been with the University of Wisconsin-Madison, serving as Professor and Chairman of Veterinary Science from 1974 to 1978. He has 108 reviewed publications in animal surgery, specializing in pulmonary circulation and cardiopulmonary pharmacology.

Dr. Will is a member of the American Physiological Society, the Society For Experimental Biology and Medicine, Sigma Xi, the American Association for the Advancement of Science, the American Heart Association, and the American Veterinary Medical Association. He is a Fellow of the Royal Society of Medicine.



Scott Hubbard-Van Stelle attended the University of Wisconsin-Madison from 1974-1976. He received his Associate of Applied Science degree in 1978 from the Madison Area Technical College and became a certified Veterinary Technician.

Since then, he has worked at the University of Wisconsin-Madison as a Research Specialist for 18 years and currently as a Laboratory Animal Training Coordinator.

He became a member of the American Association of Laboratory Animal Science in 1979 and was certified as a Laboratory Animal Technologist in 1993.



Hong Cao (S'97) received the B.S. and M.S. degrees in electrical engineering from Nanjing University, Nanjing, China in 1992 and 1995, respectively. He received the Ph.D. degree in electrical and computer engineering from the University of Wisconsin-Madison in 2001.

Currently, he is a Senior Software Developer with Epic System Corporation, Madison, WI, working on the enterprise electronic medical record (EMR) database system and integration of medical instruments into the EMR system. His research interests include medical instrumentation, RF catheter ablation of cardiac tissue and hepatic tumors, and medical information systems. He is contributing author to J. G. Webster (Ed.), *Minimally Invasive Medical Technology* (Bristol, UK: IOP, 2001).



Supan Tungjitsolmun (S'96–M'00) was born in Bangkok, Thailand, December 5, 1972. He received the B.S.E.E. degree from the University of Pennsylvania, Philadelphia, in 1995, and the M.S.E.E. and the Ph.D. degrees from the University of Wisconsin, Madison, in 1996, and 2000.

He is on the faculty of the Department of Electronics, Faculty of Engineering, and the Research Center for Communications and Information Technology, King Mongkut's Institute of Technology Ladkrabang (KMITL), Bangkok, Thailand. His research interests include finite-element modeling, radio-frequency cardiac ablation, and hepatic ablation.

Dr. Tungjitsolmun is a member of Tau Beta Pi, Eta Kappa Nu, and Pi Mu Epsilon.



Vicken R. Vorperian received the M.D. degree in 1985 from the American University of Beirut, Beirut, Lebanon. He did a fellowship in cardiac arrhythmias and electrophysiology at the Vanderbilt University, Nashville, TN; and a fellowship in cardiac pacing and catheter ablation at the University of Michigan, Ann Arbor.

He is Clinical Associate Professor of Medicine in the Department of Medicine, University of Wisconsin-Madison and is an Electrophysiologist in the Cardiac Electrophysiology Laboratory, the University of Wisconsin Hospital, Madison. He is also a member of the Arrhythmia Consultants of Milwaukee S.C., a private practice group in cardiac arrhythmias and clinical cardiac electrophysiology.



Young Bin Choy (SM'00) was born in Seoul, Korea, on Aug 17, 1976. He received the B.S. degree in 1999 from the School of Electrical Engineering, Seoul National University, Seoul, Korea. He received the M.S.E.E degree in 2000 from the University of Wisconsin-Madison. His research was measuring the mechanical compliance of the endocardium to determine the relation between the penetration depth of the RF cardiac catheter ablation electrode and the force. He is currently a Ph.D. candidate at the University of Illinois at Urbana-Champaign.

He was an Engineer in LG Corporate Institute of Technology, Seoul, Korea, from January to June 1999.



Dieter Haemmerich (S'00) was born in Vienna, Austria, on May 22, 1971. He received the B.S.E.E. degree from the Technical University of Vienna, Vienna, Austria, in 1997 and the M.S.B.M.E. and the Ph.D. degree from the Department of Biomedical Engineering, University of Wisconsin, Madison, in 2000 and 2001, respectively.

He is currently an Assistant Scientist in the Department of Surgery, University of Wisconsin, Madison. His research interests include finite-element analysis of radio-frequency ablation and tissue impedance measurement.



John G. Webster (M'59–SM'69–F'86–LF'97) received the B.E.E. degree from Cornell University, Ithaca, NY, in 1953, and the M.S.E.E. and Ph.D. degrees from the University of Rochester, Rochester, NY, in 1965 and 1967, respectively.

He is Professor of Biomedical Engineering at the University of Wisconsin-Madison. In the field of medical instrumentation he teaches undergraduate and graduate courses, and does research on RF cardiac and hepatic ablation. He is editor of *Medical instrumentation: application and design, Third Edition* (New York: Wiley, 1998), *Encyclopedia of electrical and electronics engineering* (New York: Wiley, 1999), and *Minimally invasive medical technology* (Bristol, UK: IOP, 2001).

Dr. Webster is the recipient of the 2001 IEEE-EMBS Career Achievement Award.