Continuous measurement of left ventricular volume in animals and humans by conductance catheter

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ABSTRACT An eight-electrode conductance catheter previously developed by us and used to determine stroke volume in dogs was applied in human beings and dogs to measure absolute left ventricular volume quantitatively. For calibration we developed the formula \( V(t) = \frac{1}{\alpha}(L^2/\sigma_0)G(t) - V_0 \), where \( V(t) \) is time-varying left ventricular volume, \( \alpha \) is a dimensionless constant, \( L \) is the electrode separation, \( \sigma_0 \) is the conductivity of blood obtained by a sampling cuvette, and \( G(t) \) is the measured conductance within the left ventricular cavity. \( V_0 \) is a correction term caused by the parallel conductance of structures surrounding the cavity and is measured in two ways. The first method, applicable in the anesthetized animal, consists of temporary reduction of volume to zero by suction. The second method uses a transient change in \( \sigma_0 \) by injection of a small bolus of hypertonic saline (dogs) or 10 ml of cold glucose (humans) into the pulmonary artery. The validity of the formula was previously established for the isolated postmortem canine heart. The predicted linearity, slope constant \( \alpha \), and accuracy of \( V_0 \) for the left ventricle in vivo were investigated by comparing the conductance volume data with results from independent methods: electromagnetic blood flow measurement for stroke volume and indicator dilution technique for ejection fraction (dogs), thermal dilution for cardiac output (12 patients), and single-plane cineventriculography for \( V(t) \) (five patients). In all comparisons, linear regression showed high correlation (from \( r = .82 \) [\( n = 46 \) ] to \( r = .988 \) [\( n = 20 \) ] ) while \( \alpha \), with one exception, ranged from 0.75 to 1.07 and the error in \( V_0 \) ranged from 0.5% to 16.5% (mean 7%). After positioning of the catheter, no arrhythmias were observed. It is concluded that the conductance catheter provides a reliable and simple method to measure left ventricular volume, giving an on-line, time-varying signal that is easily calibrated. Together with left ventricular pressure obtained through the catheter lumen, the instrument may be used for instantaneous display of pressure-volume loops to facilitate assessment of left ventricular pump performance. 


PUMP FUNCTION of the left ventricle is commonly determined in the cardiac catheterization laboratory by measuring left ventricular pressure and by obtaining a ventriculogram. From the latter, left ventricular volume and ejection fraction are obtained, while the pressure tracing is used to determine maximal dP/dt. A difficulty with these indexes is that they are dependent on preload and/or afterload.1,2

A solution to this problem might lie in the combination of ventricular pressure with volume, especially when considering the end-systolic pressure-volume relationship. At least in the isolated heart, it has been shown that the slope of this relationship, \( E_{max} \), is not dependent on loading conditions.3 Application of this concept to assess pump function in human beings has been initiated4,5 but is hampered by two factors: (1) There is a general lack of experimental studies on ventricular pressure-volume relationships of the heart in situ. (2) It is hard to obtain a ventriculogram simultaneously with ventricular pressure, and the conversion from the radiographic image to a time-varying ventricular volume is complex and time consuming. Moreover, it is not possible with this technique to monitor pump function continuously, e.g., during interventions.

A method that combines the measurement of left ventricular pressure and volume by means of a conductance catheter was developed in our laboratory. The instrument has previously been applied to measure car-
diac output and stroke volume in dogs, and the first results of its application in humans were presented previously. This article describes how the conductance catheter is used to determine absolute left ventricular volume in humans and dogs, and how the results compare with those obtained by standard methods.

**Materials and methods**

Studies were performed in anesthetized mongrel dogs and in patients undergoing left heart catheterization for diagnostic purposes.

The conductance catheter (custom made by Cordis Europa NV, Roden, The Netherlands) and the conditioning amplifier to measure conductance and convert it to volume (Model Sigma 5; Leycom, Oegstgeest, The Netherlands) have been described previously. In principle, eight electrodes are equally spaced near the far end of a catheter positioned along the left ventricular axis. An example of a catheter used in patients, differing from those used in dogs, since it has a lumen for pressure measurement and a pigtail, is shown in figure 1. The electrode distance, L, is chosen so that with electrode 1 within the apex, electrode 8 is situated just above the aortic valve. The 20 kHz current (0.07 mA root mean square) applied between electrodes 1 and 8 is well below the safety limit set by the Association for the Advancement of Medical Instrumentation, which is 0.2 mA root mean square at 20 kHz. The voltages measured between adjacent electrodes have an order of magnitude of 1 mV root mean square. Time-varying left ventricular volume, V(t), follows from the measured conductance in the left ventricular through

\[ V(t) = \frac{1}{\alpha} \left( \frac{L^2}{\sigma_b} \right) G(t) - V_c \]  

in which \( \alpha \) is a dimensionless constant, \( \sigma_b \) is the specific conductivity of blood measured by a calibrating cuvette, and \( G(t) \) is the sum of the conductances \( G_n(t) \) measured between the five pairs of adjacent electrodes:

\[ G(t) = \sum_{n=1}^{5} G_n(t) + 1/3 G_0(t) \]  

\( V_c \) is a correction term caused by the conductance, \( G^p \), of structures surrounding the ventricular cavity:

\[ V_c = \frac{1}{\alpha} \left( \frac{L^2}{\sigma_b} \right) G^p \]  

Equation (1) differs from the formula originally derived in that it incorporates the slope factor \( \alpha \) and the correction term \( V_c \). For an isolated postmortem canine left ventricle we found that \( \alpha = 0.8 \) and \( V_c = 31 \) ml, while the relation between \( V \) and \( G \) was linear from 0 to 55 ml. In that study, a model was described relating \( V \) to \( G \) analytically with a spheroidal model of the left ventricle. For the same canine ventricle the model predicted an almost identical relationship \( \alpha = 0.7, V_c = 28 \) ml, which was very linear over the same range, while for a human left ventricle the model-predicted relation was virtually linear up to 200 ml.

This study is concerned with validation of the conductance method in vivo; therefore we investigated the shape, slope, and zero-volume intersection point of the relationship between \( (L^2/\sigma_b)G(t) \) and \( V(t) \).

To obtain ventricular volume by independent methods, we used integrated blood flow (\( Q_b \)) during ejection measured by electromagnetic flowmeter (dogs), ejection fraction measured by indicator dilution (dogs), cardiac output measured by thermal dilution (humans), and time-varying volume measured by contrast cineventriculography (humans). To estimate the correction factor \( V_c \), two different techniques were applied, a summarized description of which has been given previously.

**V, obtained by suction (dogs).** The first method to estimate \( V_c \) consists in temporarily reducing cavity volume to zero. In such a situation, all current flows through the tissues surrounding the cavity and the measured conductance, \( G^p \), is the parallel conductance, since cavity conductance is zero. In the canine experiments, volume was reduced to zero by suction through a multiple-hole catheter in the left ventricle while inflow was prevented either manually or by inflating a balloon in the left atrium, which occluded the mitral ostium. Suction was applied until ventricular pressure fell below zero. Since the blood in the right ventricle also contributes to \( G^p \), it was reduced to a minimum by caval occlusion. Occasionally, the blood was removed from both ventricles by external manual compression.

**V, obtained by dilution.** The second method to estimate \( V_c \) is based on the circumstance that the conductance \( G \) is linearly related to the specific conductivity of blood, \( \sigma_b \). Combining equations (1) and (3) yields

\[ G(t) = \frac{\alpha}{L^2} \sigma_b V(t) + G^p \]  

Thus, if \( \sigma_b \) is changed by an intervention, the relationship between \( G \) and \( V \) [equation (1)] changes, from which \( G^p \) may be solved. By means of an indicator, \( \sigma_b \) was changed in a transient fashion. In dogs we injected a 0.5 to 1.5 ml bolus of hypertonic saline solution (6M with \( \sigma = 75 \) S/m); in patients we used a quantity of 10 ml of cold glucose solution (2° to 4° C, \( \sigma = 0 \) S/m). The injection was made into the pulmonary artery. Upon

**FIGURE 1.** Conductance catheter (No. 7F), 10 cm, with pigtail for use in humans, schematically shown positioned along left ventricular axis. Note fluid channel for pressure measurement and electrical connector for conductance.
arrival of the bolus in the left ventricle, the salt increased $\sigma_b$ (and thus $G$) while the cold glucose decreased $\sigma_b$ slightly.

During the intervention, end-diastolic (ED) and end-systolic (ES) values of $G(t)$ were sampled by computer on a beat-to-beat basis, and $G_{ES}$ was plotted as a function of $G_{ED}$ during the beats while $\sigma_v$ was changing. The following equation was derived from equation (4):

$$G_{ES}(\sigma_b) = G_{ED}(\sigma_b) + \frac{\alpha}{L^2} \sigma_v (V_{ES} - V_{ED})$$

The slope of this parametric equation in $\sigma_v$ equals $1 - EF$ (ejection fraction). Provided ejection fraction remains constant during the injection, $G^p$ may be deduced from the relationship between $G_{ES}$ and $G_{ED}$, which in the limit $\sigma_b \to 0$ gives $G_{ES} = G_{ED} = G^p$. Thus $G^p$ is the intersection point between the identity line ($G_{ES} = G_{ED}$) and the line obtained by linear regression of the experimental $G_{ES}, G_{ED}$ points. From equation (3), $V_c$ is then obtained from $G^p$.

The use of this method relies on the constancy of $G^p$ during the intervention. Since the diluted blood enters the coronary circulation this assumption might be violated. Therefore the influence of the hypertonic saline was investigated by injecting a bolus of 1.5 ml diluted by a factor 10 into the main stem of the left coronary artery in dogs.

**Studies in dogs.** Testing of the catheter was performed in mongrel dogs weighing 15 to 38 kg. After premedication with 5 ml of Hypnorm (10 mg of fluanison and 0.2 mg of fentanyl per milliliter) intramuscularly and 0.5 ml of atropine subcutaneously, anesthesia was initiated with 15 mg/kg iv sodiumpentobarbital (Nembutol) and maintained with an intravenous infusion of methadone (2.5 mg/hr) and droperidol (12.5 mg/hr). Respiration was maintained with a 3:1 mixture of $N_2O$ and $O_2$ administered by a Dräger-Pulmonat respirator. Blood volume and pressure were maintained by an intravenous infusion of dextran (Macrodex). The chest was opened via a midline sternotomy and a dual-sensor, catheter-tip micromanometer (Millar PC 780 N) was introduced through the left common carotid artery to measure left ventricular and aortic pressures. The lead II electrocardiogram (ECG) was also recorded. The balloon-tipped catheter for mitral occlusion was placed via the left atrial appendage, and a conductance catheter with appropriate electrode distance (5 to 8 cm total) was introduced into the left ventricle via the right common carotid artery. Correct position of the catheter was verified by palpation of the apex and again after termination of the experiment by opening the ventricle. The transient emptying of the ventricle was performed through the fluid channel of the Millar catheter or through a multiple-hole catheter introduced into the left ventricle via the left subclavian artery. An electromagnetic flow probe (Skalar Corp., Delft, The Netherlands) was placed around the root of the aorta and loose ligatures were placed around both venae cavae and the descending aorta.

To determine ejection fraction by independent means we used a dilution method that employs ferromagnetic fluid (Ferrofluid type AO1; Ferrofluidics Co., Burlington, MA) as indicator. A small bolus (1 ml) of the fluid was injected into the left ventricle late in diastole, and its presence was detected by measuring the change in the self-inductance of a pick-up coil placed around the heart. The ventricular blood, made slightly ferromagnetic by the indicator, acts as a magnetic core to the pick-up coil. We have previously shown that with this technique dilution curves with flat plateaus are obtained, 12 thus allowing for calculation of ejection fraction in the same manner as from a first-pass isotopic dilution curve. 13

For the injection of hypertonic saline, a balloon flotation catheter (Gould Statham model SP 50005 No. 5F) was placed with its tip in the pulmonary artery. In two experiments a pair of ultrasonic crystals (Schuessler, Cardify by the Sea, CA) was placed on the endocardial surface of the left ventricle to monitor equatorial diameter.

Changes in stroke volume and ejection fraction were produced by venous and/or aortic occlusions, volume loading, and administration of dobutamine (Dobutrex, 4 to 10 $\mu$g/kg/min).

**Studies in patients.** For studies in patients the catheter was equipped with a fluid channel and a pigtail (figure 1). This facilitated placement of the tip in the apex and eliminated risk of endocardial damage. Since the end of the pigtail points toward the ventricle, satisfactory pressure tracings could be secured in most cases. The channel was also used for a guidewire (Cordis size 0.025 or 0.032 inch) to facilitate passing the catheter through the aortic valve. Measurements were performed in 12 patients undergoing left heart catheterization for diagnostic purposes after informed consent was obtained. The subjects ranged from 1.50 to 1.83 m in height and from 61 to 86 kg in body weight. In this early stage, patients were selected without shunts or valvular abnormalities. Four patients had angiographically normal coronary arteries, while eight had stenoses of various degrees involving one to three branches; two of them had histories of myocardial infarction.

By means of transcutaneous arterial puncture, catheters were introduced through the right external femoral artery with a sheath (Cordis F8). After selective right and left coronary arteriography (all patients), cineventriculographic studies were performed in seven patients by standard injection of dye into the left ventricle through a No. 7F Eppendorf catheter, but the data on left ventricular volume obtained from the angiogram were not used for comparison with the conductance data secured later during the procedure. In the other five patients we were able to obtain a cineventriculogram simultaneously with conductance measurements by injecting angiographic dye into the pulmonary artery. For this purpose, a No. 7F Eppendorf catheter was introduced transcutaneously into the right femoral vein and advanced to the pulmonary artery. Subsequently, a conductance catheter was placed in the left ventricle.

To verify the position of the catheter in the ventricle, the site of the aortic valve on the angiographic screen was compared with the location of electrodes 7 and 8. During held respiration, 40 to 50 ml of angiographic dye (Isopaque) was injected at a rate of 25 ml/sec into the pulmonary artery by a power injector (Angiomat type 3000). As soon as the dye entered the left ventricle, a cineangiogram was recorded in the 45 degree right anterior oblique position. Subsequently, during respiratory arrest, the injection method to estimate $V_c$ was performed by hand-injecting the cold glucose solution into the pulmonary artery while recording conductance $G(\sigma_v)$ continuously. In those cases in which the glucose had no visible effect, the angiographic dye ($\sigma = 0.3$ S/m) was used as a satisfactory alternative.

In all patients a thermal dilution catheter (Gould, No. 7F) was placed in the pulmonary artery. By injection of 10 ml of cold glucose solution, cardiac output was determined from the thermal dilution curve immediately after the injection with use of an LSI 11/02 computer and standard formalism. Measurements were repeated until cardiac output values converged, and were subsequently taken three times during held respiration. The average cardiac output from these latter three measurements was then converted to average stroke volume. Stroke volume was also obtained by averaging 10 consecutive heartbeats as recorded by the conductance catheter just before or after thermal dilution measurements. Calibration for blood conductivity, $\sigma_v$, was done before and after each measurement.

**Data acquisition and analysis.** The conditioning amplifier converting the voltages from the conductance catheter to vol-
...gives the five segmental conductances \( G_s(t) \), which can be calibrated individually, and has an output giving a calibrated summed signal \( G(t) \) [equation (2)]. These six signals, along with the ECG and left ventricular pressure, were written on an ink-jet recorder (Elema-Schönander type Mingograf 81), to allow direct inspection of the pulsatile variations in segmental left ventricular volume. Calibration for the conductivity of a blood sample was also incorporated into the conditioning amplifier.

All pertinent signals — ECG, left ventricular pressure, \( G(t) \), and arterial pressure or aortic blood flow — were written on an eight-channel heat-stylus recorder (Hewlett-Packard type 7758A) in the canine experiments. The data recorded in patients were stored on a 14-channel analog tape recorder (Honeywell type 5600C) and analyzed later.

For calculation of volume, the five segmental signals from the catheter, after amplification, were fed into the analog-digital converter of a DEC LSI-11/23 computer that was also used for computing \( V_c \), stroke volume, ejection fraction, and other parameters, and for plotting results on an X-Y digital plotter (Tektronix type 4662). A trigger pulse derived from the R peak of the ECG was used to compute the RR interval. In the canine experiments aortic blood flow or aortic blood pressure were used to determine beginning and end of ejection. Stroke volume was calculated by digital integration of the flowmeter signal in dogs. In patients, the conductance-derived stroke volume was computed by taking maximum and minimum values of the \( G(t) \) signal while assigning a constant arbitrary value to \( V_c \) in equation (1). Furthermore, the conductance-derived \( V(t) \) signal was differentiated digitally to obtain a flow signal \(-dV/dt\) during filling and ejection.

The instantaneous indicator dilution signal from the injection of ferromagnetic fluid was written with high magnification on the ink-jet recorder and ejection fraction as follows was calculated:

\[
EF = \frac{R_1 - R_{i+1}}{R_i}
\]

in which \( R_{i+1} \) is the level of the signal representing the residual amount of magnetized blood in the left ventricle after the contraction numbered \( i \) following the injection. At least three steps were taken into account from which an average ejection fraction value was computed. Conversely, ejection fraction from the conductance signal was calculated through equation (5) after injection of hypertonic saline solution. In all calculations, the value of \( \alpha \) in equations (1), (3), and (5) was assumed to be 1.0.

The films taken during cineventriculography were projected and each image of the left ventricle was traced. The tracings and the 1 cm square grid were fed into the DEC LSI-11/23 computer with a digitizer (Summagraphics BITPAD-1). By means of the single-plane area-length method without empirical corrections, time-varying left ventricular volume was obtained at 25 points/sec. Volume data were calculated at the same points in time from the conductance data.

All data were analyzed statistically for linear correlation. Because data derived from the electromagnetic, indicator dilution, and contrast ventriculographic methods cannot be considered true measures of stroke volume, ejection fraction, or \( V(t) \), the data points from all methods were considered dependent on unknown true values. Thus correlation coefficients were computed in \( Y = aX + b \), and the standard error in the slope, \( S_a = (a/r) \sqrt{\sum (1 - r^2)(n - 2)} \), was calculated. [In the correlation between conductance-derived volume and values obtained from another method, the slope, \( a \), provides an estimate of the factor \( \alpha \) in equation (1) and \( b \) an estimate of the mismatch in \( \alpha V_c \)].

**Results**

Uncalibrated segmental conductance signals \( G_s(t) \), as well as their sum \( G(t) \), obtained in a patient are shown in figure 2. Clearly shown in most of the signals are ejection (decrease of \( G \)) and three phases of filling: the rapid phase, a period of diastasis, and atrial contribution to filling, shown as an increase in \( G \) starting with the P wave of the ECG.

Figure 3 shows data from one cardiac cycle in a dog, plotted and calibrated by computer after \( V_c \) was obtained by the zero-volume technique. Note the similarity in shape and amplitude of the \(-dV/dt\) and the electromagnetic flow signal during ejection. The high heart rate in dogs generally obscures the separate manifestation of the filling phases.

The two methods to obtain the \( V_c \) term are shown in figures 4 to 6. Figure 4 shows how a constant value \( G^p \) is reached after left ventricular pressure becomes negative through suction, in spite of ongoing ventricular contractions. Approximately 0.5 to 1 min after release of the suction, a regular contraction resumes after initial bradycardia. The procedure could be repeated at least twice and in some dogs up to five times, enabling us to investigate the reproducibility of the \( G^p \) measurement, which was better than 4%.

Figure 5 shows the effect of 1 ml of hypertonic...
saline on the G(t) signal, which rises to a peak in about 5 beats and then returns to its control level after 1 to 2 min. The value of Gp shown here was calculated from equation (5). In reference to this level, the mean value of G(t) rose by about 25%. This increase is almost totally accounted for by the change in blood conductivity, σb, which was shown by the experiment in which left ventricular diameter was recorded by ultrasonic crystals. Injection of hypertonic saline revealed a small (2% to 3%) increase in end-diastolic and end-systolic diameter after arrival of the bolus in the left ventricle. During the washout period of 1 to 2 min, end-diastolic diameter remained slightly elevated, while end-systolic diameter increased about 9% above control and systolic left ventricular pressure decreased by 5 mm Hg (0.7 kPa, seen also in figure 5). After 2 min all values returned to control levels.

In another experiment, 1.5 ml of 0.6M saline (as opposed to 6M) was injected directly into the left coronary artery main stem while G(t) and diameter were monitored. Since coronary flow represents 10% to 20% of cardiac output and the saline is diluted in its passage through the lungs, this maneuver probably mimics the effect on the myocardium of the injection of normal hypertonic saline. The same gradual, transient decrease in systolic left ventricular pressure (and in maximal left ventricular dP/dt, see figure 5) was seen as before, as well as similar transient increases in left ventricular diameter and conductance, amounting to 2% for end-diastolic dimension, and about 9%, much more gradually, for end-systolic dimension. To avoid these changes, apparently caused by an effect on the myocardium, we used data to measure Vc only during the increasing phase of G(t) as shown in figure 5 because penetration of salt into the wall is still limited then. Likewise, in the human studies only the decreasing phase of G(t) caused by the cold glucose solution was taken into account.

Figure 6 illustrates the use of equation (5) to measure Gp by linear regression between Gs and Gt. In the dog (figure 6, a) G increased by 20% in reference to Gp (0.27 S), while the decrease in G for the patient (figure 6, b) was about 25%. Ejection fraction values were 0.58 (dog) and 0.81 (patient).

The conductance method, at least for the canine postmortem heart, is linear down to zero volume as previously shown. This is important, since both the suction method (zero volume) and dilution method to obtain Vc are based on this linearity, and both should give the same value. This was investigated in a study of 26 dogs, the results of which are shown in figure 7. To eliminate effects of different σv values, L2Gp data

FIGURE 3. Left, ECG (lead II) and calibrated volume after correction for Vc. Right, left ventricular pressure (P1V, 20 kPa = 150 mm Hg), derivative of volume (−dV/dt), and aortic blood flow from electromagnetic (EM) flow probe in a dog weighing 21 kg. Catheter 6.5 cm (L = 0.95 cm), σb = 0.625 S/m, stroke volume = 17.8 ml, cardiac output = 2.54 liters/min, Vc = 39 ml. From electromagnetic flow: stroke volume = 16.2 ml. Abscissa: 1.0 sec.
were plotted, reflecting conductive and geometric properties of the wall and surrounding tissues.

The linearity of the conductance method in vivo is shown in figures 8, a, 9, and 10. In figure 8, a, the conductance is seen to measure changes in stroke volume in a dog over a fivefold range and the result is typical for those obtained in other dogs, with r ranging between .95 and .99, the slope (a ≡ α) between .80 to 1.05, and the intercept (b) between −1.3 and +0.5 ml.

Figure 8, b, shows stroke volume values obtained by the catheter plotted against those obtained by the thermal dilution method in 12 patients. Since hemodynamic interventions were not applied, the results testify to the possibility that stroke volume can be measured quantitatively in humans, not to the linearity of the method.

The linearity within the cardiac cycle is manifested by data shown in figures 9 (dog, integrated flow probe signal during ejection) and 10 (patient, ventriculographically derived volume). The slight curvature of the relationship in figure 9 was present in most dogs, but the correlation coefficient was always very high with low uncertainty in the slope (Sa).

The data in figure 10 are representative of those obtained in all five patients in whom simultaneous measurements were made. In addition to showing linearity, figure 10 testifies to the validity of the measurement of V_c (229 ml); the error in its value (−2.7 ml) amounts to just over 1%. The results obtained in the five patients are given in table 1, which gives the slope (mean value .86), intercept (mean value 19.3 ml), r value, standard errors in slope (Sa) and estimate (SEE), and the relative error in V_c (b/V_c, mean value 6.8%). Figure 11 represents a different way of showing the accuracy of the V_c measurement obtained from injection of hypertonic saline in dogs, by plotting ejection fraction values as calculated from equation (5) against those obtained by the ferromagnetic fluid dilution method.

Finally, figure 12 shows calibrated pressure-volume loops obtained by the conductance catheter. In the dog (figure 12, a) the descending aorta was occluded for 10 sec, causing pressure to increase and stroke volume to
The decrease in spite of a slight increase in end-diastolic volume. The end-systolic pressure-volume relationship is seen to be represented by a practically straight line. Figure 12, b, shows a similar plot for one cardiac cycle in a patient.

**Discussion**

In previous reports from our laboratory describing the conductance catheter we have discussed its application to measure stroke volume and cardiac output in dogs and its theoretical background. The present report is concerned with calibration of volume in absolute sense, in humans as well as animals. Results in preliminary form were presented on various occasions. The first recording obtained in humans and calibrated in terms of stroke volume was published by our group.

The origins of the conductance method of measuring a time-varying quantity of blood in the body can be traced to the first description of thoracic impedance plethysmography, which has been used to determine cardiac output. To derive an analytic relationship between thoracic impedance and cardiac volume is virtually impossible because of the inhomogeneity and time-varying contents of the thorax. By applying the current source inside the ventricle, the ensuing electrical field will be confined chiefly within the cavity, which is the main reason why our method functions quantitatively.

Earlier attempts to measure left ventricular volume with intraventricular electrodes failed to establish

![FIGURE 5](image)

**FIGURE 5.** Procedure to obtain $V_c$ by bolus injection of 1.5 ml of hypertonic saline into pulmonary artery. *Top trace,* ECG (lead II); *second trace,* left ventricular pressure ($P_{LV}$, 13.3 kPa = 100 mm Hg); *third trace,* left ventricular $dP/dt$; *bottom trace,* summed conductance, $G(t)$. Dog (24 kg), $\sigma_b = 1.02$ S/m, catheter 5.5 cm ($L = 0.8$ cm), $V_c = 30.1$ ml, ejection fraction = 0.70, stroke volume = 15 ml.

![FIGURE 6](image)

**FIGURE 6.** End-systolic conductance ($G_{es}$) as function of end-diastolic conductance ($G_{ed}$) during entrance of hypertonic saline (a) or cold glucose solution (b) into the left ventricle. Intersection with identity line not shown. In this and following figures, $S_a$ indicates standard error of the slope. a, Dog (19 kg), ejection fraction = 0.57, $G_P = 0.27$ S, $\sigma_b = 1.22$ S/m, catheter 5.5 cm ($L = 0.8$ cm), $V_c = 13.5$ ml. b, Male patient 45 years old (80 kg; 1.67 m), ejection fraction = 0.78, $G_P = 0.76$ S, $\sigma_b = 0.55$ S/m, catheter 9 cm ($L = 1.29$ cm), $V_c = 229$ ml.
quantitative relations between stroke volume and impedance partly because a two-electrode system was used, in which electrode polarization is known to cause problems. The signals reported by Geddes et al., however, bear qualitative resemblance to left ventricular volume.

Our conductance catheter obviates the above problem by means of a multielectrode set-up in which no voltages are measured from the current-carrying electrodes. A small modification of our system was introduced by McKay et al., who used a 12-electrode catheter and a lower frequency of excitation. These investigators, however, used just one pair of recording electrodes and did not succeed in establishing a quantitative relationship between impedance and volume.

The crux of the matter, as far as calibration in terms of absolute volume is concerned, lies in application of the correct theory along with methods to obtain the necessary calibration values. Our previous results in the isolated postmortem heart, as well as those shown here, establish the validity of a linear relationship between conductance and volume down to zero V. No measurements were made in the postmortem human heart, which is much larger than a dog’s heart, but the spheroidal model predicts a linear relationship between G and V from 0 to 200 ml provided the electrode separation is matched to heart dimensions (11 cm between electrodes 1 and 8). Moreover, the results shown in figure 10 and table 1 clearly show a linear relationship in the human left ventricle over a very large volume range: the smallest $V_{ls}$ is 9 ml, the largest $V_{ls}$ is 227 ml.

The positive intercept on the G axis was clearly caused by the conductance $G^p$ of tissues surrounding the cavity: left ventricular wall, right ventricle, and lung tissue. Since the value of $L^2G^p$ may differ substantially between individual dogs (figure 7) and less in patients (table 1; $V_c - \sigma_s$), its value must be individually measured by one of the two methods described. Obviously, the method of causing a transient change in $\sigma_s$ by injection of hypertonic saline or cold glucose is to be preferred and, according to the results shown in figures 7, 10, and 11 and in table 1, functions satisfactorily. In canine studies we noticed that the decreasing effect on $\sigma_s$ of 10 ml of cold glucose, although measur-
able, was much smaller than the increasing effect of 1 ml of hypertonic saline. The effect of cold glucose is probably derived primarily from its temperature, slightly reducing the ionic activity of plasma; the temperature dependence of blood resistivity is well known.24 The hypertonic saline, on the other hand, significantly increases the ionic strength of plasma. For this reason, the saline method is to be preferred and in one case, 5 ml of slightly hypertonic saline (0.8M) was used in a patient without subsequent adverse hemodynamic effects. The quantity (6 mg/kg) is far below that used therapeutically in cases of hypovolemic shock25,26 and must be considered harmless. This is corroborated by the small effects found in dogs on contractile indexes such as maximal dP/dt, systolic pressure decrease (figure 5), and systolic diameter increase. Other investigators using hypertonic saline of approximately similar or larger quantities reported slight-to-moderate cardiovascular responses.27 A survey of these responses was given by Geddes et al.28

Apparently, the assumption that end-systolic and end-diastolic volume remain constant during the saline injection is valid during the initial phase. Even if this should not be the case, such as when radiopaque dye was used, the method is valid as long as ejection fraction remains unchanged.

The second assumption for correct functioning of the saline injection method — the constancy of Gp — was also found to be valid as testified by direct infusion of saline into the coronary artery. Since changes in left ventricular diameter and total conductance were essentially similar, an increase in myocardial conductance,

TABLE 1
Results and coefficients from data in five patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Slope (sex/age)</th>
<th>Intercept (b (ml))</th>
<th>r</th>
<th>n</th>
<th>Sa (ml)</th>
<th>Vc (ml)</th>
<th></th>
<th>VED-Ves (ml)</th>
<th>angio(ml)</th>
<th>σb (S/m)</th>
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<tr>
<td>6 (M/49)</td>
<td>1.05</td>
<td>+3.56</td>
<td>.977</td>
<td>22</td>
<td>.05</td>
<td>6.91</td>
<td>285</td>
<td>0.4%</td>
<td>163-57</td>
<td>0.56</td>
</tr>
<tr>
<td>7 (M/45)</td>
<td>0.75</td>
<td>-2.73</td>
<td>.988</td>
<td>20</td>
<td>.03</td>
<td>4.44</td>
<td>229</td>
<td>1.2%</td>
<td>149-33</td>
<td>0.55</td>
</tr>
<tr>
<td>9 (M/53)</td>
<td>0.44</td>
<td>+38.7</td>
<td>.956</td>
<td>24</td>
<td>.03</td>
<td>5.37</td>
<td>234</td>
<td>16.5%</td>
<td>131-9</td>
<td>0.58</td>
</tr>
<tr>
<td>11 (F/49)</td>
<td>0.99</td>
<td>+51.1</td>
<td>.967</td>
<td>23</td>
<td>.06</td>
<td>12.0</td>
<td>353</td>
<td>14.5%</td>
<td>227-74</td>
<td>0.46</td>
</tr>
<tr>
<td>12 (M/62)</td>
<td>1.07</td>
<td>+6.07</td>
<td>.858</td>
<td>32</td>
<td>.10</td>
<td>12.9</td>
<td>398</td>
<td>1.5%</td>
<td>86-17</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Sa = standard error of the slope; ED = end-diastolic; ES = end-systolic; V = volume.

V (catheter) = a V (angio) + b (linear correlation). The slope, a, is an estimate of α; the intercept, b, is an estimate of the error in αVc.

Range over which data were analyzed.
stroke volumes are identical while contraction and relaxation are virtually simultaneous, this is not considered a disturbing factor.

The problem of a precise value for $\alpha$ and the factors causing variation between individuals will remain unsolved as long as no gold standard for (stroke) volume measurement is available for comparison. The uncertainty of cardiac output values measured by thermal dilution is well known, which means that both the scatter and the slope value of the linear regression line in figure 8, $b$, may be explained by the uncertainty in the horizontal axis variable.

Essentially, the same applies to the data in figure 11

If any, was too small to disturb the measurement. A simple calculation, in which blood comprises 5% of total wall volume, confirms the finding.

The slope of the relationship between conductance and volume is governed by electrode distance ($L$), blood conductivity ($\sigma_b$), and a dimensionless constant ($\alpha$) [equation (1)]. $L$ is known while $\sigma_b$ is easily measured. In patients, $\sigma_b$ was found to vary minimally (=1% to 2%) except immediately after injection of the dye. In studies of anesthetized dogs over several hours, $\sigma_b$ tends to increase with time and requires recalibration after infusions or every half hour.

The slope constant $\alpha$ was shown to have a value of 0.7 in the spheroidal model of the left ventricle. This was somewhat lower than the experimental value (0.8) for the isolated heart and the values observed in vivo (0.78 to 1.05 in dogs, 0.44 to 1.05 with mean value of 0.86 in humans). We have started calculations with the spheroidal model, showing that $\alpha$ may be inversely correlated with $G_p$, but these predictions require experimental verification. This is difficult because of the substantial experimental uncertainty in $\alpha$, which is related, in turn, to the uncertainties of the volume methods with which the conductance technique must be compared. On the other hand, the theoretical model may also require some expansion to include the presence of the right ventricle. Since its contents vary during the cardiac cycle along with left ventricular volume, the effect of the pumping right ventricle is expected to increase the slope constant $\alpha$ without affecting the intercept. Since right and left ventricular

![Figure 11](image1.png)

**FIGURE 11.** Ejection fraction (EF) calculated from conductance vs that calculated from ferromagnetic indicator in seven dogs (18 to 32 kg). Variations in ejection fraction were produced by dobutamine and aortic occlusions.

![Figure 12](image2.png)

**FIGURE 12.** Left ventricular pressure-volume loops. Volume calculated from conductance. *a*, Dog (22 kg), vagotomized. Left ventricular pressure measured by micromanometer-tipped transducer. Variations in pressure and volume were produced by occlusion of descending aorta. $\sigma_b = 0.85$ S/m, catheter 7 cm ($L = 1.0$ cm), $V_c = 52.3$ ml. *b*, Male patient, 53 years old (74 kg; 1.59 m), $\sigma_b = 0.555$ S/m, catheter 10 cm ($L = 1.43$ cm), $V_c = 234$ ml. Left ventricular pressure was measured through the fluid channel of conductance catheter. 20 kPa = 150 mm Hg.
because indicator dilution techniques to estimate ejection fraction all have substantial inaccuracies, mostly because of incomplete mixing of the indicator in the left ventricle. These circumstances are also borne out by the relatively large errors in the slopes (Sa) of figure 8, b, and 11.

Likewise, single-plane cineangiography is fraught with inaccuracies, as illustrated by the different experimental correction factors (0.724 to 0.938) used in the literature. If these had been applied, the α values in table 1 and figure 10 would have been somewhat larger. Clearly, the interindividual variation in α in patients is larger than that observed in dogs studied with flow probes. In one patient (No. 9), $V_{ES}$ measured angiographically was as low as 9 ml, implying a highly unlikely value of 0.93 for his ejection fraction. Thus the low value for α of 0.44 may well be attributable to an inaccurate angiographic value for volume.

In addition, use of the pulmonary artery to inject angiographic dye produces ventriculograms of less-than-ideal contrast. Still, this was the only way to obtain data simultaneously with conductance without having to insert two arterial catheters. Furthermore, this method was better than comparing nonsimultaneous conductance data with angiograms by direct left ventricular injection, which causes ventricular preload changes.

The patients reported in this study were selected on the basis of absence of shunts or valvular abnormalities because these would have made comparison of cineangiographic and thermal dilution data even less accurate or impossible. In a few cases, patients with extensive coronary artery disease (four vessels or more) were excluded from the study to minimize the duration of the catheterization. In most cases in the study, the extra time required was around 30 min, part of which was caused by the time needed for the comparisons with thermal dilution data and pulmonary angiograms.

Omitting these, the addition of the conductance measurement would add around 15 min to the standard procedure.

Generally, the tip of the catheter was positioned in the apical region fairly easily, sometimes accompanied by transient arrhythmias. Once the catheter was in position, arrhythmias disappeared. No complications with the procedure have been encountered.

The proven ability to obtain a continuous, calibrated, on-line display of left ventricular volume is one of the most attractive aspects of the conductance catheter. In this respect, the instrument holds promise in its ability to follow short-term interventions by pacing or vasoactive substances as qualitatively shown by others. Thus, although it may be hard to show that the method is more accurate than cineventriculography, for example, its easy application, on-line possibilities, and continuous display offer great advantages. As opposed to other continuous methods for determining left ventricular volume such as nuclear scintigraphy or echocardiography, the instrument combines left ventricular pressure measurement with left ventricular volume. This enables one to obtain dynamic pressure-volume loops (figure 12) in the control state and during interventions from which $E_{max}$ may be readily obtained to assess contractile state. In addition, on-line differentiation of the signal (figure 3) might be applied to assess left ventricular filling dynamics.

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Continuous measurement of left ventricular volume in animals and humans by conductance catheter.

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