DEVELOPMENT AND EVALUATION OF AN IMPEDANCE CARDIOGRAPHIC SYSTEM TO MEASURE CARDIAC OUTPUT AND OTHER CARDIAC PARAMETERS

JULY 1, 1969 TO DECEMBER 31, 1970

FINAL PROGRESS REPORT

Performed under Contract No. NAS 9-4500

by

University of Minnesota

Minneapolis, Minnesota

for

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

Manned Spacecraft Center

Houston, Texas

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Final Progress Report

by

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and A.H.L. From, M.D. Co-Investigators

University of Minnesota College of Medical Sciences
Minneapolis, Minnesota

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FOREWORD

The success of this project is due to several factors. A vital feature has been the unusually close relationship between electrical engineers, physiologists, and physicians. The project has advanced from the initial stage of the impedance technique as a promising laboratory concept to the present system incorporating very sophisticated electronics and evaluated in a wide spectrum of clinical and research applications. It is now a reliable, simple to operate, safe, and noninvasive means to monitor several parameters of the cardiovascular system.

The contributions of my colleagues and co-investigators, Dr. Arthur From, Mr. Robert Patterson, and Mr. David Witsoe are acknowledged with great gratitude. The project could not have been completed without the dedicated technical services of Miss Barbara Ristuben and Mr. Neil Strawhorn. Mrs. Vivian Nordgren added immeasurably in the skillful preparation of the manuscript.

The enormous contributions of the clinical and research scientists outside of the University of Minnesota served as a vital link between the engineering development and the resultant practical applications of the Impedance Cardiograph.

Obviously, without the financial support of the NASA, Manned Spacecraft Center, the project could not have been accomplished.

W. G. Kubicek

Part I History of this Project

This contract was started in June 1965. At that time Dr. George Armstrong was the first monitor. The original concept of this project was derived from some earlier work done in this laboratory under an Air Force contract. The original plan was to attempt to improve the impedance approach to measuring cardiac output and other parameters of cardiac function sufficiently to justify its use in an inflight experiment. Subsequently the planning for an inflight experiment was separated from this project. Some progress was made toward an inflight experiment by funding us to purchase a sophisticated Honeywell tape recorder to be used to record data telemetered from a space flight to a suitable ground station and then to reach our laboratories by way of telephone lines. The NASA Manned Spacecraft Center also contracted with the Spacelabs, Inc. to produce some miniaturized models of the impedance system. This was to serve as a beginning for a more updated system to be used in prolonged space flight.

The main body of work accomplished in this laboratory has been a combination of electrical engineering, physiology and medicine. The Minnesota Impedance Cardiograph as it exists today is the product of several years of rather sophisticated electrical engineering combined with physiological and clinical testing of the instrument. A second important feature of this project was to provide a broad scientific evaluation of the impedance approach to obtaining information about the

cardiovascular system. In 1967 we were provided funds to construct several of these instruments and to place them in selected clinical laboratories around the country. Travel funds were also provided to allow the principal investigator to visit each location and to give a lecture on the progress with the system up to that date. Our two engineers also were able to travel to some of these locations to assist in the setting up and operation of the equipment. This has resulted in an excellent yield of data as evidenced by the list of papers given at the First Symposium on Impedance Cardiography held at the NASA Manned Spacecraft Center in June 1969. A perusal of the subsequent pages listing the publications to date will indicate the rather wide scope of research and published articles relative to the impedance system.

The Impedance Cardiograph has been advanced from a laboratory apparatus with potential value in 1965 to a highly sophisticated electronic system with an extremely promising future in both clinical and research applications.

An updating of the Impedance Cardiograph has been made in order to incorporate a number of electrical safety features (Figs. 1 and 2). Both the current source output and the voltage pickup amplifier leads now have transformer isolation. The shields on the patient cables have been disconnected from ground in order to reduce capacity to ground. This will greatly reduce possible 60 Hz leakage currents to ground.

The ground wire used for the ECG has been changed to an active ground circuit. If the current in leads 3 (the ECG

ground lead) exceeds approximately one microampere, the circuit opens and leaves a minimum impedance to ground of 5 meg ohms. In the new design the maximum current to ground with 115 VAC, 60 Hz connected in parallel with all four patient leads is 40 microamperes. This complies with recommended hospital safety standards for electrical equipment.

The original formula for ventricular stroke volume is used by a number of investigators including this laboratory.

$$\Delta V = \rho \frac{L^2}{Z_o^2} T(dZ/dt)_{min} \quad \text{(cc)} \quad \text{(Eq. 1)}$$

where

ΔV = ventricular stroke volume (cc)
ρ = the electrical resistivity of blood at 100 kHz (average value 150 ohm-cm)
L = the mean distance between the two inner electrodes (2 and 3) in cm. (Figs. 1 and 2)
Z_o = the mean body impedance between the two inner electrodes in ohms
$(dZ/dt)_{min}$ = the minimum value of dZ/dt occurring during the cardiac cycle in ohms per second (see Figure 10).
T = the ventricular ejection time in seconds as obtained from the dZ/dt waveform (see Figure 5).

Cardiac output is calculated from the stroke volume and pulse rate as shown below

C.O. = $\Delta V \cdot PR/1000$
C.O. = cardiac output in liters/min
ΔV = stroke volume in cc
PR = pulse rate in beats/min determined by measuring the time interval between the beat used to calculate the stroke volume and the previous beat.

A <u>thoracic resistivity constant</u> has been derived as follows:

$$K = \frac{C^2 Z_o}{4\pi L} \quad \text{ohm centimeters} \quad \text{(Eq. 2)}$$

where:

C = the average circumference of the chest (cm)
Z_o = Impedance (ohms) between leads 2 and 3
L = the average distance (cm) between leads 2 and 3 (figs. 1 and 2).

This is useful in observing the formation or reversal of pulmonary edema or other conditions involving fluid accumulation in the thoracic cavity.

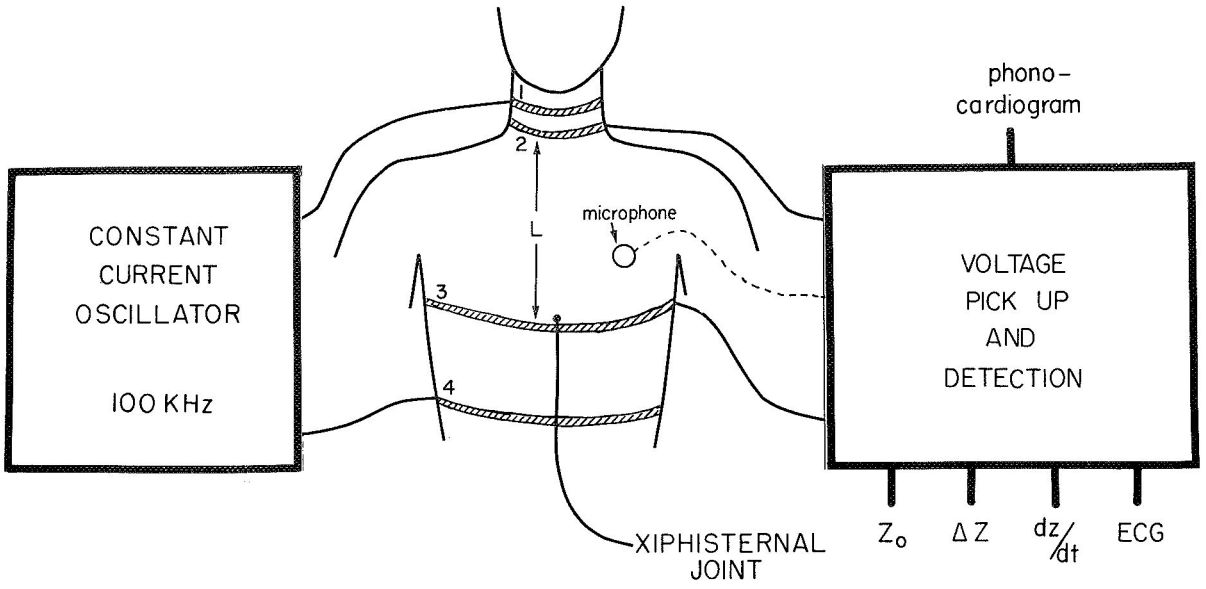

Figure 1. A diagram of the main features of the Minnesota Impedance Cardiograph Model 304. Heart sound microphone, Hewlett Packard, model 21050-A.

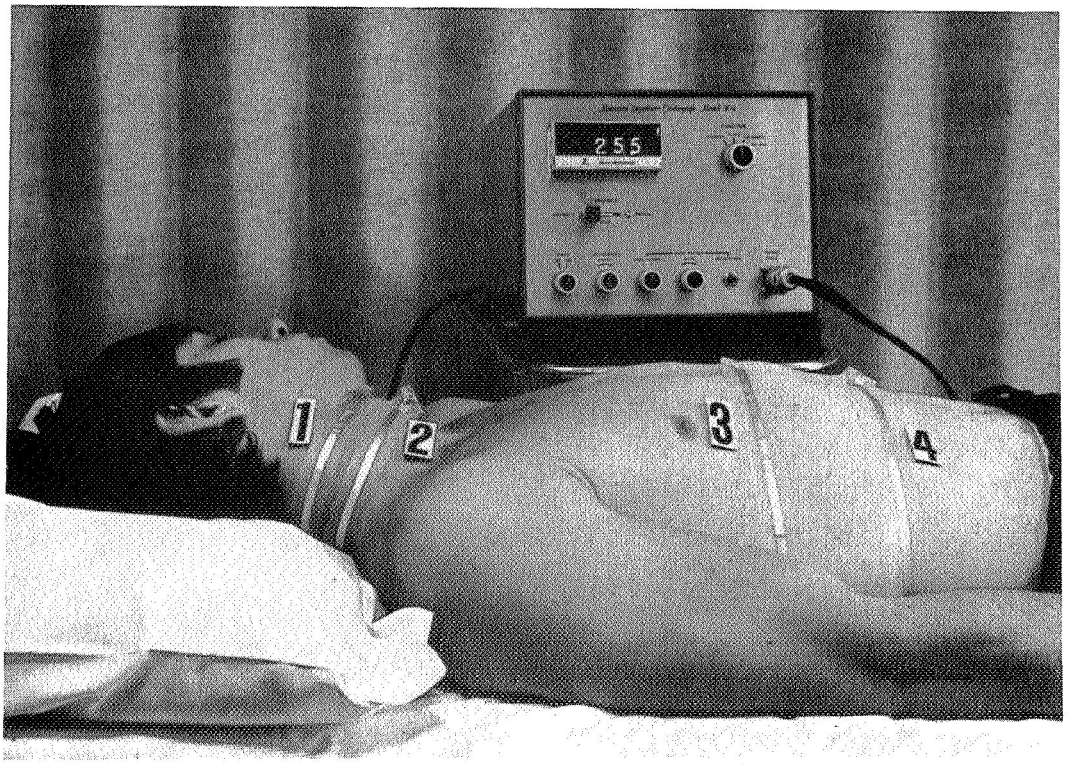

Figure 2. A photograph of the Impedance Cardiograph connected to the aluminized Mylar disposable tape on electrodes. Electrode Tape No. M6001, 3M Company, Medical Products Division, 3M Center, Saint Paul, Minnesota 55101.

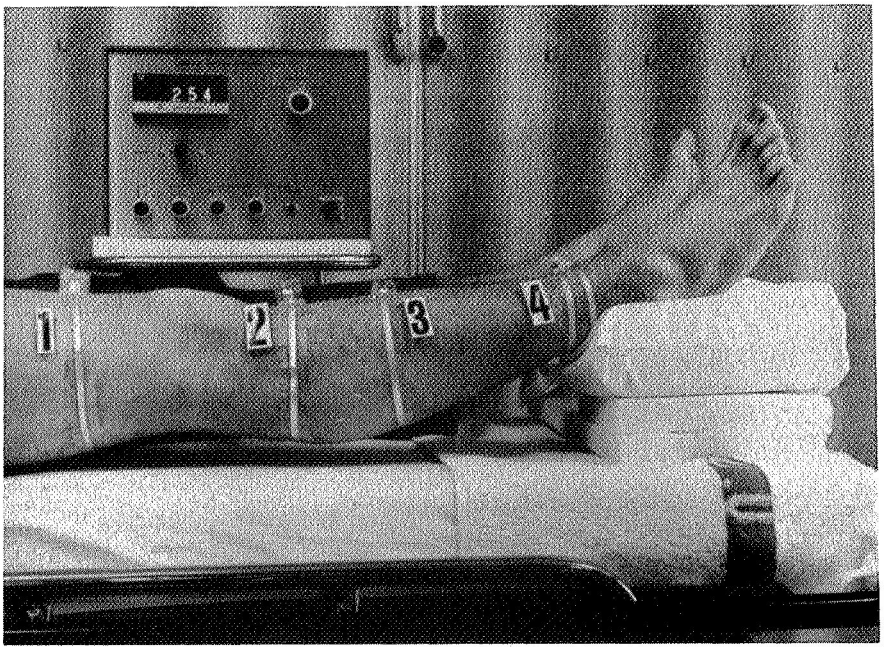

Figure 3. A photograph of the impedance system connected to observe circulation in the leg.

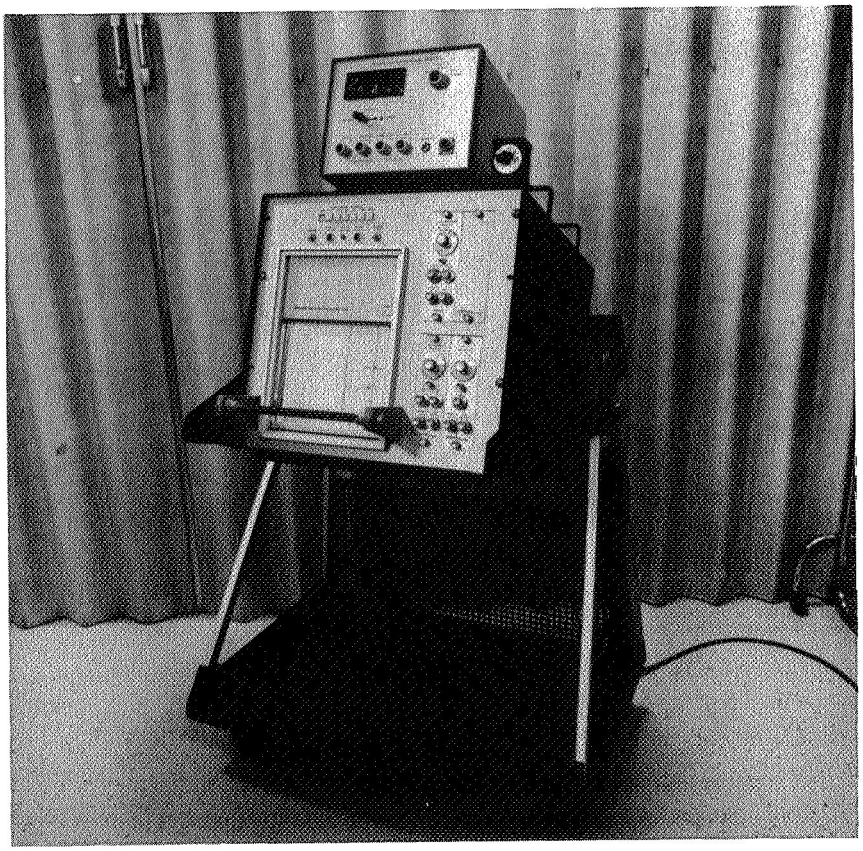

Figure 4. A photograph of the Impedance Cardiograph mounted on a mobile Brush recorder to facilitate its use in various locations in the hospital.

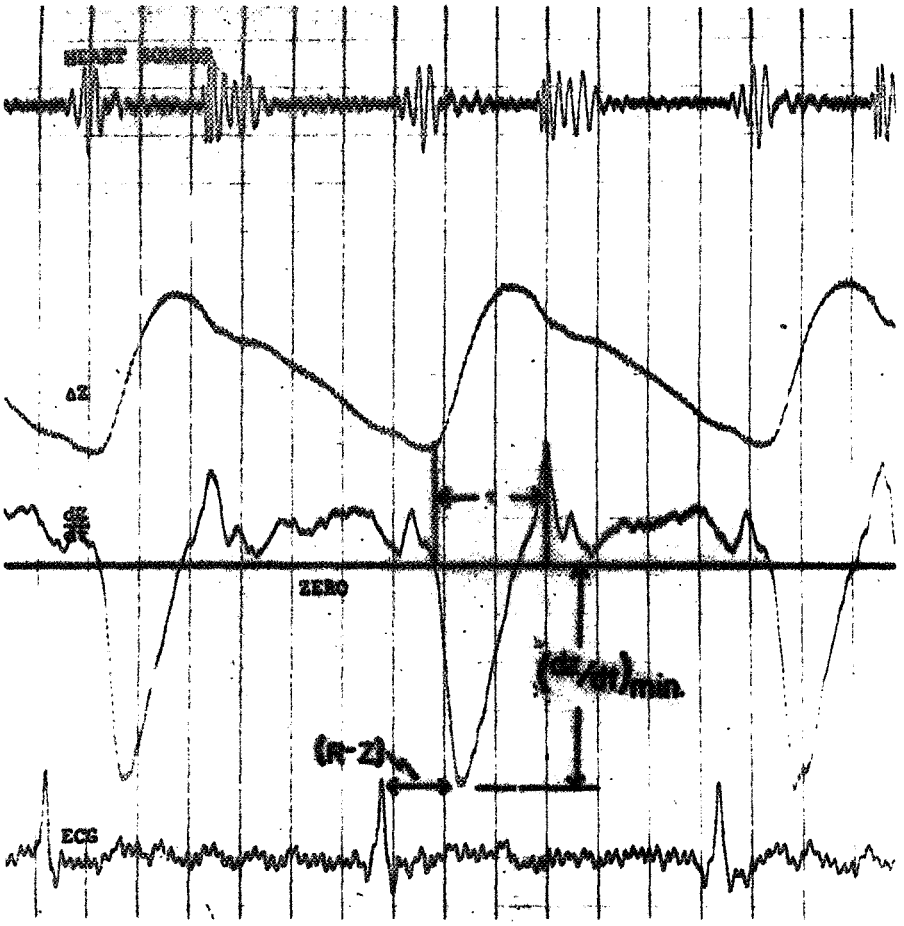

Figure 5. A record of heart sounds, (ΔZ), (dZ/dt) and ECG on a normal adult human being. The (R to Z) interval is useful in determining cardiac contractility and other parameters of cardiac dynamics. The interval shortens during exercise, for example while $(dZ/dt)_{min}$ increases.

Dr. Loren Heather has suggested the ratio of $(dZ/dt)_{min}$ divided by the (R to Z) interval as a sensitive index of cardiac response to exercise.

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Measurement of Leg Volume Change by Electrical Impedance Change

An approach to the problem of measuring leg volume change via change in electrical impedance was to confine the calf of the leg in a thin calibrated metal band 7.6 cm wide, as shown in Figure [6] . The initial length (or circumference) of the band can be obtained from a length calibration marked on the band. The length (circumference) of the band can then be changed by turning the calibrated micrometer screw.

The fundamental concept was to attempt to improve the accuracy of the resistivity constant K_1 in the formula used to compute leg volume change:

$$\Delta V = K_1 \frac{L^2}{Z_o^2} \Delta Z \qquad \text{eq. 3}$$

$$\text{Therefore:} \quad K_1 = \frac{\Delta V Z_o^2}{\Delta Z L^2}$$

By rearranging the resistivity formula for a volume conductor;

$R = \rho \frac{L}{A}$ and substituting circumference C into the cross sectional area A, substituting our Z_o for R and labelling $\rho = K_2$, the following resistivity constant results:

$$K_2 = \frac{C^2 Z_o}{4\pi L} \qquad \text{(see eq. 2)}$$

Since each individual must have a somewhat characteristic ratio of bone, water, blood, muscle, fat, connective tissue, skin, etc. for a given cross section through the leg, it is reasonable to assume that there would be a considerable individual to individual variation in the value of K_2. It has been suggested that for women this value could be influenced

by alterations in water retention during the menstrual cycle.

The above reasoning leads to the possibility that the proper value for K_1, eq. 3, may be K_2, eq. 2. The obvious advantage would be to provide a resistivity constant adjusted for each individual's body characteristics rather than relying upon a fixed constant.

Then substituting K_2 for K_1 in eq. 3

$$\Delta V = \frac{C^2 Z_o}{4\pi L} \cdot \frac{L^2}{Z_o{}^2}\Delta Z$$

$$= \frac{C^2 L}{4\pi Z_o}\Delta Z$$

Analysis of eq. 4 reveals the following

1. $\frac{C^2}{4\pi}$ = A the cross section area
2. A X L = volume of the segment of leg involved
3. Since Z_o is primarily resistive,

   $1/Z_o$ = conductivity - mhos.
4. Thus eq. 4 in its final form;

   ΔV = (volume) (conductivity)ΔZ eq. 5

The hypothesis that $K_1 = K_2$ was tested as follows:
Step 1 -- The four impedance electrodes were attached to the leg as illustrated in Fig. 3. A thin plastic insulating sheet was wrapped smoothly around the leg covering the area between electrodes 2 and 3. The metal band (Figure), was then carefully placed around the leg. The band was then tightened only enough to eliminate "slack" between the leg and the band, producing only a minimal constriction of the tissue between electrodes 2 and 3.

Step II --

1. Initial recording of the leg circumference C from the length calibration on the metal band.
2. A simultaneous recording of Z_o on a strip chart recorder and the digital display on the front panel. The recording was done through the ΔZ output terminal to obtain the accuracy necessary for the ΔZ value.

Step III --

1. The micrometer screw was turned two, four, or eight turns (decreasing C). --ΔV = approximately 5 cc, 10 cc and 20 cc respectively.
2. A simultaneous recording of ΔZ was made at each change in C.

Step IV -- The reverse of step III.

A typical total volume of the segment of leg involved, 825 cc.

The change in leg volume (ΔV) was calculated from the change in circumference between step II and step III or step IV. This value for ΔV was inserted into (eq. 3) and the value of K_1 calculated. The ratio K_1/K_2 was calculated for each run on the various individuals.

Results:

Table I contains the data from this series of experiments upon six young adult men and two adult young women. All were apparently healthy with normal peripheral circulation.

Table I

Subject	Sex	K_1	K_2	K_1/K_2
1	M	218	216	1.01
2	F	203	226	0.89
3	M	180	193	0.93
4	M	202	214	0.96
5	M	195	195	1.00
6	F	228	225	1.05
7	M	224	197	1.13
8	M	214	223	0.96
$K_1 = \frac{\Delta V Z_o^2}{\Delta Z L^2}$ $K_2 = \frac{C^2 Z_o}{4\pi L}$			Mean	0.99

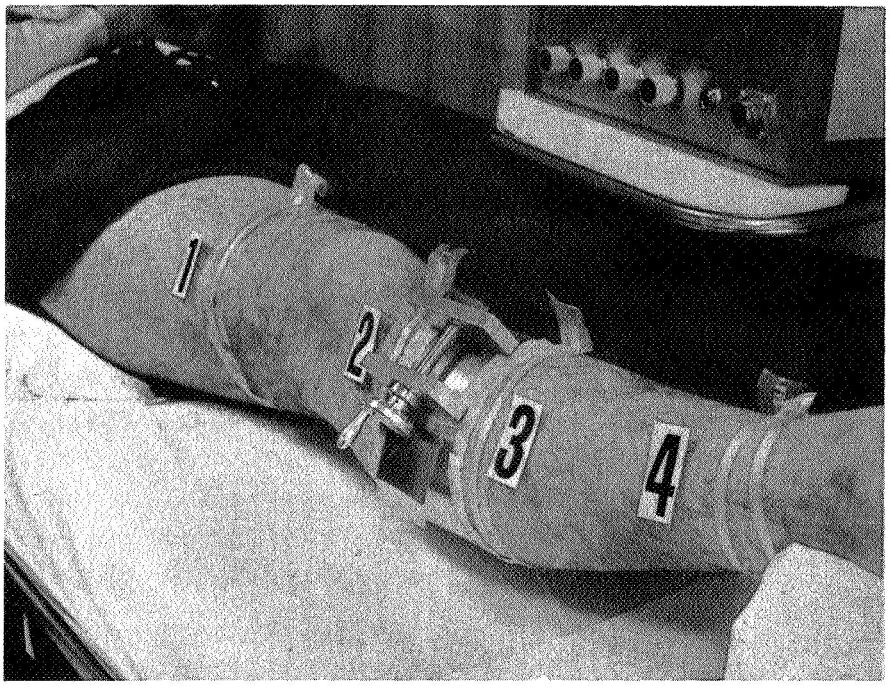

Figure 6. A view of the thin metal band placed around the calf of the leg. The band has a total length (circumference) scale marked on the edge to provide the initial circumference measurement. The micrometer screw is calibrated in 1/1000 inch graduations to provide an accurate measurement of circumference change and thus leg segment volume change ΔZ. A thin sheet of insulating material is under the metal band for electrical insulation.

The four impedance detecting electrodes are in the standard configuration.

Part III

Studies on the Applications of Transthoracic Impedance (Z_o) Measurements

A. At the Veterans Administration Hospital, Minneapolis, Z_o data were obtained on forty one patients suffering from a variety of chest diseases. The main objective of this investigation was to determine if a correlation existed between the resistivity constant

$$K = \frac{C^2 Z_o}{4\pi L} \quad \text{ohm cms}$$ (Eq. 2) p 3 and various lung diseases.

Table II contains the list of patients considered to have a K value in the range of normal individuals (600 to 699).

Table III lists the patients with a K value considered above the normal range.

Table IV contains the list of patients with a K value below the normal range.

Although certain logical trends can be seen between, for example, patient no. 23, with severe emphysema and asthma K = 1010, and a patient (no. 37) with a congealed tuberculosis K = 453, the total picture is probably clouded by the various combinations of chest diseases possible in a given individual. Emphysema alone would be expected to produce a high K value due to the increased amount of air in the chest. On the other hand, an old congealed tubercular lesion could be expected to produce a low K value due to its high electrical conductivity. If both such conditions should be present in a patient, one could offset the other with a resultant K value in the normal

range. Patient no. 10 with severe emphysema and cor pulmonale illustrates such a case. The emphysema would increase the K value while the cor pulmonale apparently resulted in pulmonary vascular congestion and tended to decrease the K value with the resultant value in the normal range.

A more detailed study should be conducted where complete pulmonary function data were available to improve the separation of such patients into more clearly defined groups.

Table II

GROUP ONE K = 600 - 699 (normal range)

PATIENT	DIAGNOSIS	K	Z_o
1. M.C.	Cor pulmonale	682	30.1
2. L.W.	Bronchial Asthma	675	25.5
3. P.B.	Primary hypoventriculation syndrome	613	31.1
4. G.T.	T.B.	662	25.6
5. G.H.	T.B.	672	32.9
6. T.E.C.	T.B., chronic bronchitis	687	30
7. P.B.	Asthma many years, myocardial infarct	667	30.6
8. L.H.	Chronic bronchitis, chronic cough	601	31.4
9. C.H.G.	Emphysema	622	32.1
10. L.	Severe emphysema, cor pulmonale	653	23.2
11. J.D.	Cold	652	26.1
12. E.P.	Rt. ventricular failure	650	29.7

Cold ▫ chronic obstructive lung disease

$$K = \frac{C^2 Z_o}{4\pi L}$$

C = average chest circumference

LUL = left upper lobe

ASHD = arteriosclerotic heart disease

Table III

GROUP TWO K = 700 or greater (above normal range)

PATIENT	DIAGNOSIS	K	Z_o
13. H.H.	Emphysema, chronic bronchitis	793	31.4
14. M.K.	Cold, Asthma	821	29.1
15. B.B.	Asthma	1038	27.5
16. O.K.	Asthma, Obesity	1302	30.7
17. H.M.	Bronchial asthma, allergies, wheezing, normal chest x-ray	830	20.2
18. T.G.	Chronic bronchitis, chronic cough	980	29.8
19. M.	Cor pulmonale	700	30.8
20. A.M.	Chronic bronchitis	770	34
21. G.P.	Severe emphysema, cor pulmonale	837	38.1
22. H.Z.	Bronchial asthma	712	28.6
23. T.	Severe emphysema, asthma	1010	41.5

Table IV

GROUP THREE K = 599 or less (below normal range)

PATIENT	DIAGNOSIS	K	Z_o
24. C.A.	Emphysema, biventricular failure, ASHD	580	24.5
25. N.N.	Asthma for 20 years, LUL pneumonia on admission, bilateral pleura effusion, emphysema, chronic bronchitis	563	33.2
26. J.M.	Silicosis and diffuse pulmonary nodularity and fibrosis on x-ray, lymphosarcoma by biopsy of lymph node	485	23.6
27. E.P.	chronic bronchitis and emphysema	572	24.9
28. E.N.	Asthmatic Bronchitis	484	26.3
29. R.J.	Asthma and cold	565	32.4
30. E.P.	Chronic Bronchitis, LLL Pneumonia	488	25.4
31. L.C.	LUL lesion	452	28.2
32. R.K.	ASHD, cold	488	28.5
33. T.T.	Cold, Cor pulmonale	587	22.7
34. I.M.	Asthma	588	23.9
35. B.H.	T.B.	460	26.7
36. W.A.	T.B.	457	29.2
37. E.H.	T.B.	453	26.8
38 H.G.	T.B.	574	29.5
39. N.J.	T.B.	577	29.7
40. W.L.	Diabetes mellitus	557	28.6
41. E.B.	T.B. vs Neoplasm	494	27.9

B. A part of this contract was a supplemental addition to provide funds for Dr. Ben Eiseman, Department of Surgery, Denver General Hospital and University of Colorado Medical School, Denver, Colorado, to conduct an evaluation of the use of the thoracic impedance (Z_o) as a guide to intrathoracic fluid volume.

This investigation produced very encouraging results for Z_o measurements to detect pulmonary edema and other thoracic fluid accumulations. This work on 52 patients treated at the Denver General Hospital was published in the Annals of Surgery, May 1970.

In order to avoid any possibility of misquoting these authors a copy of the reprint is included here in its entirety.

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Clinical Evaluation of Transthoracic Electrical Impedance as a Guide to Intrathoracic Fluid Volume

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A CLINICAL need exists for sensitive means to detect intrapulmonary fluid accumulation. Pulmonary insufficiency such as that which occasionally follows nonthoracic trauma [2, 5] is notoriously difficult to reverse once there is accumulation of intrapulmonary fluid, and gas exchange becomes inefficient. Treatment ideally should begin prior to the onset of the vicious cycle of fluid accumulation, hypoxia, and more fluid accumulation.

Previously [4] we described studies on experimental animals utilizing transthoracic electrical impedance as a measurement of alterations in intrathoracic fluid volumes. Impedance changed as much as 45 minutes prior to detectable alterations in central venous pressure, pulmonary compliance, arterial pressure or changes in blood gases in these experimental preparations.

This report is a clinical evaluation of transthoracic electrical impedance as a measurement of intrathoracic fluid changes in 52 patients.

Material and Methods

Fifty-two patients treated in the Denver General Hospital form the basis of this study. As summarized in Table 1, six patients were studied acutely. In three fluid was removed from the chest by thoracentesis, and three had total body fluid reduced by membrane dialysis. The remaining 46 patients were studied because they were suspect of subsequent intrapulmonary fluid alterations. Of these patients, 15 sustained thoracic trauma, ten had nonthoracic trauma, and 14 patients were undergoing cardiac surgery. Seven patients had a variety of systemic illnesses.

Impedance was measured using the Minnesota Impedance Cardiograph Model 202 as designed by Kubicek [3] (Fig. 1). Four Mylar circular aluminum strip electrodes * were employed. Two such strips encircled the neck and two the upper abdomen, one at the level of the xiphoid, the other around the lower abdomen (Fig. 2). The outer electrodes (Nos. 1 and 4) provided an electrical field from a constant current oscillator at 100 kHz four Ma. The voltage between the two inner electrodes (Nos. 2 and 3) was displayed on a digital voltmeter and can be considered proportional to impedance. In essence this voltage reflected electrical impedance of the chest as a cylinder between electrodes two and three. A typical study patient is illustrated in Figure 3.

Impedance usually was monitored at least daily and was correlated with arterial blood gases, central venous pressure, arterial pressure, radiographic appearance of the chest, and general clinical course. In the 44 long-term studies the evaluation period lasted 5 to 25 days.

Electrodes once placed were maintained carefully in their original positions since

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FIG. 1. Minnesota Impedance Cardiograph Model 202. (*From* Pomerantz, M., Baumgartner, R., Lauridson, J., and Eiseman, B.: Transthoracic Electrical Impedance for the Early Detection of Pulmonary Edema, Surgery, 66:260, 1969.)

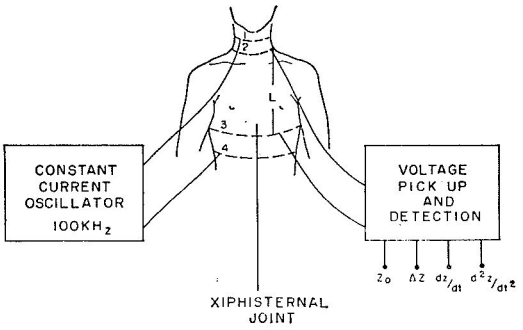


FIG. 2. Electrode placement for impedance measurements. (*From* Pomerantz, M., Baumgartner, R., Lauridson, J., and Eiseman, B.: Transthoracic Electrical Impedance for the Early Detection of Pulmonary Edema, Surgery, 66:260, 1969.)

movement of as little as six cm. could alter the impedance five ohms.

Results

Acute Removal of Intrathoracic Fluid

In all six patients where fluid was removed acutely (three by dialysis, three by thoracentesis) impedance reliably reflected measurable fluid loss.

In the three patients undergoing thoracentesis for pleural effusion there was a linear relationship between the amount of fluid removed, and increase in impedance (Fig. 4). In the case illustrated in Figure 4, impedance rose one ohm for every 200 cc. of effusion removed.

Trauma

Of the 25 patients monitored following trauma 17 developed some degree of pulmonary insufficiency as reflected by arterial blood gases, central venous pressure or radiographs of the chest. Impedance invariably paralleled the above findings and frequently preceded changes in these other values reflecting more acutely alteraations in intrapulmonary fluid volumes.

Seven of the ten patients with nonthoracic trauma developed some degree of

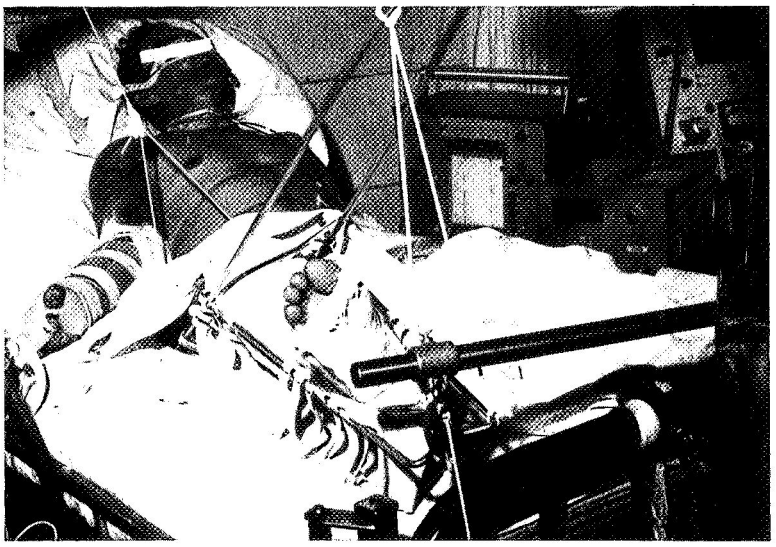


FIG. 3. Typical patient monitored with Impedance Cardiograph and Recorder.

TABLE 1. *Clinical Impedance*

I Acute Studies	
1) Dialysis	3
2) Thoracentesis	3
II Chronic Studies	
1) Cardiac	14
2) Trauma	
(a) Thoracic	15
(b) Nonthoracic	10
3) Miscellaneous	7
Total	52

* 3M Company Medical Products Laboratory, St. Paul, Minnesota 55101.

pulmonary insufficiency. Two of these patients died of the "respiratory distress syndrome" [1] with fluid overload as the cause of death. In these cases impedance remained low, below 19–20 ohms, and at autopsy the wet, hemorrhagic lungs weighed over 900 Gm. per side in each case.

Ten of the 15 patients with thoracic trauma developed some degree of pulmonary insufficiency. All of these patients recovered. As the pulmonary contusions cleared, and blood gases returned to normal, impedance rose indicating clearing of fluid from the lungs.

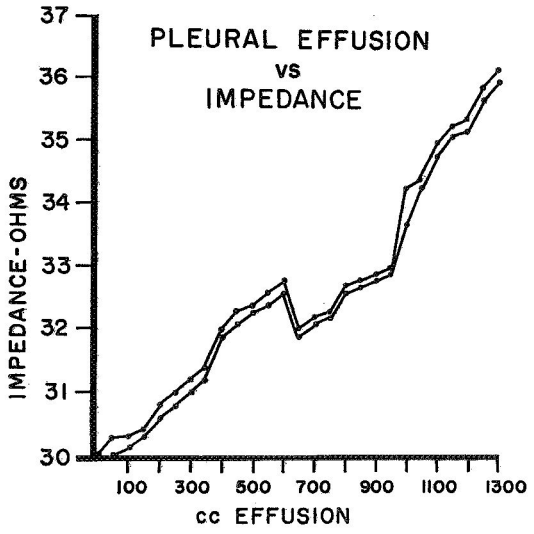


FIG. 4. Impedance versus fluid removed by thoracentesis.

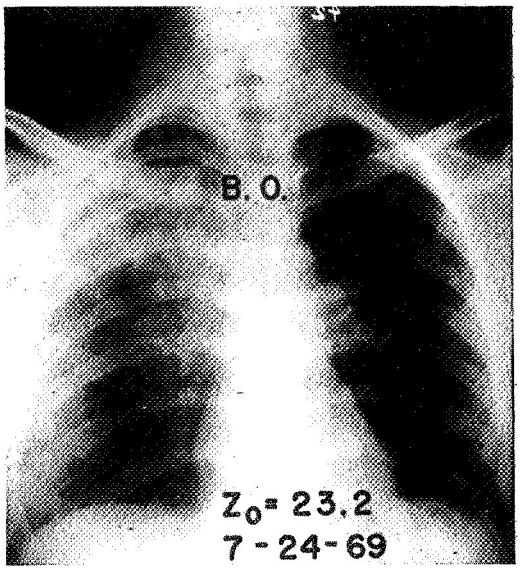


FIG. 5. B. O. Initial films having contused lung and impedance of 23.2 ohms.

The following case demonstrated clearly how impedance changes reflect changes in pulmonary fluid volumes following clearing of a contused lung.

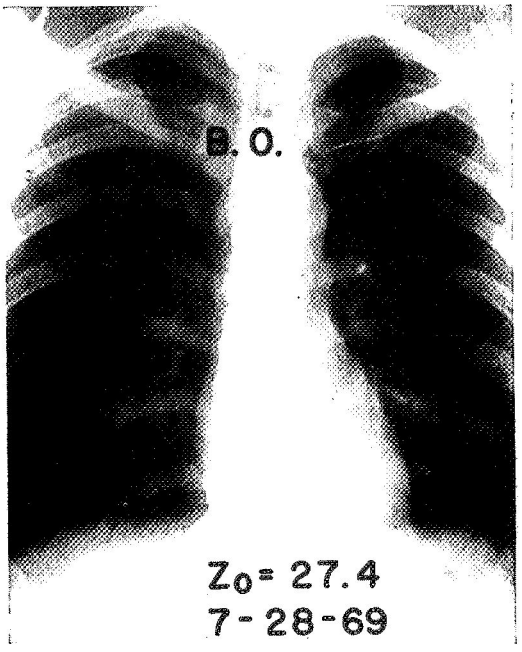
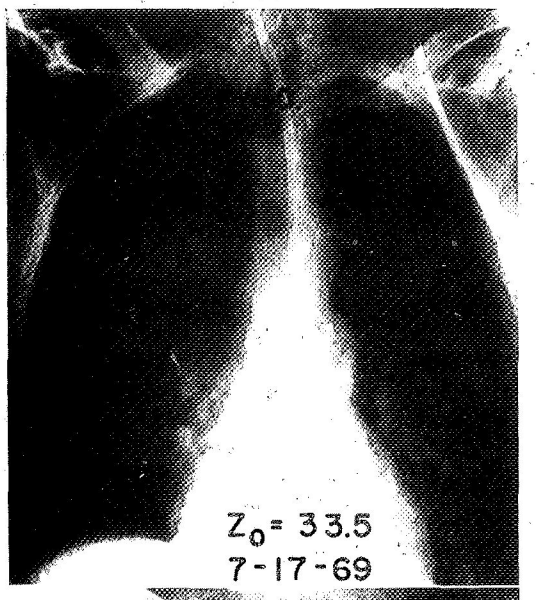


FIG. 6. B. O. Film showing clearing of contusion and impedance of 27.4 ohms.



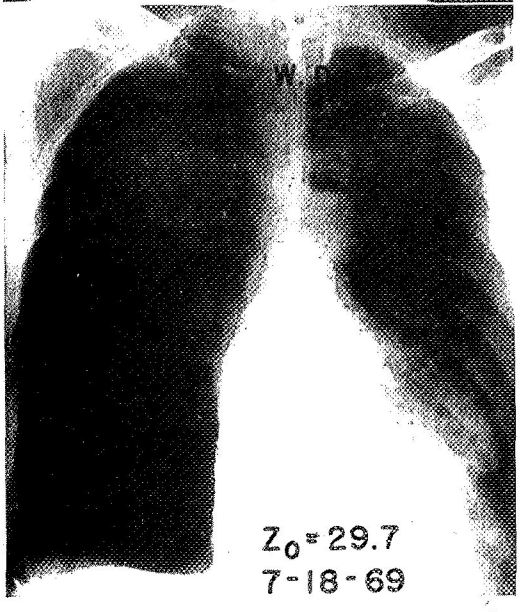


FIG. 7. (top) W. D. Initial postoperative film and impedance of 33.5 ohms.

FIG. 8 (bottom). W. D. Two days postoperative films with left lower lobe infiltrate and impedance of 29.7 ohms.

Case Report

Case 1. B. O., a 26-year-old man sustained a pulmonary contusion secondary to an auto accident. Admission impedance was 23.2 and evidence of a pulmonary contusion was noted in the right upper lung field (Fig. 5). On the following day impedance remained stable and his pulmonary contusion persisted. Three days later impedance rose to 27.4 and the chest film was clear (Fig. 6).

Cardiac Cases

Impedance measurements in all 14 cardiac surgical patients accurately reflected the status of intrathoracic fluid volumes. Those patients in congestive heart failure preoperatively, treated with vigorous medcal therapy, all showed a rise in impedance as they improved their cardiopulmonary dynamics. All pump cases were perfused using a bubble oxygenator and hemodilution. Postoperatively impedance was characteristically lower than immediate preoperative levels indicating increased fluid within the lungs. Invariably over the next 7 to 10 days however, impedance rose to above preoperative levels as cardiopulmonary dynamics improved.

The following case represents how impedance reflected pulmonary fluid volumes in cardiac surgical patients.

Case 2. L. S. was a 65-year-old man with ventricular aneurysm and congestive heart failure. Admission impedance was 20.6. After treatment for congestive heart failure resulting in diuresis

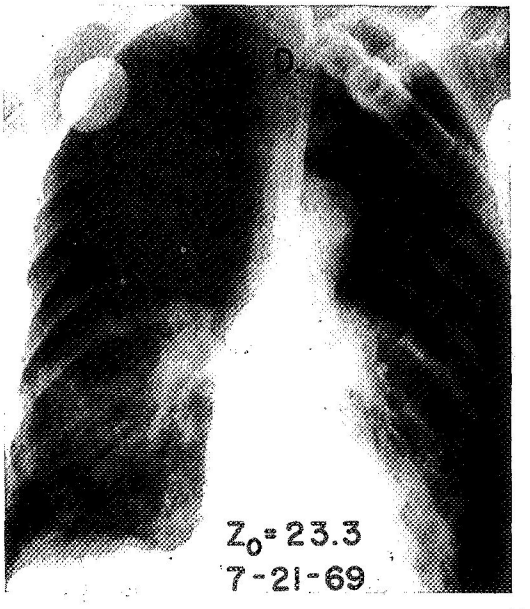


FIG. 9. W. D. Four days postoperative film with bilateral lower lobe infiltrate and impedance of 23.2 ohms.

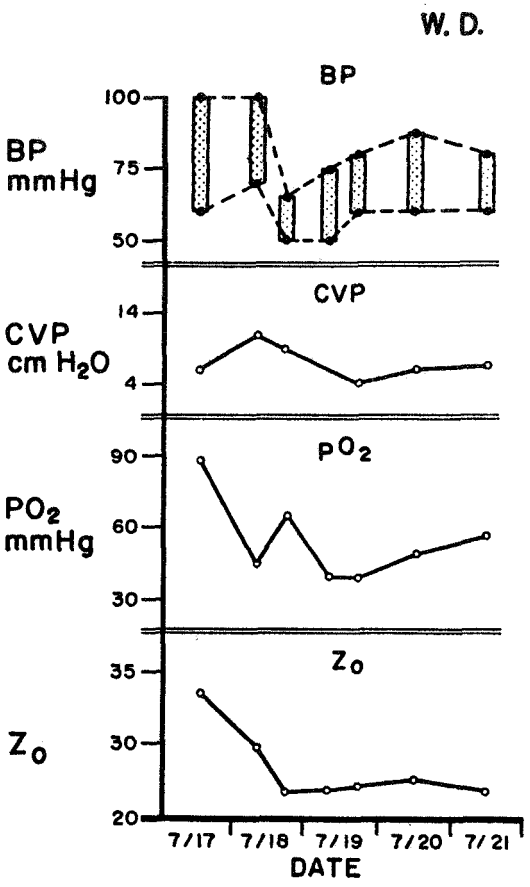


FIG. 10. Hospital course of Patient W. D.

of 25 pounds, impedance rose to 32.0. While he was in good cardiopulmonary status, both preoperatively and following aneurysmectomy his impedance remained stable.

Systemic Illness

Three of the seven patients with a severe systemic illness developed respiratory insufficiency. Two of these patients recovered while one (W. D.), developed the "respiratory distress syndrome" [1] and died. Impedance measurements reflected the status of intrapulmonary fluid volumes as described below (Cases 3 and 4), and paralleled the clinical course of each patient.

Case 3. W. D., a 73-year-old emphysematous man underwent cholecystectomy for empyema of the gallbladder. On the first postoperative day the chest film was normal and the patient's impedance was 33.5 ohms (Fig. 7). On the following day the impedance dropped to 29.7 and the chest x-ray revealed a left lower lobe infiltrate (Fig. 8). On the next 2 days the patient's impedance dropped to 23.5 and 23.3, respectively, at which time bilateral lower lobe infiltrates were noted (Fig. 9). His hospital course until death is illustrated in Fig. 10. At autopsy his lungs weighed 1,000, and 900 Gm., respectively.

Case 4. W. S., a 56-year-old alcoholic was admitted with the diagnosis of hemorrhagic pancreatitis. Pulmonary insufficiency followed and respiratory support was necessary. A rise in impedance corresponded with diuresis and improvement in pulmonary function (Fig. 11).

In the first of these two cases impedance decreased as the patient developed progressive pulmonary insufficiency resulting in death. In the latter case a rise in impedance was associated with improvement of the patient's pulmonary status.

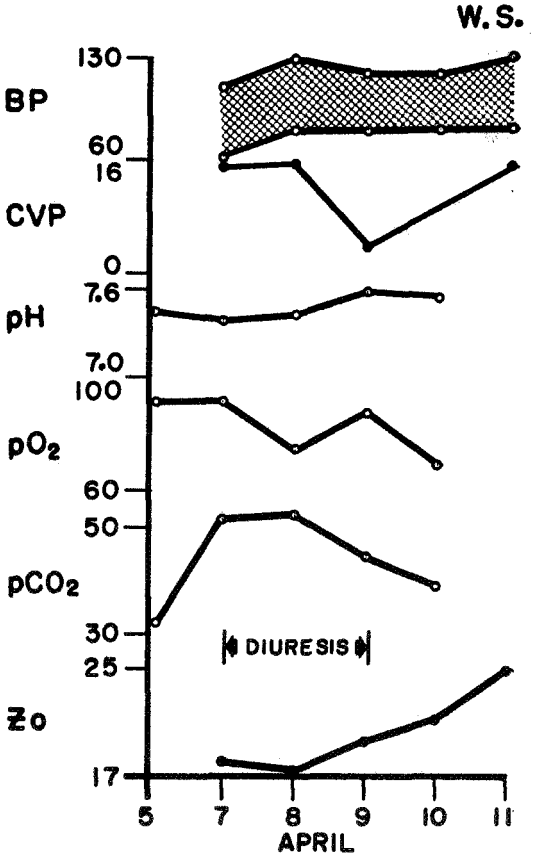


FIG. 11. W. S. Clinical course showing a rise in impedance associated with a diuresis and a decrease in P_{CO_2}.

Discussion

There is an obvious need for an accurate technic to determine changes in intrathoracic fluid volumes prior to the onset of pulmonary edema. Once pulmonary edema occurs in the severely injured or postsurgical patient alveolar ischemia leads to increased vascular permeability and more resistant edema. Alterations in transthoracic electrical impedance provides a means for the early detection of pulmonary fluid accumulation before the onset of frank pulmonary edema. As employed in postoperative and post-traumatic patients, this device has provided early warning in those patients who might develop pulmonary edema or pulmonary insufficiency. Treatment could therefore be started earlier.

There are certain obvious problems that remain in the system at this time. Hyperventilation changes measurable impedance as much as one to 1.5 ohms. Therefore, changes in impedance in hyperventilating patients—such as often occurs following severe trauma—must be greater than 1.5 ohms to be significant. In addition the circular electrodes must not be moved since this markedly alters measurable impedance.

We have not had sufficient experience to define an absolute figure for normal transthoracic electrical impedance. Therefore, each patient must serve as his own control. Currently impedance of 25.0 ± five ohms seems to represent the normal for adults. Patients with emphysema have a higher baseline impedance reflecting an increased amount of air—a poor conductor—within the chest. Although impedance may be altered by gross changes in body length and width of chest, we found no constant numerical correlation with the thoracic cylinder being measured or the circumference of the chest.

Such problems probably are solvable with further clinical experience. They do not detract from the over-all value of impedance measurements as a guide to intrathoracic fluid volumes. Alterations from baseline measurements consistently occurred in seriously ill patients where there was significant intrathoracic fluid accumulation.

Summary

In a clinical study of 52 patients transthoracic electrical impedance accurately reflected alterations in intrathoracic fluid volumes. This simple, rapid, noninvasive technic paralleled and often preceded classic methods for detecting pulmonary insufficiency.

Continued clinical trial of transthoracic electrical impedance as a monitor of alterations in intrathoracic fluid volumes is warranted. An important potential use is in the early detection of intrapulmonary fluid accumulation as occasionally follows trauma.

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Discussion

Dr. William H. Lee, Jr. (Charleston): I particularly wanted to congratulate Dr. Clowes and discuss his paper, although the other two were most intriguing also. Dr. Clowes gave us a great deal of insight into a problem that not only involves sepsis but also is of extreme interest because of the pathophysiologic situation which develops following thermal burn and following prolonged pump oxygenator perfusion.

Several years ago it was my pleasure to participate with Dr. Clowes in a similar study which

involved the thermal burn model, and I would like to report one aspect which I think is relevant to Dr. Clowes' study.

(Slide) One of the factors of most importance, it seemed to us, in the court of these investigations was to have available a method by which one could assay quantitatively the leakage of plasma in the lung or the permeability factor which Dr. Clowes has mentioned. Attempting to go to the laboratory to solve this, we have modified a method previously described by Wineberg in which radioactive albumin, a molecule of about 80,000 molecular weight, is injected intravenously and the thoracic duct is cannulated in the neck. One then monitors the level of radioactivity in plasma, thoracic duct lymph, and in the case of these experiments we also assayed radioactivity from bronchial washings to try to determine the timing and quantitation of leakage into the bronchoalveolar system.

As you will note here, some 30 minutes after the injection is made in a group of ten animals—that should be 12 animals in the central group—that the risa level in blood rises to about 6,000 counts per minute, and a similar rise is seen in a group of dogs which is subjected to a thermal burn, in this particular set of experiments, and another group which are infused with 3.5 cc./Kg. of plasma taken from a burned dog. The level is fairly constant for the 4-hour observation period.

(Slide) The risa level in lymph during this period of time in the control group rises slowly but the differences between the control group and the burned and infused group are significant, both at 30 minutes and persisting for 4 hours. This, then, is a quantitative means of assaying the degree to which permeability of the capillary bed has been altered by the pathophysiologic insult.

(Slide) Finally, the risa level in bronchial washings similarly displays increased activity within 30 minutes, persisting at 4 hours.

I believe that this is a useful tool for the laboratory to continue studies of alterations in permeability resulting from prolonged pump oxygenator perfusion and thermal burn; further, I think that Dr. Clowes has added sepsis to the other two pathophysiologic states, which may result in pulmonary vascular seepage, and that there is an intriguing similarity between these three conditions.

DR. JOSEPH M. VAN DE WATER (Boston): I would like to add our enthusiasm for transthoracic electrical impedance to that of Drs. Eiseman, Pomerantz, and Baumgartner and to add a small footnote to their fine work.

At the Peter Bent Brigham Hospital we have been using this technic in our continuing study of patients with post-traumatic pulmonary insufficiency. We have found that changes in impedance correlate well with changes in pulmonary extravascular water volume (PEWV) when there are no additional fluid shifts in the pleural space or within the mediastinum.

(Slide) The actual measurement of PEWV involves a comparison of the volumes of distribution of tritiated water, a freely diffusible ion, and Evans blue dye, a nondiffusible marker. Both are injected together as a bolus into the right atrium while samples are collected simultaneously from an artery, as in the standard dye dilution cardiac output technic. The tritiated water will have a longer mean transit time than the Evans blue dye.

(Slide) The difference between these two values is multiplied by the cardiac output to obtain PEWV.

(Slide) For example, this is an anephric patient undergoing hemodialysis. His transthoracic electrical impedance initially was 19.3 ohms. At the end of dialysis it was up to 22 ohms. At the same time his PEWV dropped from a level of 45 to one of 10 ml./l. of total lung capacity.

(Slide) This unfortunate patient developed pulmonary insufficiency as a result of aspiration following peritonitis. Below the respective x-rays of November 12, 13, 15 and 17 are the falling values of impedance and the corresponding rising values of PEWV.

And finally, (slide) I would like to show two patients from a recent study that we did on patients undergoing mitral valve replacement. In this series, among other parameters that we followed, were the transthoracic electrical impedance, PEWV, and the physiologic pulmonary shunt. Plotted along the abscissa are the days beginning with pre-op. and going through post-op. day 15. The heavy bars represent the means for all members of the group. The group as a whole showed no striking changes, but patients G and F deviated markedly from the mean. Instead of progressively rising towards preoperative levels, their impedance values progressively fell, and, indeed, both patients expired. If you study the PEWV of these two patients you can actually separate them. Patient G had a markedly elevated PEWV, whereas F had a low normal one. Looking at the physiologic pulmonary shunt, we see the same thing: G, a very high physiologic pulmonary shunt; F, a low normal one. There was no mystery clinically; and of course, at autopsy patient G had heavy, wet lungs; patient F had virtually no fluid within the lungs, but did have a hemopericardium, pleural effusion, and bleeding into the chest wall as a result of a bleeding diathesis.

In conclusion, I would like to say that we share Dr. Eiseman's enthusiasm for transthoracic electrical impedance, and feel that it is not only a simple and early means of detecting problems in the lungs, but is also an accurate one.

DR. MARVIN POMERANTZ (Closing): I would like to thank Dr. Van de Water for his comments regarding our impedance measurements showing the accuracy of this relatively simple technic for determining changes in intrathoracic fluid volumes.

The first two papers presented in this session pointed out several facts of importance. First, that sepsis is a frequent cause of pulmonary insuffi-

ciency. Dr. Hardy listed 14 causes of postoperative pulmonary insufficiency. To this can be added trauma itself, and emboli from the pump oxygenator as emphasized by Dr. Lee. The one common factor in most of these conditions is an increase in intrathoracic fluid volume.

(Slide) The most important question that arises, however, is once you have determined that patients have increased intrathoracic fluid volumes, what do you do?

This slide demonstrates an experimental study in which pulmonary edema was produced by the intravenous administration of alloxan. Alloxan is supposed to cause pulmonary venule vasoconstriction, and therefore pulmonary edema. This is also thought to be the common pathway in the production of the pulmonary insufficiency that we have been discussing. The importance of this is that the change in impedance, or the change in the amount of fluid within the chest, appears to be directly proportional to the amount of fluid administered. Therefore, once the syndrome occurs, the obvious thing to do is to markedly restrict fluid administration.

Finally, I would like to illustrate the accuracy of impedance measurements with two more patients. (Slide) This young girl was in an automobile accident and sustained a fractured pelvis and a torn iliac artery. Postoperatively she developed the respiratory distress syndrome, and, as you can see, most of her studies remained entirely normal, except her impedance, which never rose above 13. At autopsy her lungs weighed over 2,000 Gm.

The corollary (slide) to the above patient is a young boy who sustained a bilateral pulmonary contusion and on admission had an impedance of 15. As impedance gradually rose, he was able to come off the respirator, and maintain a normal arterial P_{O_2}. During the recovery period his impedance rose to the normal of approximately 25.

In summary, we feel that a transthoracic electrical impedance is an accurate and simple method to detect changes in intrathoracic fluid volume.

DR. WATTS R. WEBB (Dallas): Dr. Clowes has described the hemodynamics that occur in the pulmonary insufficient lung, occurring from many different syndromes. We have studied this experimentally using the hypovolemic shock model which produces physiologic and pathologic changes very comparable to those that Dr. Clowes has shown so beautifully here.

In trying to analyze the increased rise in pulmonary arteriolar resistance that occurs, we have measured pulmonary arteriolar wedge pressures, small pulmonary vein pressures, and left atrial pressures. The first thing that we see is a rise in the small pulmonary vein pressure, so that there develops a large gradient between the small pulmonary vein and the left atrium. With the development of congestive atelectasis and increasing pulmonary capillary congestion, there develops a gradient between the pulmonary arterial wedge and the small pulmonary vein. So we think that the first change probably is an increased reactivity of the small pulmonary vein, and then with increasing pulmonary congestion a bottleneck at the capillary level.

The studies presented by Dr. Hardy have shown the changes that come to our attention as we carefully reevaluate our results and attempt to see why our patients are having difficulty, even patients that otherwise we might think are doing well.

Our own work in this field has utilized radioactive xenon to evaluate the ventilation and the blood flow to the lungs of these patients following operation or different types of trauma. Very briefly, with appropriate scintillation counters in place, the patient can breathe radioactive xenon to evaluate his ventilation, or inject radioactive xenon intravenously to evaluate blood flow to the various regions of the lung. In brief, our studies correlate very well with those of Dr. Hardy and Dr. Neely, and also those of Dr. Eiseman in showing very profound changes that persist long after the patient is radiologically and clinically normal.

I think it is interesting to speculate how many of the problems of the postoperative patient are the result of things we can do nothing about—the original blast injury to the lung, for example—and how much of it is the consequence of our own ministrations, rather than accepting these disasters as due to the patient's disease or as acts of divine providence.

Certainly, overinfusion of noncolloid substances has been well documented, and even though there is a necessity for a certain amount of saline and other electrolyte solutions in the post-traumatic and postoperative patient, we should remember that some 75% of an electrolyte solution passes into the interstitial spaces in a very few minutes. This means that 75% of all the saline or Ringer's lactate is in the interstitial fluid of the lung and the other tissues of the body. This produces edema that is not necessarily associated with an increase in central venous pressure.

We should also remember that in assuming a physiologic function of the patient, such as breathing for them, we often only incompletely perform the functions that our normal lungs do. For example, while we may ventilate adequately, we do not humidify the air, we do not warm it, and certainly we often do not sterilize, or essentially sterilize the air, as do our own respiratory passages. In fact, our ventilators all too often are a source of massive bacterial colonization.

Also we should remember that during operation and postoperatively the patient does not turn every few minutes, as we do. In fact, in our normal sleep, when we think we have slept like a log, motion pictures show that actually we have been spinning like a whirling dervish all night long, turning several times every hour. Certainly in the operative period, the longer the operation, the longer patients are flat on their backs, de-

veloping congestion in dependent parts of the lung.

Similarly, we tend to add oxygen because we think if a little bit is good, more is better. Soon we have poisoned the lung; destroyed the surfactant and caused many of the other problems that have been outlined here.

DR. ALBERT O. SINGLETON, JR. (Galveston): We have studied a group of patients using some less sophisticated respiratory function tests, spirometer studies, with the maximum expiratory flow rate being, in our hands, the most accurate test. Using patients undergoing abdominal and peripheral surgery, excluding thoracic surgery, we found that one-third of these patients preoperatively showed abnormal pulmonary function tests. On the other hand, studying this same group of patients postoperatively, we have found now that three-fourths of them had abnormal pulmonary function.

The pulmonary complications were about equal in those showing normal and abnormal function of course, one group being much larger than the other —but in the postoperative period all the complications and insufficiency occurred in the group showing abnormal pulmonary function studies.

In those patients who had nonabnormal surgery, even though operations were extensive, no pulmonary complications occurred, despite impaired pulmonary function.

DR. GEORGE H. A. CLOWES, JR. (Closing): This group of papers and the pertinent discussion which followed constitute a timely symposium on the pulmonary complications encountered in surgery. I consider it a privilege to have participated. In particular I should like to reemphasize some of the points made by Drs. Lee and Webb. Both have made significant contributions toward an understanding of the effects of nonthoracic tissue injury and infection upon the lungs. Time did not permit more than brief review of their data. The first point is that we generally agree that the response of the lung under these conditions follows a nonspecific pattern of vascular congestion and interstitial edema which leads to the obvious secondary changes of atelectasis and bronchopneumonia.

The second point is that these early abnormalities are caused by blood born elements derived from the site of injury or infection. Dr. Lee presented further evidence of the presence of fibrin coating of cells in these circumstances which leads to hemagglutination, a phenomenon reviewed by Neter (Bact. Rev. 20:166, 1956). Activation of the clotting mechanism then appears to be the principal cause of mechanical blockage in the pulmonary vasculature.

The other important aspect of this pulmonary response is a change in the filtration of protein containing fluid into the alveolar septa. Results which our group will publish shortly suggest that the agent responsible for this apparent increase of capillary permeability is transported in the plasma fraction of the blood. Perhaps it is a bradykinin like substance released by activation of the Kalikrein mechanism by Hageman factor or other circulating tryptic enzymes. The presence of interstitial edema may be demonstrated clinically by a decrease of transthoracic electrical impedance, so beautifully demonstrated by Dr. Eiseman and his associates, or more indirectly by a reduction of arterial oxygen tension.

Therefore, gentlemen, if increased capillary filtration and edema are features of the pulmonary response to injury or infection, let us get away from the massive use of crystalloids containing solutions. As is well known, such ions rapidly leave the circulation especially in areas such as this where membranes are altered. Rather resuscitation should be carried out with plasma or whole blood depending upon the need for red cells as determined by the hematocrit. Almost all the evidence points to the damage, particularly in the lungs, caused by flooding such very sick patients with large volumes of Ringer's lactate or saline.

DR. WILLIAM A. NEELY (Closing): The first patient that Dr. Hardy mentioned prompted this study. She was an 18-year-old girl who was involved in an automobile accident; she received 20 l. of fluid, chiefly crystalloid, from residents trying to maintain blood pressure. Her P_{CO_2} finally rose to 127 mm. Hg which returned to normal after peritoneal dialysis.

The patient who had the very high permay work in joules underwent eventual pneumonectomy. He was admitted with massive bleeding and underwent left upper lobectomy from which tumor cells were seen on biopsy. No tumor was found. Finally, we did a left lower lobectomy, and no tumor was found, but luckily 2 days later the pathologist found a small—about 3 mm.-malignant area from which the patient was bleeding.

This patient exhibited the most marked rise in pulmonary function that I have ever seen, and as Dr. Hardy alluded to, his postoperative P_{CO_2} was 67. This patient continues to smoke. He even smoked while he had Pseudomonas pneumonia.

We must ask the question, as all of you probably have: Why bother with all of these studies? We have been pleasantly surprised that they have been clinically useful in evaluating surgical patients. For instance, the patient shown that had the next to highest measure of pulmonary work, about 12 to 13 joules—after we found that function had increased, we examined him more closely and found that he had right lower lobe atelectasis.

This little device, we feel, is relatively inexpensive, especially since the advent of cheap operational amplifiers. One can buy little multipliers now for $25 or $30 which once cost $300 to $1,000 and by various manipulations connect these little amplifiers to design a computer that will do almost anything.

C. A study of the change in thoracic impedance (Z_o) during continuous intravenous infusion of lactated Ringer into anesthetized dogs.

In these experiments advantage was taken of an investigation underway in our laboratories related to hemorrhagic shock in dogs. A total of 24 dogs were used, 12 control dogs given a four hour infusion of L-Ringer only and 12 treated animals given L-Ringer plus a vasodilator (Serc).

Figure 7 shows the normalized changes in the mean values of Z_o for the 12 control and 12 treated animals. The difference between the control and treated animals was not significant.

The main points in these observations are:

1. The rise in Z_o during the shock period when the animals were hemorrhaged until the mean arterial blood pressure was reduced to 35 to 40 mm/Hg. The pulmonary vascular bed contributed to the shed blood volume and consequently Z_o increased.
2. When the shed blood was returned (D,E, Fig. 7), Z_o returned to near control levels indicating that the pulmonary vascular system regained the blood volume lost during the hemorrhage (shock) period (C, Fig. 7).
3. The time period F (Fig. 7) was devoted to a 4 hour continuous intravenous infusion of L-Ringer at the rate of 6 ml/kg body wt/hr in both series of animals.

A distinct, continuous fall in Z_o illustrated by the downward slope of Z_o indicated that the intravenous infusion of the L-Ringer was partially taken up by the pulmonary vascular

system. Other data showed that the infusion rate was greater than the rate of urine output. Consequently, the entire blood volume of the animals was being diluted by the lower impedance L-Ringer.

Subsequent pilot experiments in anesthetized dogs subjected to a higher rate of L-Ringer infusion (12 ml/kg body wt/hr) resulted in a steeper downward slope for Z_o.

These experiments confirm the work of Eiseman et al., Berman et al., and Van De Water et al., that transthoracic impedance (Z_o) is a reliable and very sensitive indicator of fluid shifts into or out of the thorax. Further, these experiments indicate that continuous observation of Z_o could provide an early warning of fluid overload during the treatment of shock.

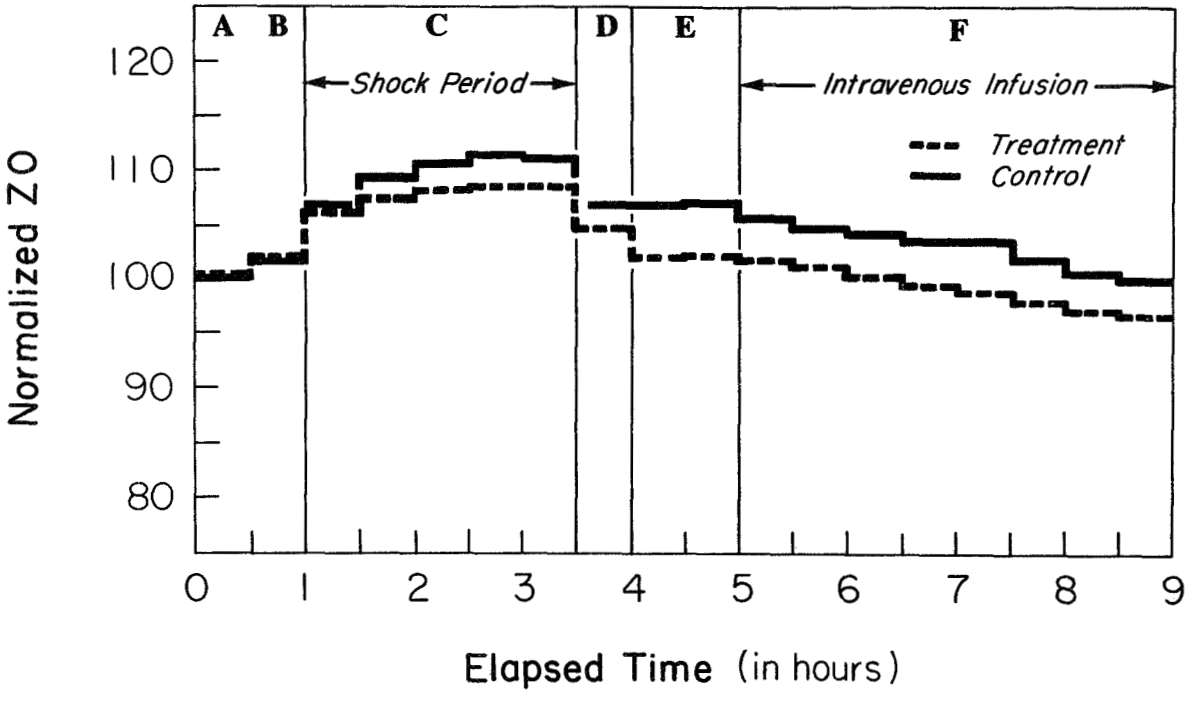

Figure 7. A graph of the changes in thoracic impedance (Z_o) during hemorrhagic shock followed by a four hour intravenous infusion of lactated Ringer (control) or Ringer plus a vasodilator compound. Note the downward slope of Z_o during the four hour infusion period indicating an uptake of some of the Ringer fluid by the pulmonary vascular bed. Ringer was infused at a rate of 6 ml/kg body wt/hr into anesthetized dogs.

Increasing the infusion rate will increase the downward slope of Z_o and thus provide an early warning of fluid overload.

Part IV

This part of the investigation was directed toward obtaining impedance records on human patients suffering from a variety of cardiac diseases, heart valve disorders or cardiac anomalies.

The primary objectives were to obtain information relative to the origin of ΔZ and secondly, to expand the scope of applications of the impedance technique.

Figure 8 is a record from a patient at the University Hospitals exhibiting extrasystoles.

One hundred sixteen patients subjected to cardiac catheterization were studied at Miller Hospital, St. Paul, Minnesota, by Dr. James Karnegis.

Figures 9-14 are examples of records obtained by Dr. Karnegis.

Table V lists the types of patients studied at the University Hospitals, Department of Surgery.

Impedance records were obtained on a total of 42 patients at the University of Minnesota Hospitals, Department of Surgery. Pre- and post-operative records were obtained on 25 cardiac surgery patients. Records were obtained on 12 patients pre-operative only, and five post-operative only, due to clinical complications. Figures 15A to 15E are examples of the types of records obtained pre- and post-operatively.

Dr. Karnegis has submitted the following statement:

"The change of impedance waveform shows deflections coincident with cardiac mechanics. Both atrial and ventricular contractions cause certain definable deflections.

Atrial contraction is related to a discrete increase in impedance, called an impedance "A" wave. These deflections are also seen in atrial flutter. In the condition atrial fibrillation, the "A" waves are lost and are replaced by irregular undulations throughout the cardiac cycle.

Ventricular contraction is related to two deflections, both of which show a decrease in impedance. One is systolic in timing and begins shortly after the beginning of the QRS complex. The other is protodiastolic in timing. These waves are called the impedance "C" and "V" waves, respectively.

Premature ventricular contractions are associated with an interruption of the usual delta Z waveform by another "C" and "V" wave. Evidence suggests that a major portion of the "C" and "V" wave is related to the effect of ventricular systole on the systemic or pulmonary venous systems, or less likely, on the pulmonary artery. An observation tending to confirm this view is the remarkable similarity of the delta Z waveform to the vena caval and pulmonary venous blood flow pattern. The contribution to the delta Z waveform by left ventricular ejection of blood is not yet completely defined."

James N. Karnegis, Director
Cardiac Catheter Laboratory
Miller Hospital
125 College Avenue West
St. Paul, Minnesota 55102

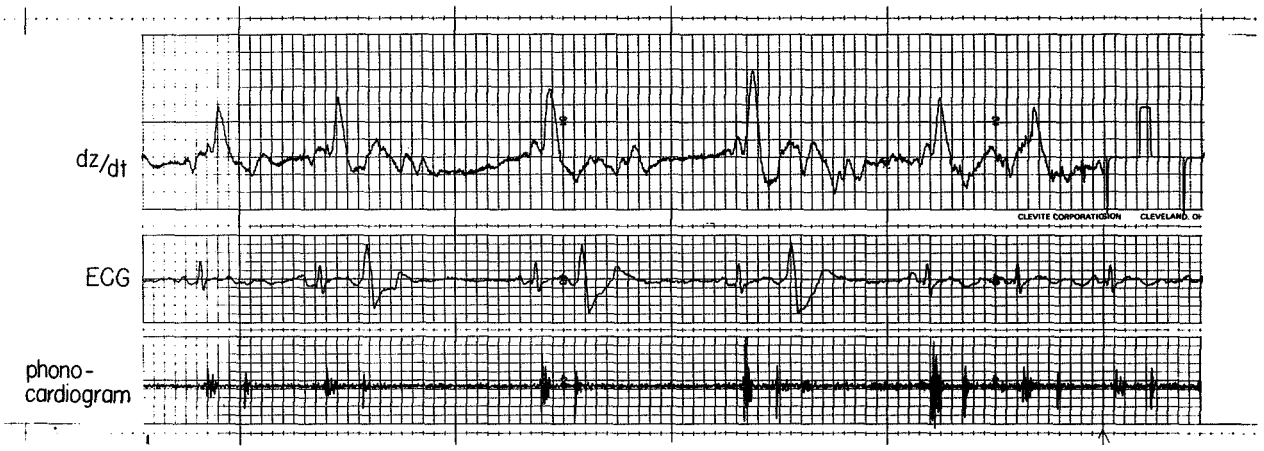

Figure 8. An example of extrasystoles indicated by the ECG while the (dZ/dt) record shows that there was little if any cardiac output during the extrasystoles. The (dZ/dt) amplitude indicates a progressively greater stroke volume during the three PVC_S presumably due to the delayed beats and thus greater ventricular filling.

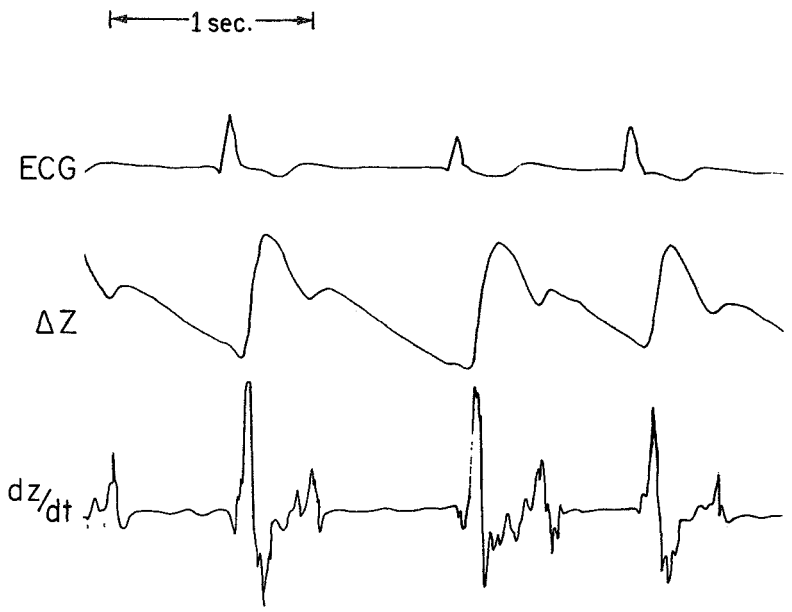

Fig. 9 Records from a patient with a 4+ mitral insufficiency

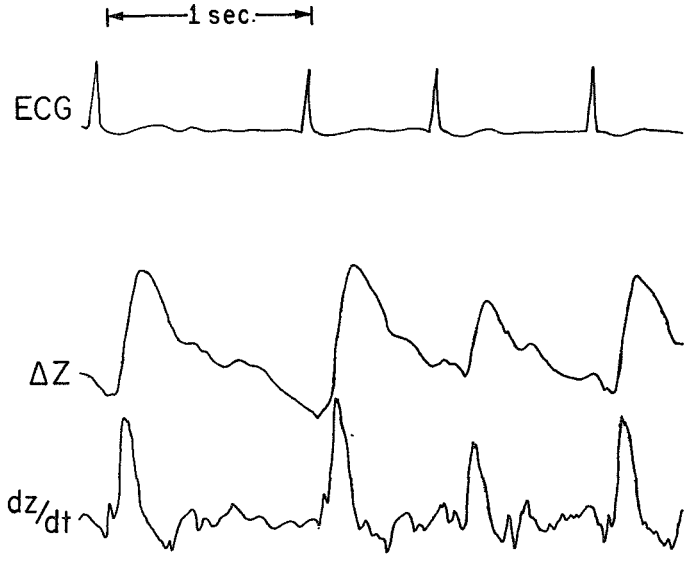

Fig. 10 Records from a patient with mitral stenosis

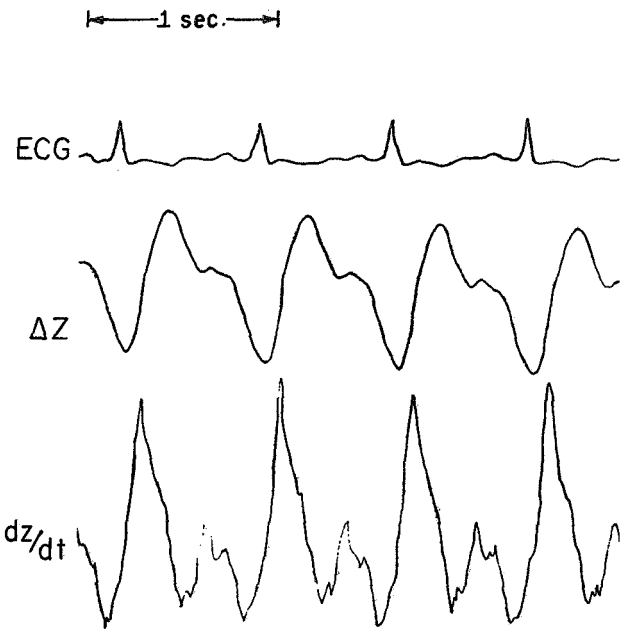

Fig. 11 Records from a patient with aortic insufficiency and cystic medial necrosis

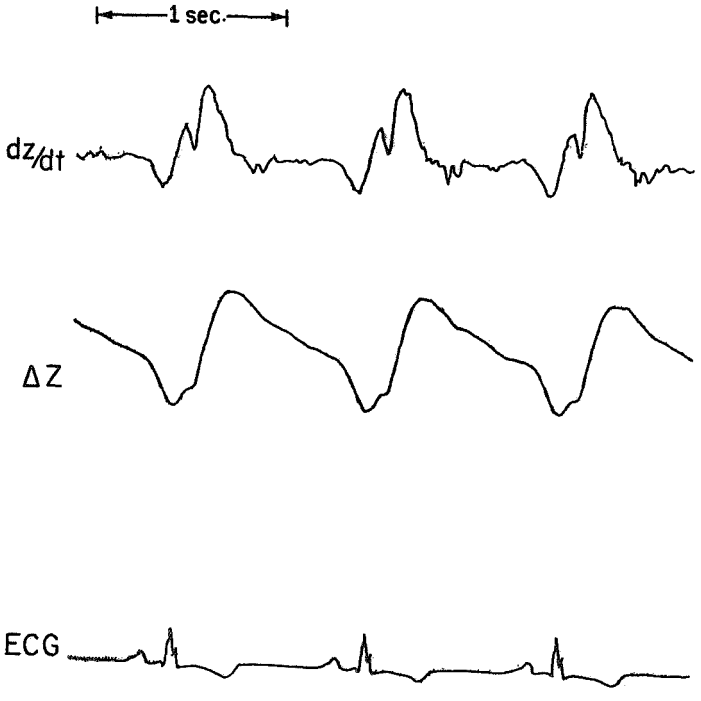

Fig. 12 Records from a patient with calcific aortic stenosis

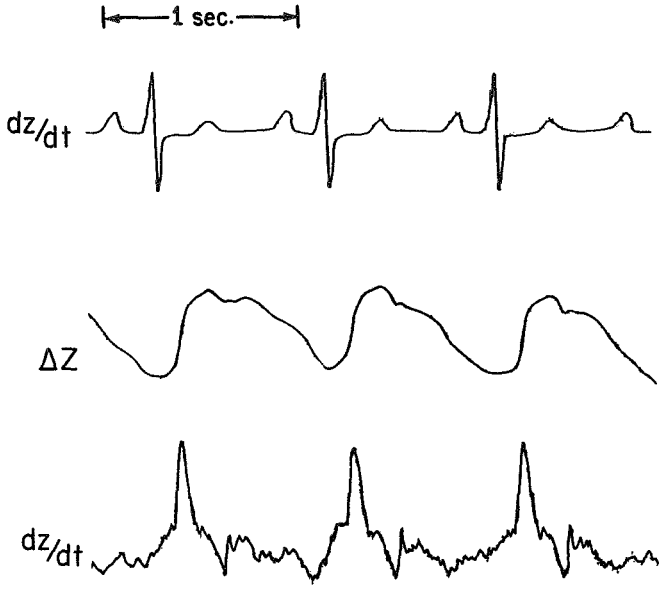

Fig. 13 Records from a patient with an atrial septal defect

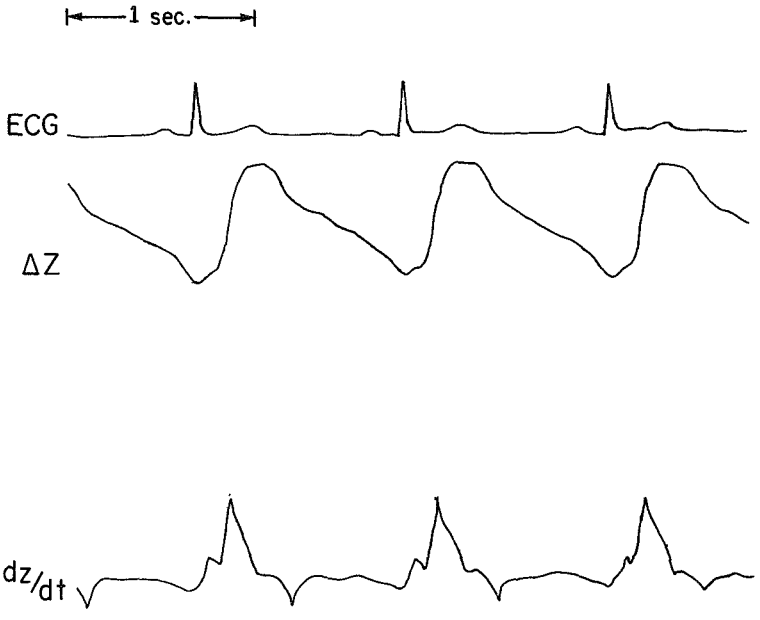

Fig. 14 Records from a patient with coronary artery disease

TABLE V

Patients Monitored at Department of Surgery
University of Minnesota Hospitals

Surgical Procedure	Pre- & Post-Operatively	Pre-operatively only	Post-operatively only
1. Aortic valve replacement	5	3	2
2. Mitral valve replacement	3	2	1
3. Ventricular septal defect	4	0	1
4. Atrial-septal defect	3	2	0
5. Patert ductus, arteriosus	3	1	0
6. Aortic and mitral valve replacement	1	0	0
7. Triple valve replacement	1	0	0
8. Aortic valve replacement, mitral commissurotomy	1	0	0
9. Aortic valvulotomy	1	1	0
10. Mitral commissurotomy	1	2	0
11. Repair of paravalvular aortic leak	0	0	1
12. Repair of paravalvular mitral leak	1	0	0
13. Tetrallogy of Fallot	1	0	0
14. Ventricular aneurism	0	1	0
	25	12	5

Figures 15A, 15B, 15C, 15D, and 15E illustrate examples of the records obtained pre- and post-operatively on cardiac surgery patients with a variety of problems. Especially the (dZ/dt) waveform shows a return toward the waveform obtained from normal individuals.

The calibrations for all of these figures are:
(dZ/dt) = 1 ohm/sec from the zero baseline
ΔZ = 0.1 ohm

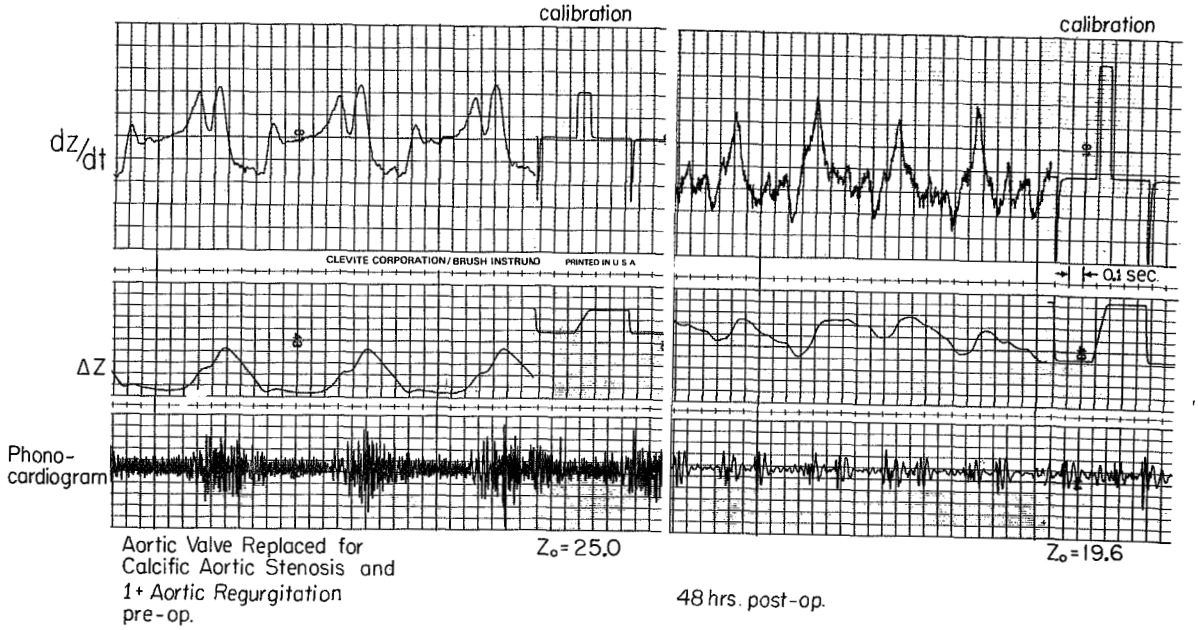

Fig. 15A

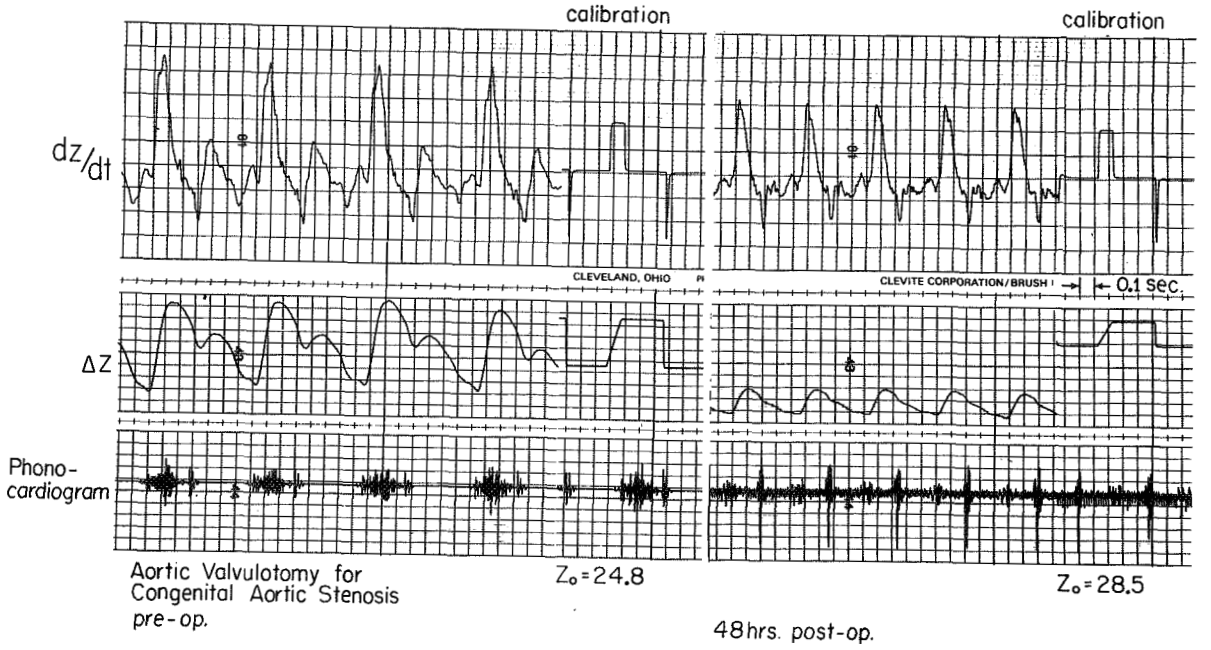

Fig. 15B

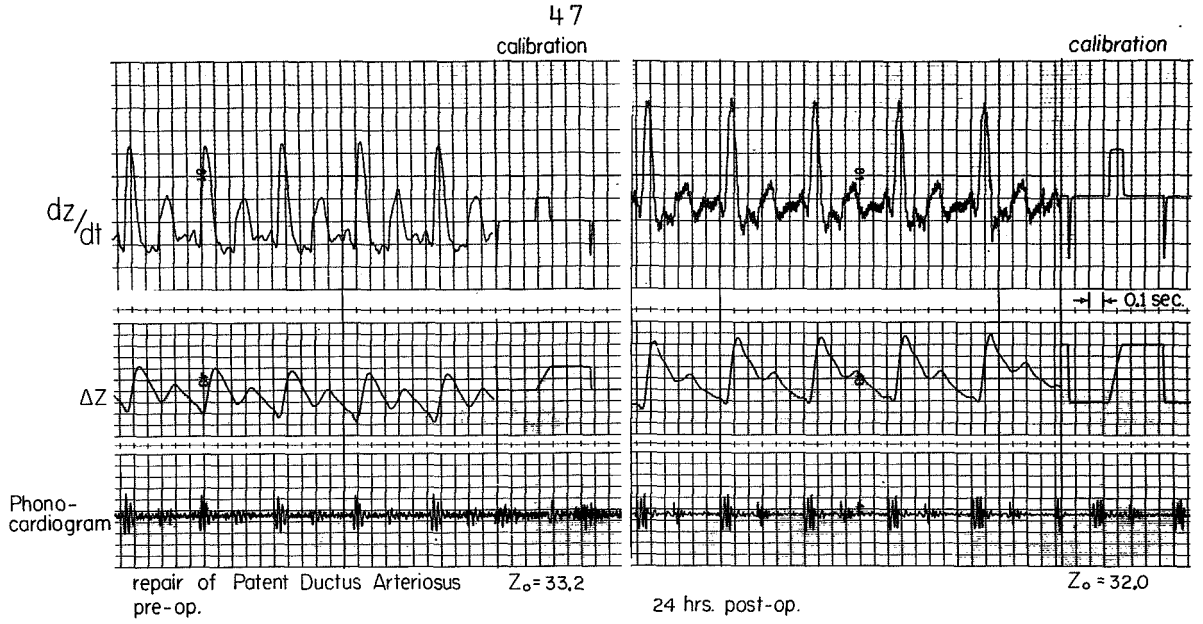

Fig. 15C

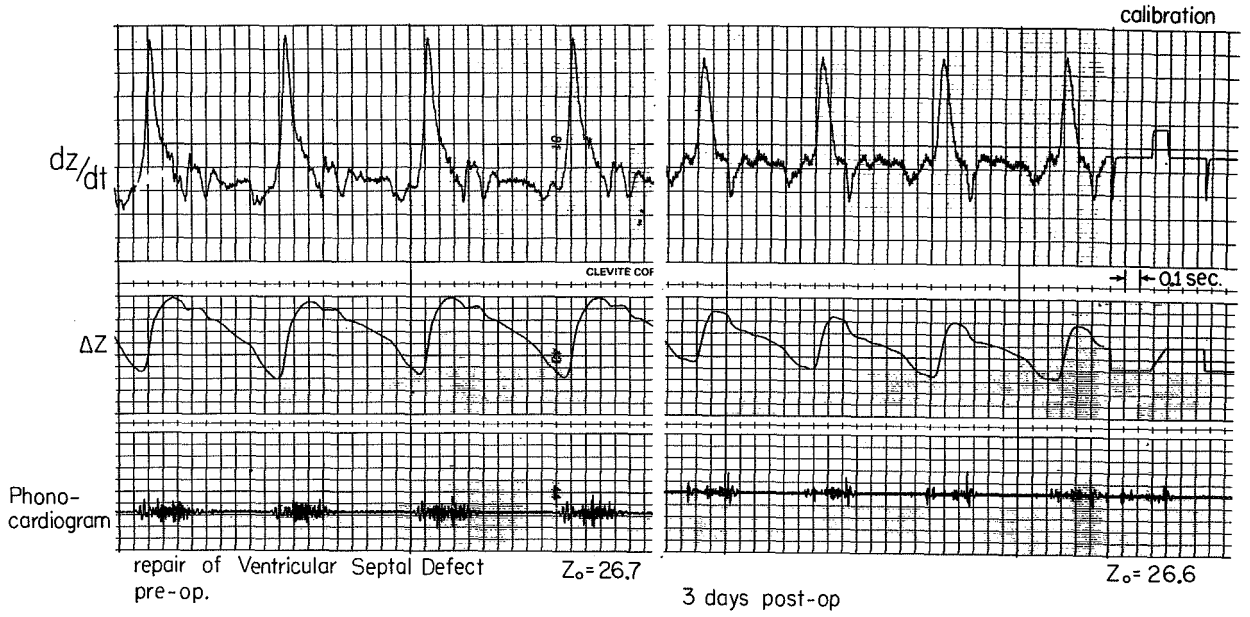

Fig. 15D

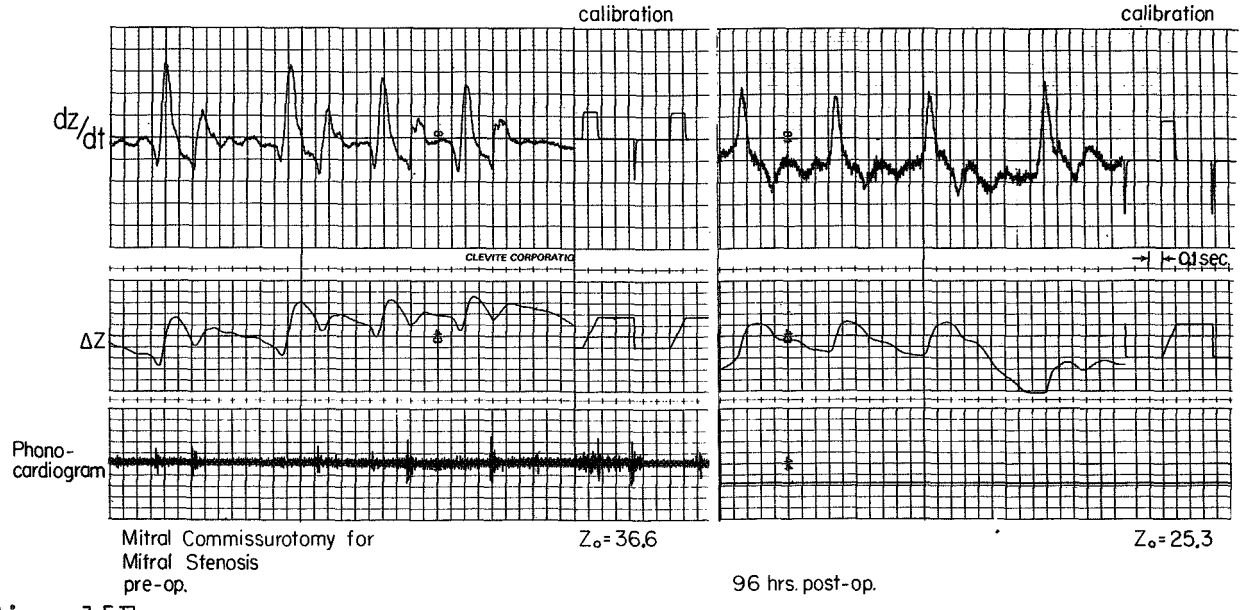

Fig. 15E

Part V. A Study of the Origin and Significance of the Thoracic Impedance Change, (ΔZ and dZ/dt) during the Cardiac Cycle

Work by Other Investigators using an Impedance Cardiograph Supplied by NASA Funds from this Contract

Karnegis (11) has reported some very encouraging observations on the Physiological Correlates of the Thoracic Impedance Waveform. His summary is as follows:

Summary

"Three major components are present. One component shows an increase in impedance, is associated with atrial contraction, and consistently follows the P wave of the electrocardiogram. The other two waves show a decrease in impedance. The first is associated with ventricular systole, and corresponds in time with the QRS complex of the ECG. The systolic wave is then followed by the third component, which also shows a decrease in impedance, but occurs in diastole. In instances of arrhythmias the deflection associated with the P wave occurs independently of the other two deflections.

The impedance change waveform is similar to the pattern of blood flow in the venae cavae and the pulmonary veins. It is possible that the impedance changes are related to the flow of blood in these venous circuits, and the heart."

Lababidi et al. (16) have reported an interesting relationship between certain points on the dZ/dt waveform and the heart sounds as follows:

"The first derivative thoracic impedance cardiogram is recorded easily without the necessity of searching for pulsations. It has sharply demarcated points that relate in time to the four heart sounds and to the opening snap in mitral stenosis. These points are consistent both in normal subjects and in those with heart disease. Thus, the impedance cardiogram can be used not only as a reference tracing for simultaneously recorded phonocardiograms, but also for directly timing intervals within the cardiac cycle."

Lababidi et al. have also submitted for publication the following article: The abstract is included here for reading convenience (17).

Evaluation of Impedance Cardiac Output in Children

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Robert E. Durnin, M.D., Paul E. Leaverton, Ph.D.
and Ronald M. Lauer, M.D.

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Pediatric Cardiology,
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University Hospitals, Iowa City, Iowa 52240

Abstract

Transthoracic electrical impedance changes may be recorded which are synchronous with events in the cardiac cycle and relate to the magnitude of cardiac output.

In 20 children without shunts or valvular insufficiency, duplicate dye dilution and impedance cardiac outputs (ICO) were carried out. The duplicate dye dilutions had a standard deviation 0.259 L/min/m^2, while duplicate ICO had a standard deviation 0.192 L/min/m^2 ($F = 1.82$, $p>0.05$). Of 53 sequential estimates, cardiac outputs measured by both indicator dye dilution and ICO had a 5.5% mean difference.

In 21 subjects with left to right shunts, the ICO correlated well with pulmonary blood flow ($r = 0.92$) rather than systemic flow ($r = 0.21$). In 13 subjects with aortic insufficiency, sequential Fick and ICO had a 50% mean difference; the impedance measurement being higher in every case.

These data indicate that the Impedance Cardiograph can provide a noninvasive measure of cardiac output when there are no shunts or valvular insufficiencies. In subjects with left to right shunts the Impedance Cardiograph provides a measure of the pulmonary blood flow. When aortic insufficiency exists, the Impedance Cardiograph is distorted such that it is consistently higher than Fick cardiac output.

The above investigators obtained a good agreement between cardiac output (CO) by the dye dilution and impedance techniques

in children without shunts or valvular insufficiency. However, of special interest here is the correlation found between the impedance CO and pulmonary blood flow rather than systemic flow in children with left to right shunts.

Also, these workers found that the impedance CO value was higher than the Fick CO in subjects with aortic insufficiency. This would be reasonable if the impedance system were measuring the total left ventricular stroke volume, and the Fick only the final average blood flow in the aorta after regurgitation had occurred.

The point here is that these observations implicate the left side of thoracic circulation as at least a large part of the source of ΔZ.

Part V, Section I. A Study of Thoracic Impedance Changes as a Function of Pressure/Volume Relationships in Segments of the Aorta and the Chambers of the Heart.

- - - - - -

Introduction

Earlier investigations (1967 Final Report to the NASA), by this laboratory into the origin of the ΔZ waveform, suggest that the pulsatile volume change of the ascending aorta was the major contributor to producing an externally observed change in impedance (ΔZ) as seen by the four band electrode method used in this laboratory. The study described in this section attempted to further isolate thoracic blood volume changes that may contribute to the formation of ΔZ by selectively infusing isolated segments of the great vessels and chambers of the heart of a dead dog.

If a specific volume change was the major contributor to ΔZ, then controlled volume changes should be reflected in the externally monitored thoracic impedance. Likewise, a duplication of the control pressure pulse - volume change determined on the alive dog should result in an impedance change (ΔZ) equivalent in magnitude to that observed on the alive animal control measurement.

Methods

This series of experiments were performed upon freshly euthanized dogs. Prior to euthanizing the dog, a series of control blood pressures and thoracic impedance measurements were recorded from the anesthetized animal. Using standard

blood pressure transducers, pressures were monitored in the ascending aorta, right and left ventricles, and right atrium (pilot experiments indicated that complete isolation of the left atrium could not be reliably achieved).

Following euthanization of the dog, a thoracotomy was performed and catheters positioned in the right atrium, right and left ventricles, ascending aorta and descending aorta. The atrium, ventricles and two segments of the thoracic aorta were then hydraulically isolated by appropriate ligature ties. The ascending aorta segment isolated the arch and the descending segment isolated the 10 cm. below the arch. Maximum volume capacities of the aortic segments were determined before closure of the thoracotomy. The thoracotomy was then closed, lungs inflated and the four impedance electrode bands were repositioned on the neck and thorax.

Measured volumes of fresh, room temperature dog blood were injected into each isolated chamber or segment in 1 or 2 cc increments. Simultaneous recordings of thoracic impedance and the pressure in the segment were taken with each step in the infusion sequence. The blood was then stepwise withdrawn from the segment before the next sequence on the same or different segment.

Occasionally, minute leaks developed in the isolated segments after closure of the thoracotomy, therefore it was not possible to obtain data from all of the desired heart chambers or aortic segments on every dog. The leaks were detected by observing a rapid decay in pressure.

Results

Seven experiments were performed in the study with varied degrees of technical success in hydraulically isolating the desired segments of the heart and aorta in each experiment. The aortic segments were satisfactorily isolated in three of the seven experiments, the left ventricle in five studies, the right ventricle in three experiments and right atrium in two of the experiments.

Figures 16, 17 and 18 are representative of the data obtained in this study. Although repeated infusions of each segment were performed on each dog, only one representative curve for each segment is presented for clarity on the graphs. Pre-euthanization control values of pressures and peak to peak ΔZ are listed on the figures. Pressure in the isolated segment for each infusion step is indicated by the number adjacent to the datum point.

Two observations can be made from the graphs. First, increased blood volumes in any of the segments resulted in a decrease in total thoracic impedance as monitored by the four-band electrode technique. Figures 16 and 18 suggest that the impedance change sensitivity to fixed volume change was greater in the aortic segments than the ventricles. Comparison of atrial and aortic segment results in figures 16 and 17 indicate these segments have similar impedance sensitivity for equivalent volume changes. Second, the change in impedance resulting from increased volume of any segment over its control pressure pulse range was less than the control ΔZ. However,

a reduced compliance may have occurred following death of the animal. In figure 18, the ΔZ resulting from increasing the ascending aorta volume to yield a pulse pressure change from 100 mm Hg. to 118 mm Hg is only 10.7% of the control ΔZ amplitude. Calculation of a similar percentage of control ΔZ for each infusion run on the ascending aorta and then determining an average percent value for the dog yielded 11.6% of control ΔZ. Similar calculations for the ascending and descending aorta infusions on three experiments are tabulated below.

Table VI

Percent of control ΔZ by infusing between control pressure pulse limits

Experiment No.	5	6	21
Ascending aorta	17%	8.1%	11.6%
Descending aorta	5.2%	2.0%	3.0%

Discussion

The ΔZ waveform obtained from man or dog exhibits an aortic pressure pulse shaped waveform with a rapid decrease of impedance at the onset of mechanical ventricular systole and a slower return to baseline during diastole. If one ascribes this observed change to a blood volume change within segments of the thorax, then that volume must be increasing during systole to account for the decrease in total thoracic impedance. The results of this study indicated that increasing the blood volume of any of the heart chambers or aortic segments tested produced a decrease in thoracic impedance.

The contribution to the origin of ΔZ by the volume change of any one of the tested segments can be examined only with respect to its temporal volume relationship to the cardiac cycle. Since the ventricles decrease volume during systole their volume change contribution to ΔZ can only be a cancellation effect on some other origin which individually would produce a ΔZ greater in magnitude than that observed on the thorax.

Examination of the data from right atrial infusion suggest that this volume change may be a contributor to ΔZ but cardiac dynamics must again be considered. The increase in volume of the atria during early ventricular systole is small and slow, while the systolic rise of the ΔZ waveform is rapid and generally reaches its peak height by mid-systole. We thus conclude that the contribution of the atrial volume change to the systolic ΔZ waveform is small if not negligible.

Earlier studies by this laboratory (1967 report to the NASA) suggested that the volume change of the ascending aorta may be a significant contributor to the observed thoracic ΔZ. The results of the current study indicate that volume changes over the control pressure pulse range produce an impedance change of approximately 12% of the control value. Although 10 to 15 cc volume changes in ascending aorta volume resulted in impedance changes equivalent to the control value, this magnitude of volume change probably does not occur in the aorta in the alive dog. Ling and Atabek[1] have reported that the aortic

[1]Ling, S.C. and H.B. Atabek, Measurement of Aortic Blood Flow in Dogs by the Hot-Film Technique. Proc. of An. Conf. on Eng. in Med. & Biol. 1966. San Francisco, Cal., Vol. 8

arch stores 25% or more of the stroke volume during the first quarter of the cardiac cycle. If we assume an average stroke volume of 15 cc for the anesthetized dog and add 25% of 15 cc or 3.75 cc to the ascending aorta volume coincident with control diastolic pressure, the change in impedance can be determined from the infusion curves similar to Figures 16-18. In Figure 16, 14.4 cc is coincident with the diastolic pressure of 125 mmHg and a ΔZ of .104Ω. At 18.15 cc (14.4+3.75) the ΔZ value is .120Ω). The .016Ω difference is 13.3% of the control ΔZ. Similar calculations for each aortic infusion run results in an average percent of control impedance change of 14.9%, 16.1% and 22.6% for experiments 5, 6 and 21 respectively. These values compare with 17%, 8.1% and 11.6% (Table VI), when diastolic to systolic pressure values were used as limits rather than increased volume of 3.75 cc. For the above calculations with 3.75 cc volume increase, the resulting change in impedance and volume occurred within (125 to 160 mm Hg) the range of diastolic to systolic pressure limits (125 to 163 mmHg) in experiment 5, but was outside the limits in experiments 6 and 21. This suggests that the control stroke volumes for experiments 6 and 21 may have been less than 15 cc and the calculation should have used a volume increase of less than 3.75 cc.

The results of infusing the aorta in these experiments suggest that aortic volume changes are not the major origin of ΔZ. It might then be argued that the systolic blood volume change of the pulmonary circulation provides the major contribution to the formation of ΔZ. However, additional experiments

(Section III) on instrumented dogs exhibiting left ventricular mechanical alternans tend to discount this hypothesis. In the absence of left ventricular ejection, but with normal right heart ejection, the systolic ΔZ waveform is very small or vanishes; thus suggesting a left-sided origin of ΔZ. Previous studies (1967 Final Report), eliminated thoracic wall circulation as an origin site. Temporal relationships between ΔZ and flow and pressure waveforms indicate that the origin is associated with a change occurring shortly after the aortic valves open.

The results of the infusion experiments described in this section indicate that the volume change of the ascending aorta, upper thoracic descending aorta, or any of the heart chambers do not by themselves provide the major contribution to the externally observed ΔZ waveform.

Figures 16, 17, 18. Thoracic impedance change resulting from stepwise increased blood volume in isolated segments. The numbers adjacent to data points indicate segment blood pressure at each infusion step. Preeuthanization control measurements are tabulated in the upper left of the graph.

RA = right atrium
Asc. A_o = ascending aorta
Desc. A_o = descending aorta
LV = left ventricle
RV = right ventricle

Dog No. 5

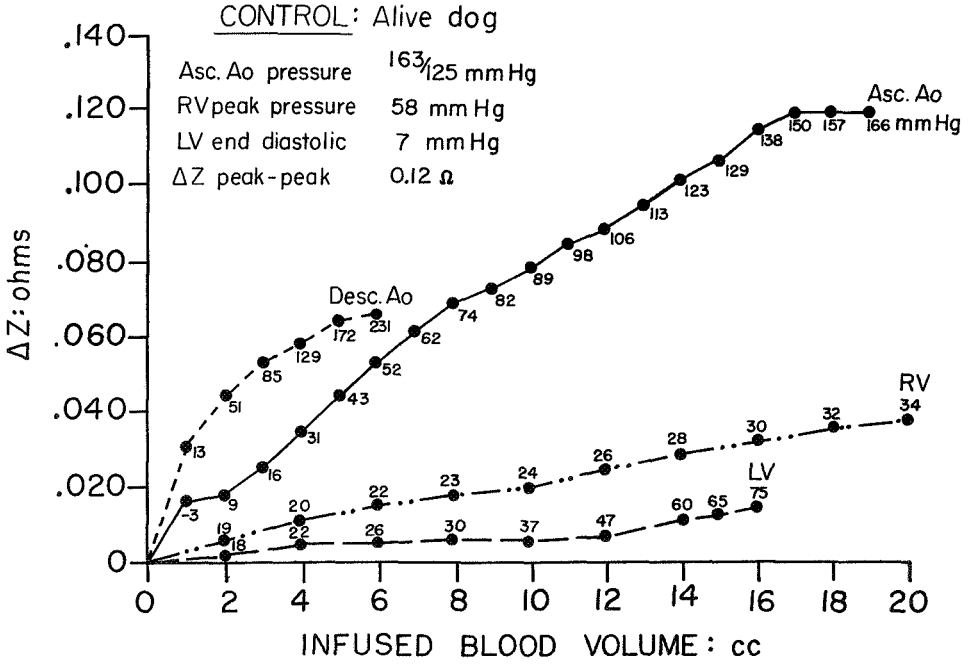

Fig. 16

Dog No. 6

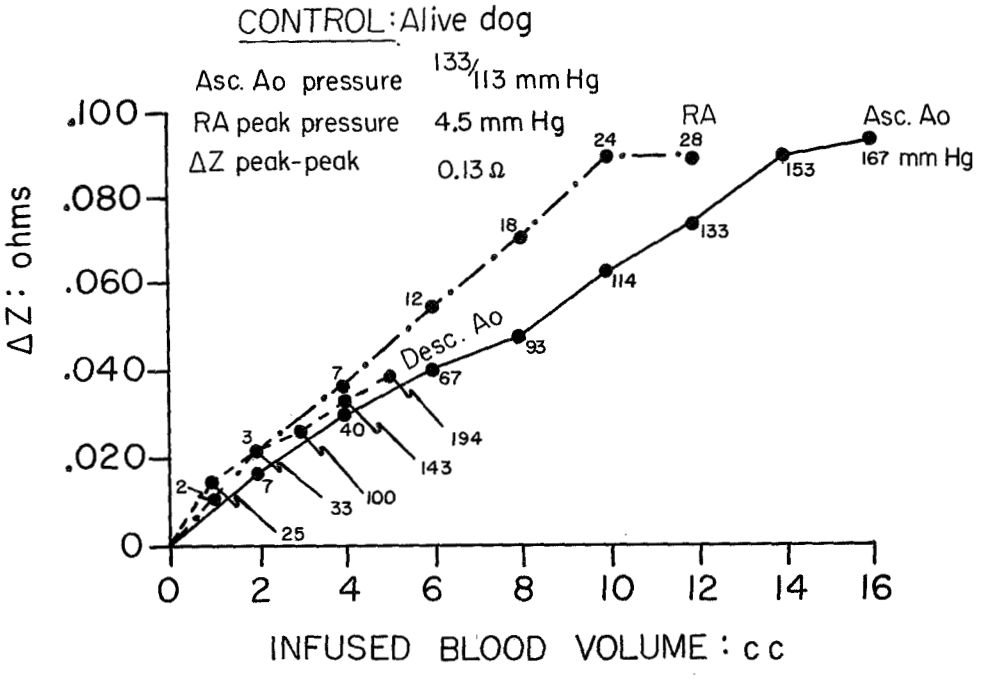

Fig. 17

Dog No. 21

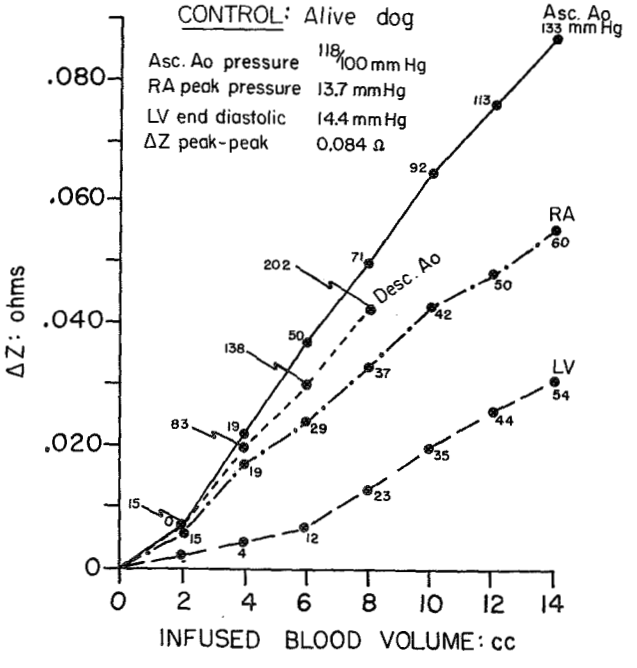

Fig. 18

Part V, Section II. A Study of Thoracic Impedance Changes as a Function of Volume Changes in the Aorta or the Pulmonary Vascular System.

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Introduction

In order to further study the physiological origin of ΔZ, an experiment was designed that used a pulsatile pump to inject equal volumes of blood into first the aorta, or second the pulmonary artery of a freshly euthanized dog. The aorta was tied off at a level near the diaphragm and close to the aortic valve. Also, all the branches of the aorta were tied off except the carotid arteries which were used to monitor pressure and to infuse or withdraw blood.

The pulmonary vascular system was prepared by cannulating the main pulmonary artery and left atrium. The blood was pumped into the pulmonary artery and drained from the left atrium into a reservoir which was returned to the pump or was connected directly back to the pump input.

The purpose of the experiment was to (1) determine if different rates of blood infusion would vary the amplitude of ΔZ, (2) determine if a localized volume change such as would occur in the aorta during ventricular ejection would produce a different ΔZ than would a similar but diffuse volume change as would occur in the lungs, (3) and determine a relationship between blood storage in the lungs and electrical impedance change.

Various investigators have reported that blood flowing in a fixed volume container will show a decrease in electrical

impedance, measured in the axial direction, with increasing flow. This suggested that it could be a possible contributing factor to the decrease in thoracic impedance that is seen during systole. Therefore, by varying the pump rates, this effect could be investigated to determine its effect on thoracic impedance change.

In theorizing about the impedance change caused by the ejection of blood from either the right or left ventricle, it is important to determine if equal blood volumes ejected into a relatively confined region such as the aorta will produce the same impedance change as a more diffuse volume change such as that ejected by the right ventricle into the lung.

As the rate of the pump infusing the pulmonary system was increased (therefore increasing the mean flow rate), there was a net increased storage of blood in the lungs in the experiment in which a reservoir was used. This increased volume of blood stored in the lungs was drawn from the pump system reservoir. By calibrating this reservoir, a relationship between impedance change and mean lung blood volume change was determined.

Methods

Mongrel dogs weighing at least 20 kg were used in the experiment. Each dog was anesthetized with sodium pentobarbital (Nembutal) at the rate of 30 mg/kg. Control records of ΔZ, aorta pressure and pulmonary artery pressure were recorded from each dog before the animal was sacrificed. Following a thoracotomy, all of the branches from the aorta were tied off

except the carotid arteries. One carotid artery was cannulated in order to infuse and withdraw blood, and the other carotid artery was catheterized in order to measure aortic pressures.

The pulmonary artery and left atrium were cannulated in order to infuse and withdraw blood from the lung. A catheter was also placed in the pulmonary artery to measure pressure.

A Harvard Apparatus pulsatile blood pump, model 1403, was used to individually pump the aorta or the pulmonary vascular system. For the aortic infusion, the pump was modified to infuse and withdraw from the same port by removing the output ball valve and sealing the input port thus providing a means to cycle the volume of blood in the aorta at various rates.

To infuse the pulmonary system, the pump was used in its standard configuration with valves to provide unidirectional pulsed flow. The output of the pump was connected to the pulmonary artery. The input of the pump was connected to a reservoir which was fed by the blood draining from the left atrium or was directly connected to the left atrium.

In all the experiments a constant stroke volume of 15 cc was used to infuse either the aorta or pulmonary vascular system through the pulmonary artery.

A total of three successful experiments were performed.

Results

Table VI shows the results of the control measurements. Control measurements of ΔZ, aortic and pulmonary pressures were made on all dogs prior to euthanization, except on dog 11 where only aortic pressure was recorded because of technical problems.

Figures 19 and 20 show the results of cycling the aorta with 15 cc of blood at a rate of from 10 to 50 cycles/min for dogs 9 and 11 respectively. Both graphs show very little change in ΔZ with changing pumping rates. With dog 8, a more flexible tube was used to connect the pump to the aorta which allowed some of the pulsatile blood volume from the pump to be stored in the tube. As the pump rate increased, this storage increased; therefore causing less blood to be delivered to the aorta.

Figure 21 shows a graph of aortic pulse pressure versus ΔZ. If it is assumed that pulse pressure amplitude linearly reflects pulse volume change, then the graph can be interpreted as showing a relationship between aortic volume change and impedance change.

Figure 22 shows the results of perfusing the lung with 15 cc pulses at rates from 10 to 50 strokes/min. In this dog the cannula from the left atrium was directly connected to the pump return. Therefore there was no change in the blood volume stored in the lungs. Figure 23 shows the same experiment on another dog with a reservoir on the venous return. An increase in mean pressure with flow rate was seen under these conditions.

Both figures however show ΔZ to be relatively independent of flow rate.

Figure 24 shows a relationship between Z_o and the blood level change in the reservoir on the venous side of the pump. This reflects the increase in pulmonary stored blood volume with increasing blood flow through the lung.

In order to relate the volume induced impedance changes to the impedance change that occur normally during the cardiac cycle, it has been assumed that pulse pressure changes reflect volume pulse changes. The corrections were made as follows:

$$\Delta Z'_{PA} = \frac{\Delta P_{cont\ PA}\ \Delta Z_{PA}}{\Delta P_{exp\ PA}}$$

$$\Delta Z'_{A_o} = \frac{\Delta P_{cont\ A_o}\ \Delta Z_{A_o}}{\Delta P_{exp\ A_o}}$$

where

ΔZ_{PA} = measured impedance change occurring during the pumping of the pulmonary system

$\Delta Z'_{PA}$ = corrected impedance change as indicated by the above relationship

ΔZ_{A_o} = measured impedance change occurring during the pumping of the aorta

$\Delta Z'_{A_o}$ = corrected impedance change as indicated by the above relationship

$\Delta P_{exp\ A_o}$ = the aortic pulse pressure measured during mechanical pumping

$\Delta P_{cont\ A_o}$ = the control aortic pulse pressure

$\Delta P_{exp\ PA}$ = the pulmonary pulse pressure measured during mechanical pumping

$\Delta P_{cont\ PA}$ = the control pulmonary pulse pressure

The results of evaluating the above equations are indicated in Table VII. The column on the far right in the table indicates the percent change the aortic volume change contributes to the sum of changes caused by the aorta and pulmonary system. It

applies only to a condition when the aorta and pulmonary system are mechanically pumped (i.e., it does not necessarily apply if the ventricles and atria are pumping).

Discussion

Figures 19 and 20 show that the impedance change, ΔZ, in the aorta is independent of pump rate or flow rate of blood. Also, Figures 20 and 22 show that the same is true for the pulmonary system. From these experiments it appears that flow induced impedance changes have little if any effect on the impedance changes recorded from the thorax with our electrode configuration.

Comparing Figures 19 and 23 for Dog 9, it can be seen that 15 cc injected into either the aorta or pulmonary artery produce about the same impedance change.

Comparing the impedance change for equal volume injections into the aorta or pulmonary system for Dog 8, Figure 21, is more difficult because of the elastic tubing used to connect to the aorta. If it is assumed that for low pump rates, little pulsatile blood volume is stored in the tubing, then a valid comparison can be made. Referring to Figure 21, it can be seen that for pump rates of 10 strokes/min pulses into the aorta, a typical impedance change was .14 ohms. Figure 22 shows an impedance change of .12 ohms for the same pumping rate for the pulmonary system, which for purposes of determining the origin of the normal cardiac impedance change indicates each region has about the same effect. It therefore appears that a diffuse volume change as occurs in the lungs has the same effect as an equal volume change occurring in the aorta.

In order to estimate the effects the aorta and pulmonary system contribute to the impedance change as seen in the living dog, Table VII was developed. The 15 cc injected into the pulmonary artery caused about the same pressure change as was seen during the control measurements, but in the aorta the pressure changes were about five times larger than the control measurements. This probably was due in part to a decrease in compliance of the aorta following death of the dog.

Table VII assumed a linear relationship between pulse pressure amplitude and pulse volume change. Therefore each impedance change recorded under the experimental conditions was corrected by the ratio of the control pulse pressure to the pump induced pulse pressure. The column on the right indicates that under these conditions the aorta contributes less to the impedance change than the pulmonary system. Changes in compliance of the aorta following death of the animal may have altered these data somewhat.

Figure 24 shows the relationship between Z_o, the thoracic impedance and pulmonary blood volume. This curve indicates that Z_o could be used as a monitor of pulmonary fluid volume changes.

TABLE VI

Control Observations on the Living Dog

Dog	ΔZ ohms	-- Aortic Pressure --- Systolic mmHg	Diastolic mmHg	Pulse mmHg	-- Pulmonary Artery -- Systolic mmHg	Diastolic mmHg	Pulse mmHg
8	.12	150	111	39	18	6	12
9	.21	149	117	32	22	2.5	19.5
11	.05	125	106	19	--	---	---

TABLE VII

Calculated Results from the Data Obtained on the Euthanized Dog

Dog	Control ΔZ	Corrected $\Delta Z'_{PA}$	Corrected $\Delta Z'_{A_o}$	Corrected $\Delta Z'_{tot} = \Delta Z'_{A_o} + \Delta Z'_{PA}$	$\frac{\%\Delta Z'_{A_o}}{\Delta Z_{tot}}$
8	.12	.105	.04	.145	27.5%
9	.21	.120	.014	.134	11.6%
11	.05	--	.015	--	--

Figures 19, 20, 21, 22, 23, and 24 illustrate these results in graphic form. The charts and their legends are self-explanatory.

For Figures 19, 20 and 21, the term "pulsing rate" was used to indicate that all of the blood volume forced into the aorta by the pump, returned to the pump during the intake part of its cycle since there was no valve in the output line of the pump and the customary intake part of the pump was permanently closed. Thus the pump simply "pulsed" blood back and forth into and out of the aorta.

For Figures 22 and 23, the term "pumping rate" was used since in the experiments on the pulmonary vascular system the pump actually pumped blood through the pulmonary artery and the lungs. The blood flowing through the lungs was collected in the left atrium and returned to the intake side of the pump which in this case had the usual one way valves in the intake and output lines.

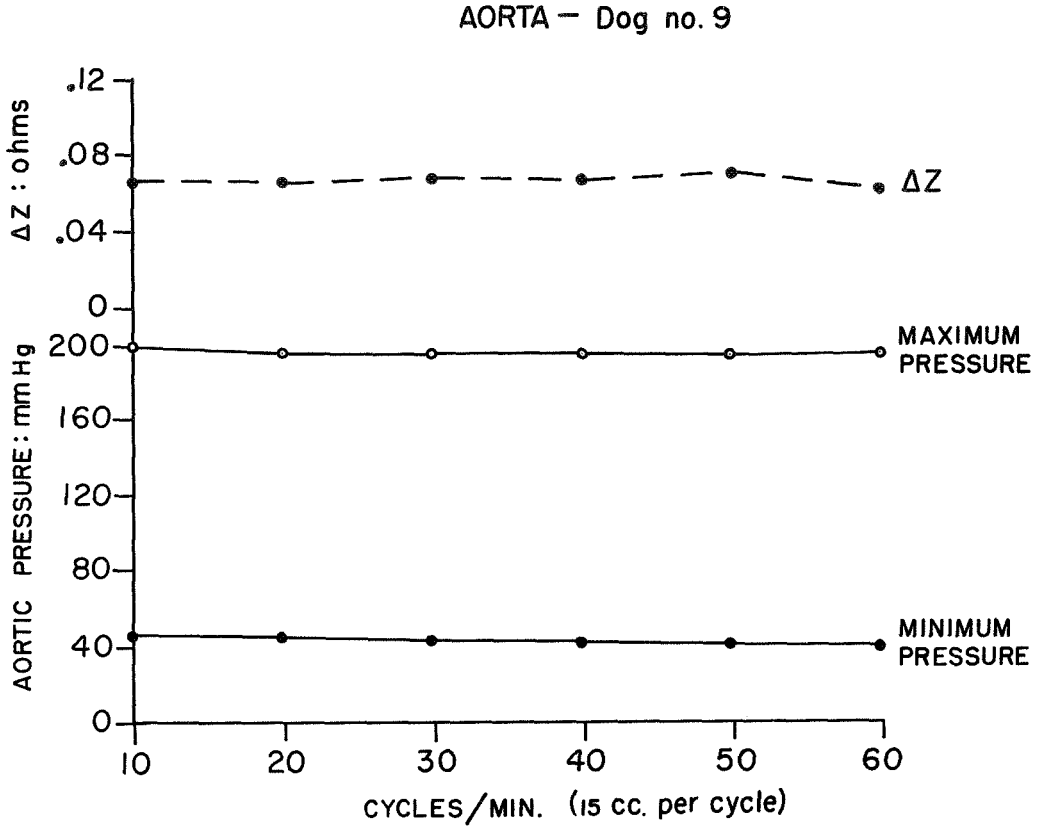

Fig. 19 Aortic pressure and ΔZ vs pulsing rate for Dog 9

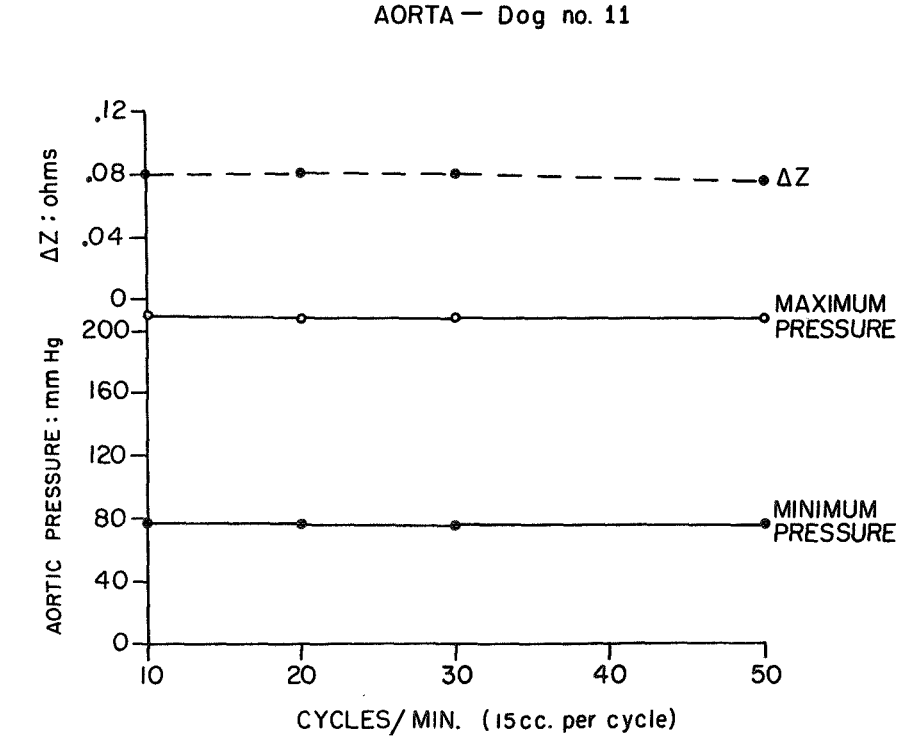

Fig. 20 Aortic pressure and ΔZ vs pulsing rate for Dog 11

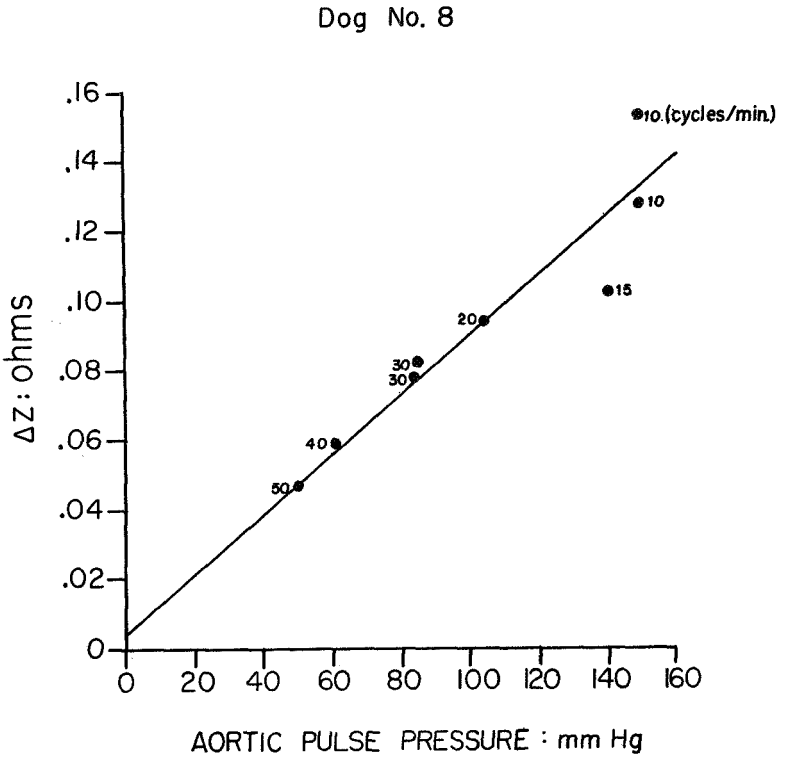

Fig. 21 Aortic pulse pressure vs ΔZ at various aortic pulsing rates

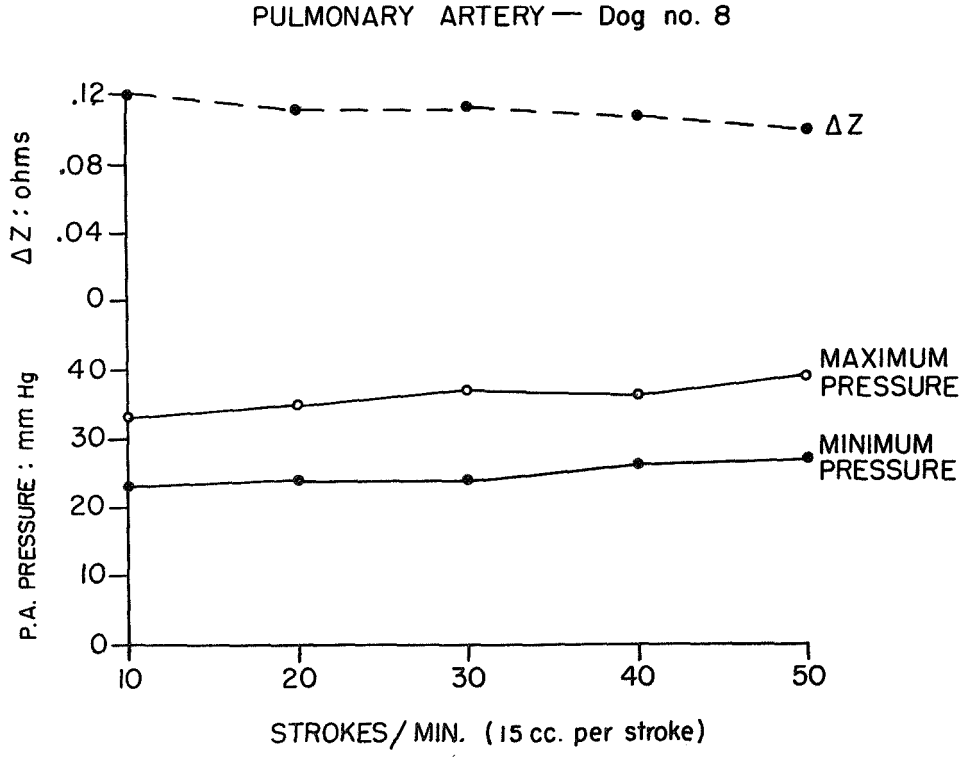

Fig. 22 Pulmonary artery pressure and ΔZ vs pumping rate, without pulmonary venous reservoir for Dog 8

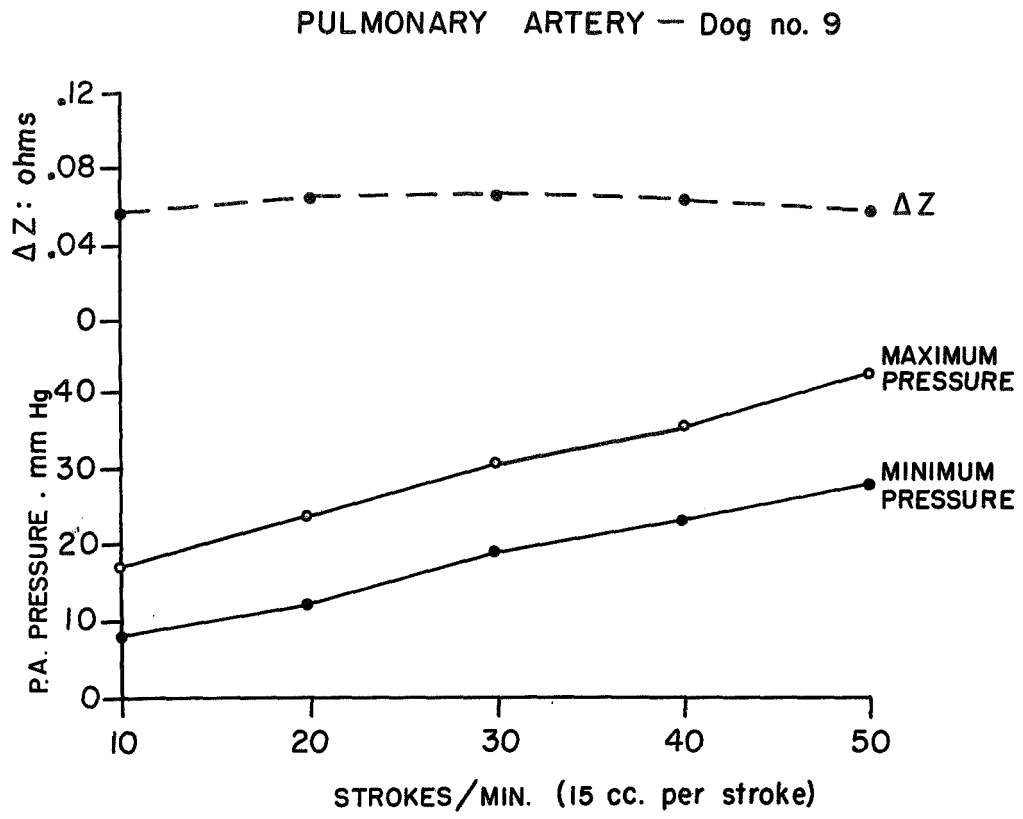

Fig. 23 Pulmonary artery pressure and ΔZ vs pumping rate, with pulmonary venous reservoir for Dog 9

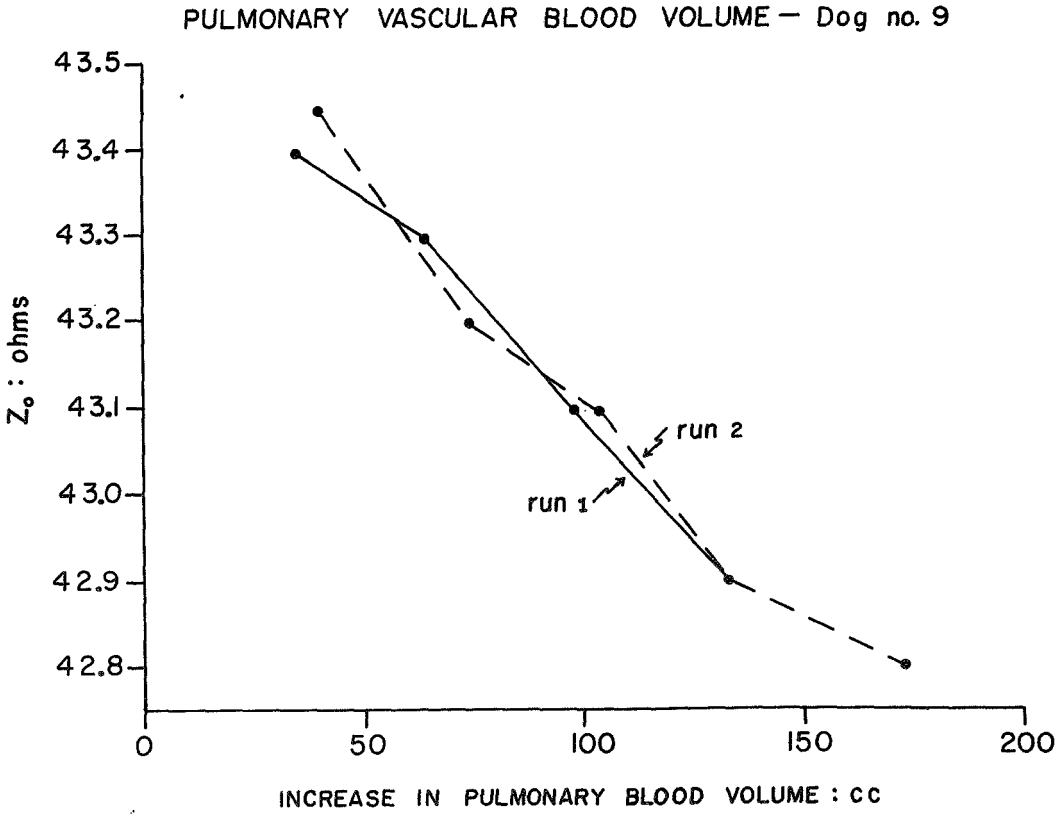

Fig. 24 Z_o vs pulmonary vascular system blood volume change for two experimental runs

Part V, Section III

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Introduction

The experiments described in Sections I and II of this report examined the role of blood volume changes of individual components of the thoracic cardiovascular system in formation of the externally observed ΔZ by isolating and modifying these volumes in the dead dog. Previous data presented to the NASA had suggested a left-sided origin of the systolic decrease in thoracic impedance (1967 Final Report). Therefore the purpose of the studies described in this section was to individually modify the function of the left ventricle and left atrium of the alive dog to assess the contribution of the left atrium and the left-sided thoracic circulation to the formation of ΔZ. The modification of the left-sided chambers was achieved by inducing left ventricular mechanical alternans and controlled fibrillation of the left atrium by electrical stimulation.

Methods

Mongrel dogs were anesthetized with sodium pentobarbitol (25 mg/kg), intubated and placed on a positive pressure respirator. A left thoracotomy was performed and electromagnetic flow transducers were placed around the main pulmonary artery and the ascending aorta. Catheters were positioned in the right and left atria, right and left ventricle, ascending aorta

and main pulmonary artery. Electrodes were then sewn into the right atrial appendage for stimulation of the atria and suitable insulating material was placed around the electrodes such that there was no escape of current to the ventricles. An additional electrode was sewn into the left atrial appendage for monitoring of the left atrial electrocardiogram. The thoracotomy was then closed and air evacuated by continuous suction. The four electrode bands for impedance measurements were placed on the neck and lower thorax in the standard positions. Control measurements were then made during which the aortic and pulmonary flow signals, impedance signals, electrocardiographic signals and two of the six pressures were recorded. Three control measurements were necessary in order to obtain the control pressure conditions from the six sites.

Using a Grass stimulator, atrial fibrillation was produced by stimulating the right atrium with an appropriate series of pulses. Since the atria of the dog spontaneously defibrillates in a few minutes after removal of such stimuli, it was possible to produce the state of fibrillation at will. During the period when the animal was in atrial fibrillation pressure measurements along with flow and impedance recording measurements were recorded. Again a series of measurements were required to obtain the pressure tracings from all six sites.

To provide dissociation of ventricular function in which the left ventricle exhibited a mechanical alternans and the right ventricle exhibited a relatively stable pattern of

ejections, 3 mg of methoxamine and 5 cc isotonic saline were mixed and administered to the dog in single doses. A complete left ventricular mechanical alternans usually resulted from this injection and disappeared after a few minutes allowing the control condition to be recorded before each additional infusion. A sequence of records were taken with mechanical alternans condition to provide adequate pressure data.

Results

Typical examples of the effect on ΔZ of eliminating atrial function by inducing atrial fibrillation are shown in Figures 25, 26 and 27. The analysis of these records and those resulting from inducing mechanical alternans involve a comparison of temporal relationships between the waveforms. The tracings are therefore presented in such a manner as to emphasize the time varying components of the signals.

The left hand panel of Figure 25 describes the control measurement preceding the onset of atrial fibrillation, while the right hand panel shows the effects of atrial fibrillation. Figure 26 is a second example of atrial fibrillation from the same experiment represented by Figure 25.

The two panels shown in Figure 27 are taken from a continuous recording of atrial fibrillation during which the animal spontaneously converted back to a normal sinus rhythm. Onset of atrial systole is defined by the sharp p wave spike in the right hand panel ECG. This waveform was achieved by connecting a wire that had been sewn into the left atrium to

one of the active electrodes of the externally monitored ECG, thus resulting in a "summed" ECG signal.

Previously reported data (1967 Report) described the occasional occurence of left ventricular mechanical alternans. These data were presented as supporting evidence for a left-sided ΔZ origin. In the current study we were able to repeatedly induce complete left-sided mechanical alternans as seen in Figures 28 through 31. These figures show a variety of ΔZ waveforms resulting from the left ventricular alternans but the condition in most dogs is best typified by the waveforms of Figures 28 and 29. The ΔZ waveform shown in Figure 31 occurred in only one of 10 or more dogs in which we have observed left-sided mechanical alternans.

Discussion

Examination of the control waveform in Figure 25 and sinus rhythm waveforms in Figure 26 suggest that the atrial contribution to the ΔZ waveform may be a pre-ventricular systole deflection characterized by a small decrease and then equivalent increase in impedance prior to the onset of the large decrease in impedance with ventricular systole (impedance decreasing upwards). If this deflection was an atrial contribution to ΔZ, one would expect that this deflection would disappear during atrial fibrillation since regular pulsatile atrial volume changes had ceased. This, in fact, was not the case as examination of the right hand panel of Figure 25 and the left hand panel of Figure 26 reveals. It appears that a large decrease in

impedance occurs at mid to end of ventricular diastole. It should also be noted that the small positive going impedance change (downward deflection) occurring just prior to pre-ventricular systole, which has been referred to by Karnegis as the A-Wave contribution of the atrium, does not disappear during atrial fibrillation but remains at about the same or slightly larger magnitude. It may then be suggested that pulsatile atrial volume changes that occur under normal conditions tend to cancel the impedance change occurring between mid and end diastole that are due to an unknown origin.

Unfortunately, similar reasoning cannot be applied to Figure 27. There is no sharp positive going impedance change prior to ventricular systole which could be attributed to the atrium but rather a small, slow decrease in impedance which occurs in the sinus rhythm case and also continues to have about the same shape during atrial fibrillation. If conclusions can be drawn about the effect of the atrium on the ΔZ waveforms, we could say at most that it must be a cancellation effect on another source or origin point which alone produces a decrease in impedance during mid to end diastole. As evident in Figure 27, this conclusion cannot be adhered to rigorously.

ΔZ waveforms presented in Figures 28, 29 and 30 during conditions of left ventricular mechanical alternans tend to support a hypothesis proposed in our 1967 Final Report that a major contribution to the systolic decrease of an impedance must be of a left-sided origin. If the results of our alternans

experiments had in general shown the waveform, seen in Figure 31, one could easily hypothesize that 50% of the ΔZ waveform is contributed by the right and 50% by the left-sided output of the heart. It must be remembered though that this observation has only been seen in one of ten or more dogs exhibiting left ventricular mechanical alternans. It is unclear why the majority of dogs should not exhibit a pronounced decrease in ΔZ with the onset of right heart output in the absence of left ventricular output, thus complementing the results of the infusion studies described in Sections I and II.

Although one would like to ascribe the impedance waveform to single origin site these data presented in this section and the data described in the previous sections tend to suggest that the ΔZ waveform is a combination of many origins and that at this time we cannot satisfactorily isolate one particular event, or one particular volume change as a major contributing factor. The impedance waveforms from dogs with alternans would suggest that a large component of the impedance change during systole is of a left-sided origin. The pump experiment described in Section II suggest the equal contribution from aortic volume changes and pulmonary blood volume changes and the static infusion experiments in Section I suggest that all volume changes have about equal sensitivity. Based upon these results we must conclude that one discrete event is not responsible for the observed changes in ΔZ occurring during the cardiac cycle.

A rather complex combination of simultaneous events occurring under highly dynamic conditions produce the resultant ΔZ. Further investigation will be necessary to completely identify all of these parameters in their proper time and rate related functions.

For Figures 25 - 31 the following notations were used:

QPA = Pulmonary artery blood flow rate

QA_o = Aortic blood flow rate

PLA = Pressure, left atrium

PLV = Pressure, left ventricle

PPA = Pressure, pulmonary artery

PA_o = Pressure, aorta

PRA = Pressure, right atrium

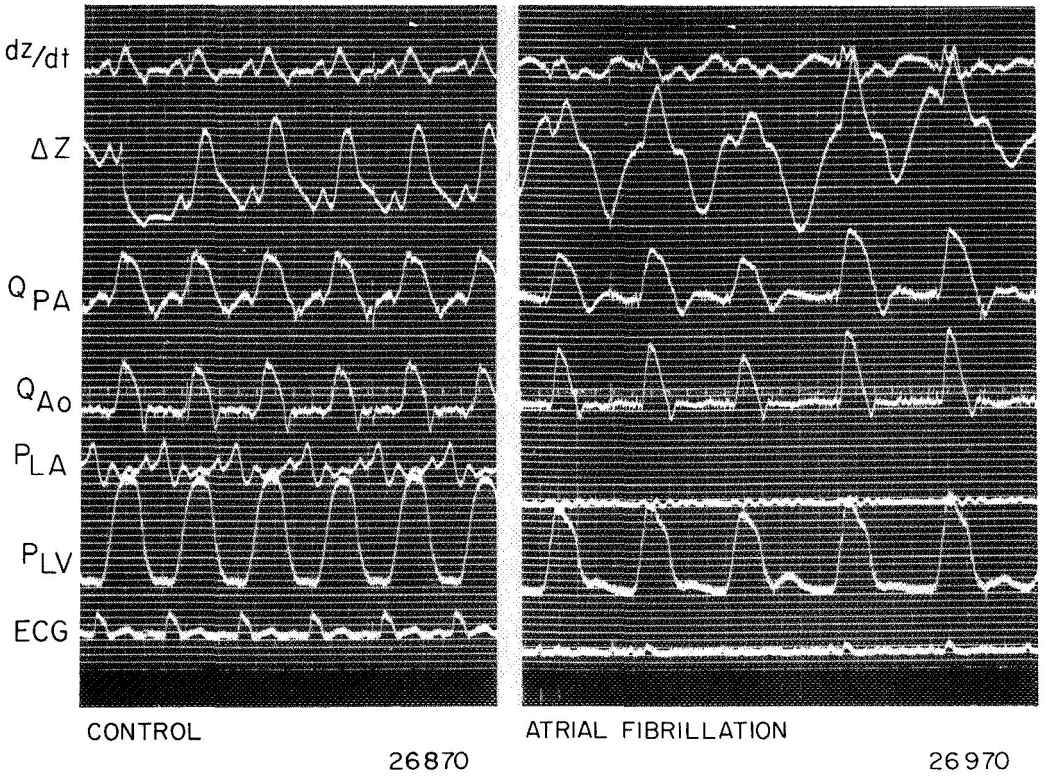

Fig. 25 Atrial Fibrillation

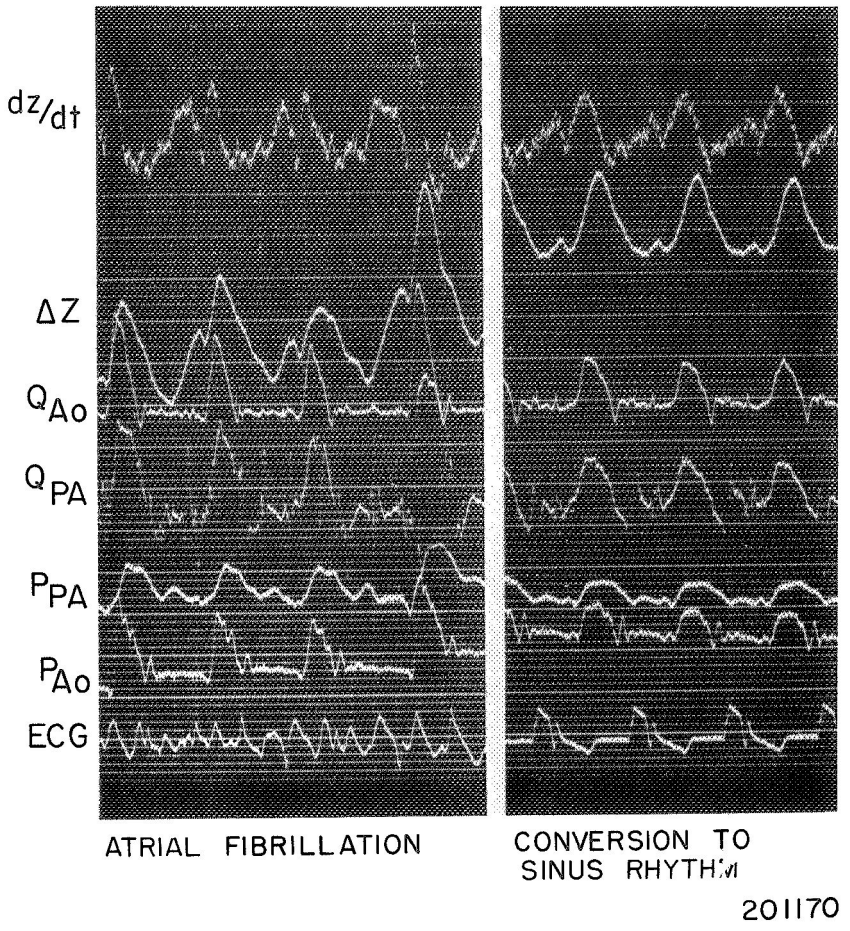

Fig. 26 Atrial Fibrillation

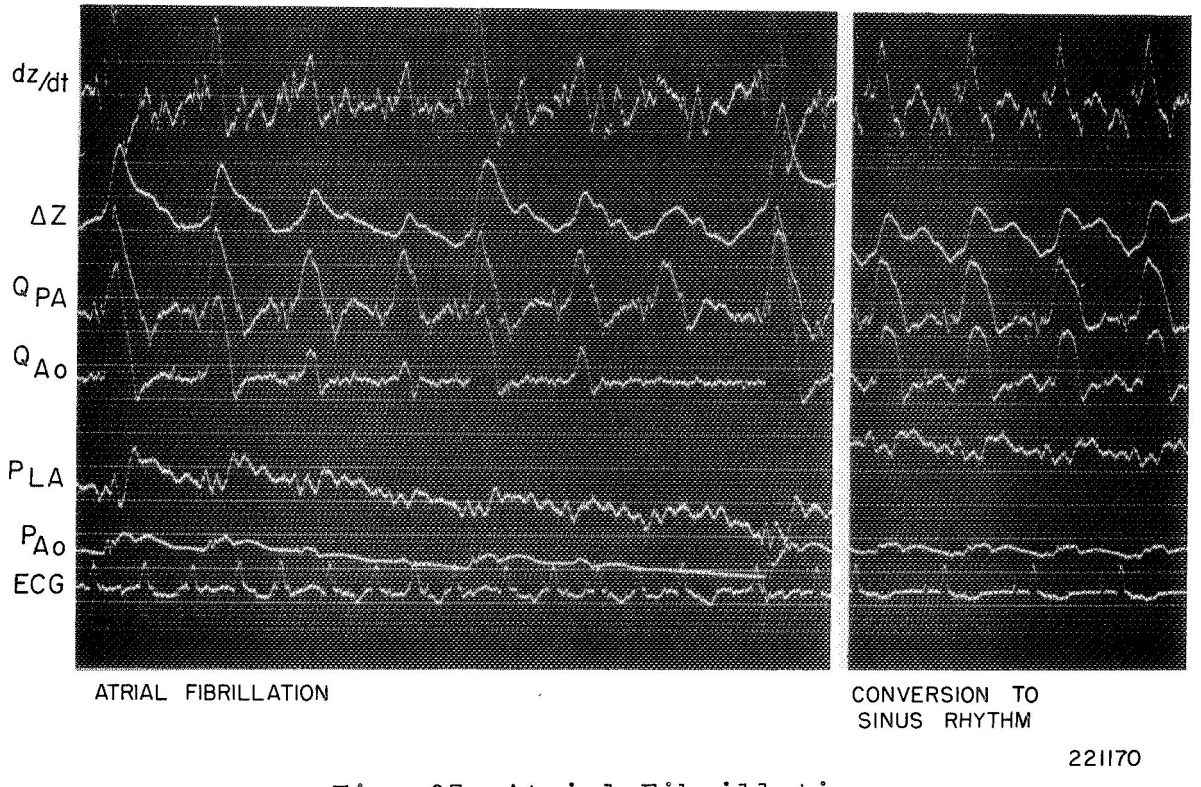

Fig. 27 Atrial Fibrillation

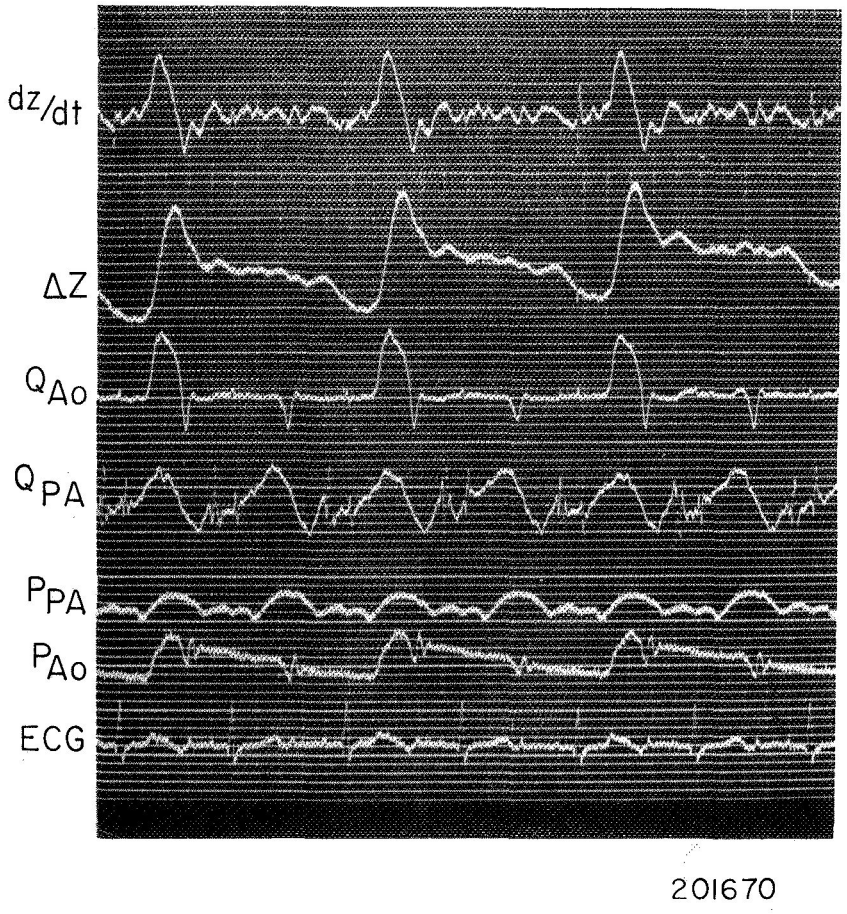

Fig. 28 Left Ventricular Mechanical Alternans

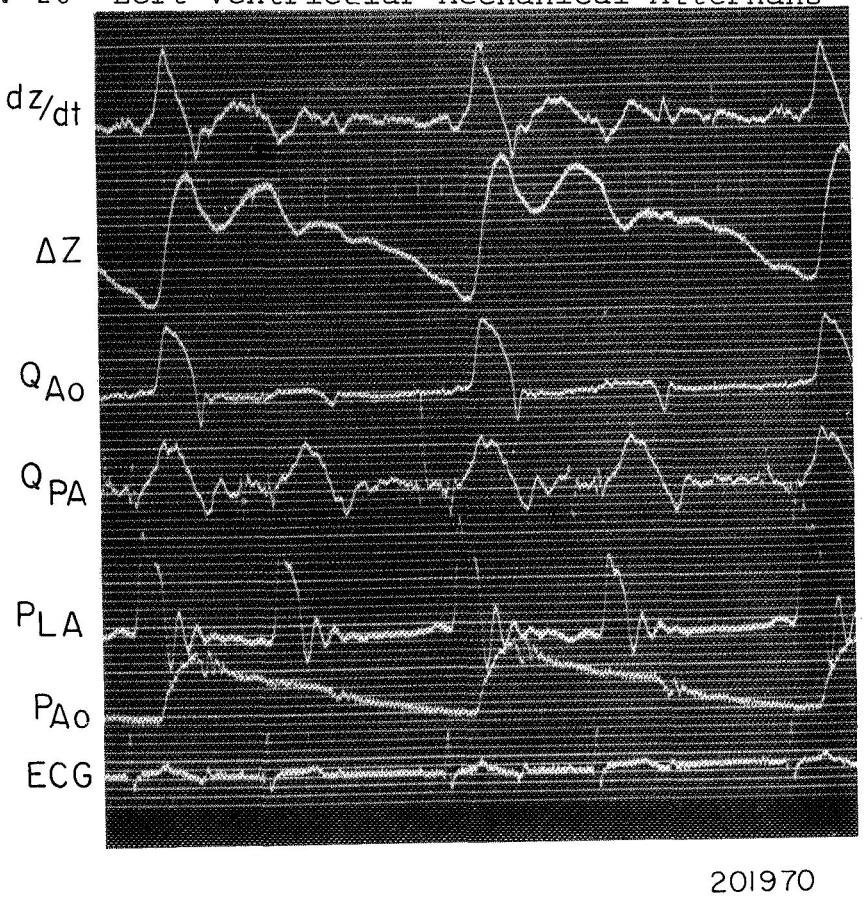

Fig. 29 Left Ventricular Mechanical Alternans

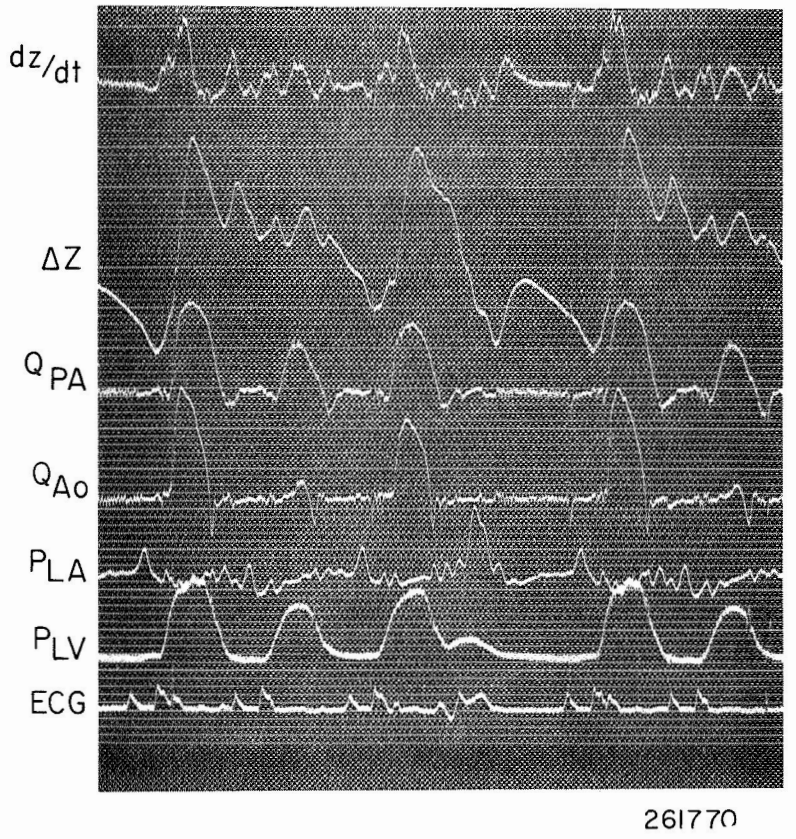

Fig. 30 Left Ventricular Mechanical Alternans

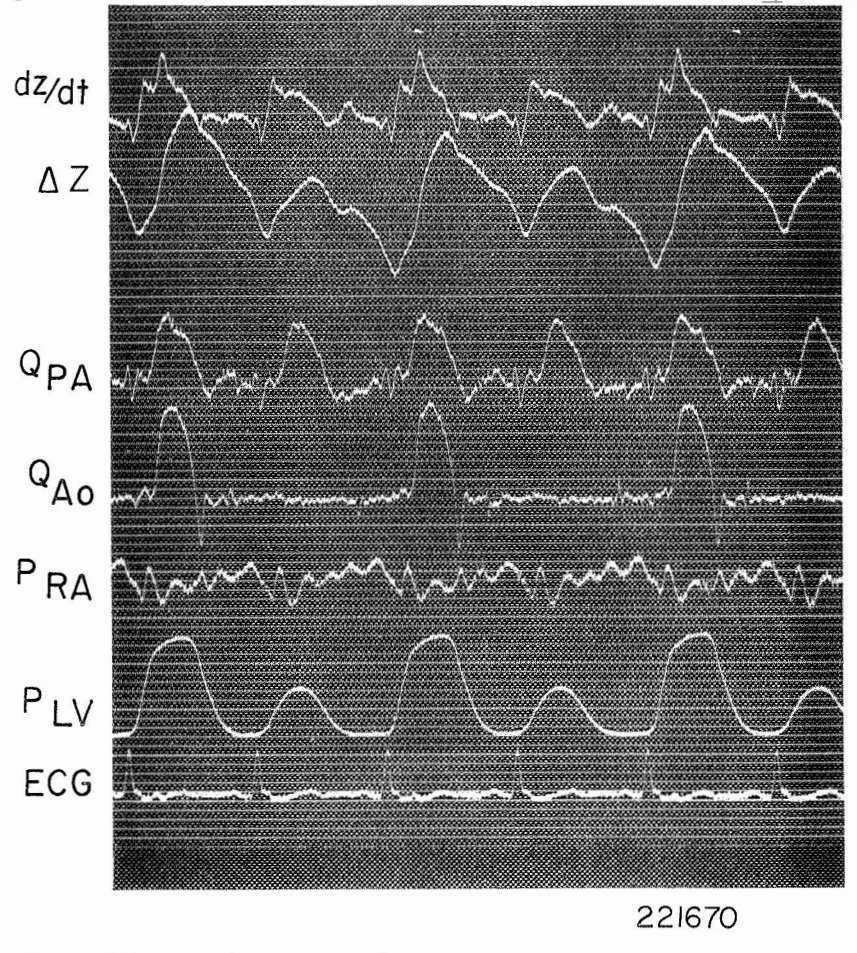

Fig. 31 Left Ventricular Mechanical Alternans