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THE DETECTION OF PULMONARY EDEMA BY MEANS OF ELECTRICAL IMPEDAN--ETC(U)
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# THE DETECTION OF PULMONARY EDEMA BY MEANS OF ELECTRICAL IMPEDANCE

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Running head: Detection of pulmonary edema by impedance

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Oct 1975

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In conducting the research described in this report, the investigators adhered to the 'Guide for Laboratory Animal Facilities and Care', as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council.

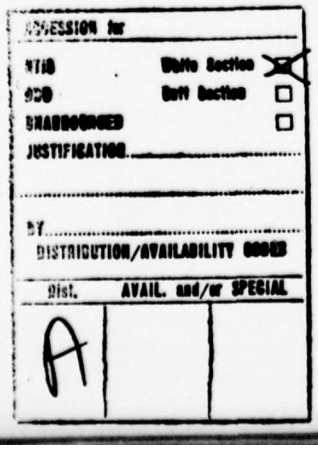
## ABSTRACT

The detection, localization, and quantification of pulmonary edema by electrical impedance were investigated using band, circumferential, and longitudinal electrode arrays in a series of four studies utilizing 35 dogs. Pulmonary edema was induced with alloxan, sucrose, and saline lavage. The ability of the various electrode arrays to distinguish between pulmonary edema and pleural effusion was also investigated. The largest absolute changes in impedance were detected by the band electrodes, although larger percent changes in impedance were measured using the circumferential arrays. The circumferential arrays indicated the possibility of differentiating between pleural effusion and pulmonary edema. The longitudinal array had essentially the same characteristics as the band array, although it permitted localization of either edema or effusion to one hemithorax. The impedance method provides a reliable quantitative index of pulmonary edema in carefully controlled experiments in dogs.



## INDEXING TERMS

Electrical impedance
Pulmonary edema
Noninvasive technique
Electrode arrays

# THE DETECTION OF PULMONARY EDEMA BY MEANS OF ELECTRICAL IMPEDANCE

Joseph C. Denniston and Lee E. Baker

The frequent development of pulmonary insufficiency following stress such as hemorrhage, burns, surgery, traumatic injury, left ventricular failure, sepsis, and shock has been long recognized by clinicians (1,4,13,18,20,24). Whatever the cause, the end result is inadequate alveolar ventilation and increased demands on the heart to maintain adequate tissue oxygenation. The seriousness of this situation is emphasized by the estimate that from 30 to 50% of adult patient deaths occurring during intensive care management are pulmonary related (18). Early deaths in combat casualties following operative resuscitation are associated almost always with pulmonary edema, congestion, and hemorrhage (24). The importance of recognizing progressive pulmonary insufficiency caused by clinically inapparent interstitial pulmonary edema has been emphasized (9). Intrathoracic fluid accumulations of any type can represent life-threatening situations.

Clinical detection of intrapulmonary fluid accumulations is based on radiography, blood gas analysis, auscultation, altered pulmonary mechanics, and by changes in arterial, central venous, and pulmonary wedge pressures. Since the values obtained from these diagnostic methods frequently remain normal until irreversible pulmonary insufficiency or cardiac failure occurs, interest has been renewed in recent years in developing a sensitive method for detecting and quantitating thoracic fluid accumulations. Indicator dilution measurements of pulmonary extravascular fluid have been used clinically with success (15,17,19,27).

Although this method appears to provide a relatively sensitive index of developing pulmonary edema, it has several clinically undesirable features: it is invasive, requires large volumes of blood, and is technically difficult. More recently, the electrical impedance method of measuring physiological data has shown promise of providing a simple, noninvasive, harmless, and painless means of detecting, quantitating, and monitoring thoracic fluid shifts (16,21-23,27,28).

Basically, the clinician has no simple means of detecting pulmonary edema early in its clinical course. He must rely heavily on the patient's history, clinical conditions, and diagnostic indices, which frequently remain normal until irreversible pulmonary edema occurs. Thus the purpose of the present study was to determine if the thoracic impedance technique would provide a simple, noninvasive means of detecting, monitoring, localizing, and quantitating pulmonary edema.

## MATERIALS AND METHODS

Four studies utilizing 35 healthy mongrel dogs, weighing from 14 to 22 kg, were conducted. Preanesthetic medication consisted of atropine sulfate (0.02 mg/kg, im) and a solution containing 0.4 mg/ml of fentanyl and 20 mg/ml of droperidol iv (0.1 ml/kg). All animals were anesthetized with pentobarbital sodium (15-20 mg/kg, iv), and an oral endotracheal airway was established.

Succinylcholine chloride (0.1 - 0.2 mg/kg, iv) was given as

required to maintain short-term respiratory paralysis during pressure-cycled respiratory assistance.

Hair was clipped and shaved from the neck, thorax, and abdomen to provide good electrical contact for the impedance electrodes. Impedance was measured by means of a Minnesota Impedance Cardiograph (4 mA, 100 kHz). Stainless steel needle electrodes were inserted to record the lead II electrocardiogram. The right femoral vein was catheterized to facilitate intravenous injections. Blood pressure was recorded from a catheter-tip pressure transducer (Millar Mikro-Tip™) placed in the descending aorta at the level of the sixth intercostal space through a right femoral arteriotomy. Data from the records were entered into a PDP-8S computer from an analog-digital converter (Gerber Scientific Corp.) for analysis.

To assess the impedance technique for detecting, localizing, and quantitating pulmonary edema, measurements of thoracic impedance were recorded in four different experimental studies.

*Study 1. Pulmonary edema induced with alloxan*

Changes of thoracic impedance were measured using the band and circumferential spot electrode arrays, depicted in Fig. 1A and B. The electrodes were allowed to stabilize for 15 to 30 min, after which a control value of basal impedance ($Z_o$) was taken at end expiration. Alloxan (300 mg/kg) was administered (iv) in 60 ml of normal saline during a 15-min period. The thoracic impedance, arterial blood pressure, and electrocardiogram were monitored during this period and during the next 105 min, unless the animal died sooner. After death, the lungs were

examined grossly and in cut-section.

*Study 2. Pulmonary edema induced with sucrose*

Two groups of six animals were studied. In group 1, the standard Kubicek circumferential band electrode array (14) was applied (Fig. 1A), and in group 2 the longitudinal spot electrode arrays $Z_1$, $Z_2$, and $Z_3$ were used (Fig. 1C).

After the electrodes were placed, the endotracheal tube was removed, the oral-pharyngeal area was cleared of any mucus secretions, a 2% solution of Lidocaine hydrochloride was applied to the epiglottis and associated structures, and the animal was intubated with a Benfield canine bronchospirometry tube ( 3) using direct visualization with a laryngoscope. The tube was advanced to the tracheal carina. The two hemithoraces were separated by inflation of the cuffs about the left main stem and tracheal components of the bronchospirometry tube. Stability of a constant basal impedance, taken at end expiration, was determined during a 10-min baseline period. A 1260-mOsm solution (70 ml) of sucrose was instilled slowly (during 1 min) into the left lung via a catheter passed down the left main stem branch of the bronchospirometry tube. The right lung was ventilated with 100% oxygen using a pressure-cycled ventilator. Mean arterial blood pressure, ECG, hematocrit, and plasma osmolarity were monitored throughout the 60-min period of study. The osmolarity and resistivity of the alveolar fluid were determined in selected animals.

The osmolarities of the sucrose solution, the plasma, and the alveolar fluid were measured with an osmometer (Precision Systems,

Waltham, Mass.). The resistivity of the alveolar fluid was determined using a variable-length conductivity cell (11).

*Study 3. Pulmonary edema simulated by saline lavage*

The band and circumferential spot (2415, 2416, 2456) electrode arrays were applied (Fig. 1A,B), and the animals were intubated with a Benfield canine bronchospirometry tube as described above. After a 10-min baseline period, 50 ml increments of saline, from 0 to 300 ml, were infused into the left lung or into both lungs. Mean arterial pressure, ECG, and thoracic impedance were monitored during the lavage.

*Study 4. Pulmonary edema simulated by plasma lavage vs. pleural effusion*

A standard thoracic drainage tube was placed into each hemithorax through a 1-inch bilateral thoracotomy in the tenth intercostal space to permit the subsequent infusion and withdrawal of blood, saline, or plasma ($37^{o}$) from the left hemithorax. The band and 2415 electrode arrays were applied (Fig. 1A,B), and the animals were intubated with a Benfield canine bronchospirometry tube, as described previously. After a 10-min baseline period, 50 ml increments of blood, saline, or plasma, from 0 to 300 ml, were infused into the left hemithorax. After withdrawal of the last of the fluids from the left hemithorax, 300 ml of plasma in 50 ml increments were infused into the left lung.

## RESULTS

*Study 1. Pulmonary edema induced with alloxan*

Alloxan produced variable effects in the animals studied. In five animals there was no edema, and mean arterial pressure, heart rate, and thoracic impedance remained constant, despite additional bolus doses (150 mg/kg, iv) of alloxan. In the five animals that developed edema, the pattern of thoracic impedance change was variable (Fig. 2A-E). For example, thoracic impedance decreased abruptly in one animal (Fig. 2A), whereas it decreased gradually in another (Fig. 2E). Data from an animal that did not develop edema are shown in Fig. 2F.

Typically, following alloxan administration, there was an initial increase in impedance (Fig. 2A,C,D,E). Respiratory management of the animals that developed pulmonary edema was difficult because fluid and foam obstructed the tracheobronchial tree. Blood pressure was maintained in all animals until hypoxia ensued. Ventilated portions of the lungs appeared normal at necropsy. Gross edema, as seen from the surface, was limited primarily to dependent lobes, particularly the diaphragmatic lobes. Sectioning of edematous lobes produced copious amounts of clear fluid and white foam from the airways.

The 2415 spot electrode array reflected the greatest change of impedance (Fig. 2). In one animal (Fig. 2D), the 2415 spot electrode array reflected a significant change in impedance, while, in contrast, the band electrode array reflected little change in impedance. A

comparison of the mean values of the thoracic impedance change ($\Delta Z$) and mean percent change in thoracic impedance ($\Delta Z/Z_o \times 100$) measured using the band and 2415 electrode arrays associated with pulmonary edema induced by alloxan in five animals is shown in Table 1. These comparisons show that the 2415 electrode array was significantly more sensitive in detecting the developing edema than was the band electrode array, regardless of whether the data were expressed as $\Delta Z$ ($P < 0.05$) or $\Delta Z/Z_o \times 100$ ($P < 0.001$).

*Study 2. Pulmonary edema induced with sucrose*

A summary of the data from the sucrose-induced edema studies is presented in Table 2. Mean arterial blood pressure declined and heart rate increased during the study. Both hematocrit and plasma osmolarity increased. All animals developed pulmonary edema, which was limited in most cases to the left diaphragmatic lobe. Cut sections of these lobes revealed copious quantities of straw-colored fluid. The mean values of osmolarity and resistivity of the alveolar fluid in this group 60 min after the introduction of sucrose were 325.8 mOsm/l and 83.2 ohm-cm, respectively.

The semilog regression of the mean change in thoracic impedance ($\Delta Z$) vs. the time course of development of pulmonary edema for the various electrode arrays employed is shown in Fig. 3. Since the volume of isotonic saline infused into the lung or thorax is linearly related to the change of impedance, these data suggest that the net movement of fluid from the pulmonary capillary compartment to the alveolar compartment

in response to the instillation of sucrose was related exponentially to time. Localization of the unilateral pulmonary edema is evident in Fig. 3B, where, with simultaneous recording from the hemithoracic electrode arrays $Z_1$ and $Z_2$, the greater slope of $\Delta Z_2$ indicates accumulation of fluid in the left hemithorax.

A comparison of the mean changes of thoracic impedance ($\Delta Z$) measured in animals with pulmonary edema of the left lung induced by sucrose indicates that the longitudinal spot array ($Z_3$) was significantly ($P < 0.005$) more sensitive (ohms) to the total accumulation of fluid than was the band array. Additionally, the hemithoracic electrode arrays ($Z_1$ and $Z_2$) enabled significant ($P < 0.005$) localization of the fluid accumulation to the left hemithorax.

*Study 3. Pulmonary edema simulated by saline lavage*

A summary of the linear regression analysis of the data obtained from this group using all of the electrode arrays vs. volume of saline infused into the left or both lungs is presented in Table 3. These data indicate that because of differences in initial values of $Z_o$, the regression of absolute values of impedance ($Z_o$) vs. volume of saline infused into the left lung for animal groups using specific electrode arrays was not correlated significantly; however, the same data treated as a change in impedance ($\Delta Z$) or percent change in impedance ($\Delta Z/Z_o \times 100$) were correlated significantly. Although grouped data on impedance (Table 3) did not correlate well with the volume of saline infused, impedance and volume of saline infused were correlated significantly in all the

individual animals studied.

The sensitivity of the band electrode array (-1.4 ohms/100 ml) in detecting fluid infused into the left lung was greater than that of the comparable transthoracic electrode array 2415 (-0.6 ohms/100 ml). However, on the basis of a percent change, the 2415 array (5.7%/100 ml) was more sensitive than the band electrode array (3.1%/100 ml). The hemithoracic electrode arrays (2416 and 2456) permitted localization of fluid accumulation to the left hemithorax; e.g., during the infusion of saline into the left lung, recorded change in impedance with the 2416 electrode array (-0.1 ohms/100 ml) was less than that recorded with the 2456 electrode array (-0.4 ohms/100 ml). This same relationship was noted when comparing the percent change in impedance (9.1%/100 ml vs. 3.1%/100 ml for the 2456 and 2416 electrode arrays, respectively). No difference was noted in the sensitivity of the band electrodes in detecting fluid in the left lung (1.4 ohms/100 ml) or in both lungs (1.4 ohms/100 ml).

*Study 4. Pulmonary edema simulated by plasma lavage vs. pleural effusion*

The infusion of blood into the left hemithorax produced the smallest change in impedance for both band and 2415 electrode arrays. The infusion of either saline or plasma into the left hemithorax caused nearly identical changes in impedance for the specific electrode array used in recording impedance from any given animal. While the band electrode array detected no difference between plasma infused into the left lung or into the left hemithorax, the 2415 electrode array appeared more sensitive to plasma within the left lung than to plasma within the left

pleural cavity. For example, one animal showed a 0.9 ohms/100 ml change in impedance during the infusion of plasma into the left hemithorax and 1.5 ohms/100 ml change during plasma lavage of the left lung as recorded from the 2415 electrode array. These findings are depicted graphically in Fig. 4.

## DISCUSSION

The initial increase in thoracic impedance (Fig. 2) observed after the iv infusion of alloxan (Study 1) most likely represents the initial decrease in pulmonary capillary blood volume (2,25) and in central blood volume (25) caused by alloxan. The decrease in impedance ($\Delta Z$) measured by the 2415 circumferential spot electrode array during the course of alloxan-induced edema always exceeded that measured by the band electrode array. The greatest change in impedance recorded from the band array (Fig. 2A) was approximately 3 ohms. This result contrasts sharply with the findings of Pomerantz et al. (21) of 8-ohm changes recorded during alloxan-induced edema studies. However, these investigators administered alloxan in 300 ml of saline, and the magnitude of their observed impedance changes may represent both vascular overload and edema formation enhanced by the volume load.

From this study it is difficult to understand the observation of Pomerantz et al. (21,22) that blood gases were not altered significantly during the alloxan studies, despite marked changes in impedance.

Ventilatory obstruction due to severe edema and the presence of cyanosis was a consistent feature in the present study. Similar observations were made by Staub et al. (25). The fact that alloxan does cause necrosis of alveolar epithelia would explain the development of alveolar edema upon destruction of this critical barrier. The functional organization of the alveolar-capillary interfaces is such that blood gas alterations do not necessarily have to accompany interstitial edema; however, the presence of severe alveolar edema always will affect gas exchange in the terminal lung units. In a single animal (Fig. 2D), blood gases were determined at 10-min intervals following the administration of alloxan. Initial control values for $PO_2$ and $PCO_2$ were 156 mm Hg and 26.1 mm Hg, respectively. $PO_2$ and $PCO_2$ continued to change during the experiment with terminal values of 26 mm Hg for $PO_2$ and 49.6 mm Hg for $PCO_2$. Alterations in blood gases in this single animal accompanied changes of thoracic impedance and were consistent with the alterations in gas exchange that would be expected from alteration of the anatomical sites affected in alloxan-induced edema. It is possible that the differences observed in this study and that of Pomerantz et al. (21) could be attributed to differences in the dose rate administration of alloxan.

Although the 2415 spot electrode array was more sensitive than the band electrode array to pulmonary edema induced by alloxan, the order of sensitivities was reversed in pulmonary edema simulated by saline lavage of the left lung. This difference can be explained by considering the current distribution within the thorax and the total tissue between the impedance detecting electrodes of each electrode array. For conceptual purposes, the thorax has been divided into three zones: apical, cardiac,

and diaphragmatic (Fig. 5B-E). For the band electrode array, it can be assumed that the pathways of current flow through the thorax are essentially longitudinal since the plotting of equipotential lines on the surface of the thorax produces "rings" around the thorax rather evenly spaced for a given potential gradient. This distribution of current is represented in Fig. 5B by parallel lines running the length of the thorax. The dashed line depicts the separation of the thorax into a left and right component by the mediastinum. With the spot electrode array, the distribution of current is limited primarily to the diaphragmatic zone (Fig. 5D). Since the distribution of current is confined to the lower diaphragmatic zone, changes in impedance in the apical and cardiac zones will affect minimally the impedance measured across the diaphragmatic zone. Thus, the impedance-detecting band electrodes reflect changes of potential in the entire thorax, while the spot-detecting electrodes examine a limited region.

A cross section of the conceptual model presented is depicted in Fig. 5A. This cross section shows separate resistances for the right ($R_{RL}$) and the left lungs ($R_{LL}$) and a low resistance path ($R_S$) due to the muscular and vascular component of the thorax. The physical system suggests the equivalent circuit shown in Fig. 5C for the band electrode array. The resistance of the lungs ($R_{RL}$ and $R_{LL}$) is shown as series resistors ($R_1 + R_2 + R_3 = R_{RL}$; $R'_1 + R'_2 + R'_3 = R_{LL}$) in parallel with the shunt resistor designated $R_{S-B}$ for the band array. Likewise, the physical arrangement suggests the equivalent circuit depicted in Fig. 5E for the spot electrode array. Here, the resistance of the lung in the

diaphragmatic area is represented as two series resistors, $R_4$ for $R_{RL}$ and $R'_4$ for $R_{LL}$, in parallel with the shunt resistor designated $R_{S-S}$.

Considering these models and the fact that edema induced by alloxan is limited almost entirely to the diaphragmatic lobes, it is apparent why the spot electrodes detected the greatest change in impedance. With the spot electrodes, the decrease in $R_4$ and $R'_4$ with edema would affect significantly the equivalent R of the circuit between the electrodes, while a similar change in $R_3$ and $R'_3$ would affect the equivalent R for the band array less, since $R_3$ and $R'_3$ are in series with "resistors" not affected by the edema.

Air trapping is another factor that might account for the differences in impedance detected by the band and the 2415 electrode arrays with alloxan edema. The diaphragmatic lobes under the influence of alloxan were edematous and air trapping was minimal. The upper lobes (cardiac and apical) were distended with air trapped by the immense amount of foam in the upper airways. During positive pressure ventilation these upper lobes were inflated, but during passive expiration, increasing amounts of air became entrapped due to the airway obstructions. Thus the increase in air within the upper lungs would be detected by the band electrode array as an increase in impedance due to the high resistivity of air. This increase in impedance within the upper lobes could offset the decrease in impedance associated with the edema in the diaphragmatic lobes and, in effect, reflect no change in total impedance as detected by the band electrode array. The spot electrode array, on the other hand,

examines only the lower portion of the lung, and thus would be affected minimally by changes in impedance in the upper regions of the lung.

With saline lavage of the left lung, the fluid was distributed uniformly throughout the cardiac and diaphragmatic lobes with additional involvement of the apical lobe. In this situation, $R'_1$, $R'_2$, and $R'_3$ all would be changed, and, since the total fluid volume infused was large, it would be detected as a significant change in impedance by the band electrodes. However, with the spot electrodes, the change in $R'_4$ would not affect the equivalent R to the same degree since $R'_4$ is in series with $R_4$, which is not affected by the lavage. Additionally, the spot electrodes would detect less total fluid accumulation than the band electrodes since the spot electrodes would be affected by only a portion (diaphragmatic zone) of the fluid infused.

The use of sucrose to induce intrapulmonary fluid shifts has been reported to provide a useful model of severe pulmonary edema (5). Taylor and Gaar (26) reported that the alveolar membrane is only slightly permeable to sucrose, while this same membrane is permeable to water and electrolytes, though less so than is the pulmonary capillary endothelium (6). Thus, the model of pulmonary edema used in Study 2, in which sucrose was instilled into one lung, allowed the development of unilateral pulmonary edema without the associated ventilation problems encountered in Study 1, in which alloxan was used. The finding of an average of 112 mEq/l for sodium, 5 mEq/l for potassium, and 83 ohm/cm resistivity of the alveolar fluid produced with edema induced by sucrose

substantiates the use of this model of pulmonary edema since these are the values usually found for edema fluid.

The hemithoracic electrode arrays ($Z_1$ and $Z_2$) permitted localization of the sucrose-induced pulmonary edema to the left hemithorax. At necropsy, the edematous left lung (limited in most cases to the diaphragmatic lobe) was swollen markedly and had displaced the mediastinum to varying degrees toward the right hemithorax. However, the degree of displacement was not as great as that observed in our pleural effusion studies (7). This may account for the significantly greater degree of localization observed with the $Z_1$ and $Z_2$ electrode arrays when detecting unilateral pulmonary edema ($P < 0.005$) than when detecting pleural effusion ($P > 0.10$).

The results of this investigation and our investigation of pleural effusion (7) indicate a distinct advantage in using band electrodes rather than the circumferential spot electrode arrays. With the exception of edema limited to the diaphragmatic zone of the lung, the bands always detected the greatest absolute change in impedance. Since the distribution of pulmonary edema within the lungs varies from patient to patient (10), the pattern of current distribution of the circumferential spot electrodes across the thorax might allow pulmonary edema to develop undetected unless it happened to occur between the detecting electrodes. The longitudinally placed spot electrode arrays ($Z_1$, $Z_2$, and $Z_3$), on the other hand, detected equally significant changes in impedance during either pleural effusion or pulmonary edema and enabled localization of

the fluid accumulation to a specific hemithorax. The advantage of the longitudinal spot array in localizing edema to a hemithorax may be of significance in the interpretation of chest films and in the immediate bedside care of a patient.

The data from Study 4, in which infusion of plasma into the left hemithorax was compared with lavage using plasma in the left lung, indicate that the band electrode array detects simulated pleural effusion equally as well as it does simulated pulmonary edema. Impedance data from man following thoracentesis indicate linear increases in impedance of 0.2 to 0.5 ohms per 100 ml of effusion fluid removed (8,22,27,28). Since the volumes of effusion fluid averaged approximately 1000 ml, total impedance changed from 2 to 5 ohms. However, the withdrawal of a static volume of effusion fluid is analogous to simulated pleural effusion of an exogenous source. The data from the pleural effusion studies (7) in dogs indicated a loss of sensitivity of approximately 30% for the band electrode array when detecting endogenous pleural effusion as opposed to detecting exogenous pleural effusion. If this percent loss is applied to the human studies described above, an effusion of 1000 ml should change the total impedance between 1.4 and 3.5 ohms. If the band electrode array does, in fact, detect pleural effusion and pulmonary edema equally well in man, then the observations of Pomerantz et al. (22), Van De Water et al. (27,28), and Dove et al. (8) of 4 to 10-ohm decreases in impedance during the course of pulmonary edema are difficult to understand, even on the basis of 0.2 to 0.5 ohms/100 ml. A total impedance change of 4 to 10

ohms would represent a fluid accumulation of at least 800 to 2000 ml with an upper limit of 2000 to 5000 ml. The combined weights of the right and left lungs of humans who die without cardiopulmonary disease usually is between 800 and 900 g. In a study by Gump et al. (12) comparing normal human lung weights with lung weights of patients that died from pulmonary edema, normal lungs weighed approximately 600 g while edematous lungs at death weighed an average of 1700 g. This represents an average increase in total lung fluid of approximately 1000 ml.

In reconsidering the impedance changes reported in man with pulmonary edema, a decrease in impedance of 4 ohms would suggest that the existing edema is incompatible with survival. However, pulmonary edema frequently is associated with concurrent pleural effusion, and the total change of impedance would reflect both the edema and effusion. This would explain the high survival rate of patients with impedance changes varying between 4 and 10 ohms. Also, fluid therapy may contribute to the changes of impedance. Despite these conflicts between experimental and clinical findings, electrical impedance has become an important new method of monitoring patients in the Intensive Care Unit.

In summary, the thoracic impedance method has been shown to provide a reliable quantitative index of pulmonary edema in carefully controlled experiments in dogs. The impedance method provides a unique means of monitoring developing pulmonary edema; however, carefully controlled clinical studies will be required to verify interpretation of impedance changes in man.

TABLE 1. Comparison of mean values of the thoracic impedance change ($\Delta Z$, ohms) and mean percent change in thoracic impedance ($\Delta Z/Z_o \times 100$, %) measured using the band and 2415 electrode arrays associated with pulmonary edema induced by alloxan.

| Electrode Array | n | Parameter | Means ± SD | Degrees of Freedom | P Values |
|---|---|---|---|---|---|
| Bands | 5 | $\Delta Z$ | 1.9 ± 1.1 | 8 | < 0.05 |
| 2415 | 5 | $\Delta Z$ | 3.2 ± 0.6 | | |
| Bands | 5 | $\Delta Z/Z_o \times 100$ | 3.7 ± 1.8 | 8 | < 0.001 |
| 2415 | 5 | $\Delta Z/Z_o \times 100$ | 18.6 ± 3.6 | | |

Comparison based on student's t test. n = number of animals. SD = standard deviation. P = significance level.

TABLE 2. Summary of data from the studies of pulmonary edema induced by sucrose

| Time (min) | Mean Arterial Pressure* (mm Hg) | Heart Rate* (beats/min) | Hematocrit* (%) | Plasma Osmolarity† (mOsm/liter) |
|---|---|---|---|---|
| 0 | 94.4 ± 12.5 | 140.9 ± 24.6 | 42.7 ± 3.4 | 313.3 ± 4.9 |
| 5 | 88.9 ± 12.7 | 152.7 ± 26.6 | --- | --- |
| 15 | 86.3 ± 10.4 | 150.2 ± 24.8 | --- | --- |
| 30 | 83.4 ± 9.5 | 152.9 ± 25.2 | 43.2 ± 3.2 | 315.5 ± 5.0 |
| 45 | 79.9 ± 9.3 | 152.3 ± 23.6 | --- | --- |
| 60 | 76.6 ± 13.2 | 156.5 ± 31.9 | 43.7 ± 3.1 | 316.8 ± 4.9 |

*Data from 11 animals. †Data from 15 animals.

TABLE 3. Summary of the linear regression of impedance (ohms) vs. volume of saline (ml) infused into either the left lung or both lungs for various electrode arrays

| Electrode Array | Infusion Site | n | N | b | a | SEE | r | P Values |
|---|---|---|---|---|---|---|---|---|
| Bands ($Z_o$) | ILL | 4 | 28 | 43.3 | -0.014 | 4.8 | -0.272 | > 0.10 |
| 2415 ($Z_o$) | ILL | 6 | 42 | 10.4 | -0.006 | 2.8 | -0.211 | > 0.10 |
| 2416 ($Z_o$) | ILL | 6 | 42 | 5.3 | -0.001 | 1.5 | -0.102 | > 0.10 |
| 2456 ($Z_o$) | ILL | 6 | 42 | 4.7 | -0.004 | 1.5 | -0.290 | > 0.10 |
| Bands ($\Delta Z$) | ILL | 4 | 28 | 0.03 | -0.014 | 0.4 | -0.954 | < 0.001 |
| 2415 ($\Delta Z$) | ILL | 6 | 42 | -0.1 | -0.006 | 0.4 | -0.842 | < 0.001 |
| 2416 ($\Delta Z$) | ILL | 6 | 42 | -0.1 | -0.001 | 0.2 | -0.660 | < 0.001 |
| 2456 ($\Delta Z$) | ILL | 6 | 42 | -0.1 | -0.004 | 0.4 | -0.711 | < 0.001 |
| Bands (%) | ILL | 4 | 28 | -0.1 | 0.031 | 0.6 | 0.984 | < 0.001 |
| 2415 (%) | ILL | 6 | 42 | 0.8 | 0.057 | 3.0 | 0.885 | < 0.001 |
| 2416 (%) | ILL | 6 | 42 | 1.8 | 0.031 | 4.2 | 0.592 | < 0.001 |
| 2456 (%) | ILL | 6 | 42 | 2.7 | 0.091 | 7.5 | 0.769 | < 0.001 |
| Bands ($Z_o$) | IBL | 5 | 35 | 44.5 | -0.014 | 2.2 | -0.549 | < 0.01 |
| Bands ($\Delta Z$) | IBL | 5 | 35 | -0.4 | -0.014 | 1.1 | -0.769 | < 0.001 |
| Bands (%) | IBL | 5 | 35 | 0.2 | 0.030 | 1.0 | 0.953 | < 0.001 |

Saline was infused in increments of 50 ml from 0 to 300 ml. $Z_o$ = absolute impedance (ohms). $\Delta Z$ = change in impedance (ohms). % = $Z/Z_o$ x 100. ILL = infuse left lung. IBL = infuse both lungs. n = number of animals. N = number of x,y pairs. b = y intercept. a = slope. SEE = standard error of estimate. r = correlation coefficient. P = significance level.

FIGURE LEGENDS

Fig. 1 Four-terminal systems for the measurement of thoracic impedance. A: Band electrode array using flexible metal bands encircling the neck, thorax (xiphoid level), and abdomen. A constant sinusoidal current was applied to electrodes 1 and 4, and the voltage reflecting thoracic impedance changes was measured between electrodes 2 and 3. B: Circumferential spot electrode array. Standard disposable ECG electrodes were applied to the thorax at the xiphoid level. A constant sinusoidal current was applied to electrodes 2 and 4 and impedances between other pairs of electrodes (1,5 - transthoracic; 1,6 - right hemithorax; 5,6 - left hemithorax) were recorded. The designations 2415, 2416, 2456 indicate that current was applied to electrodes 2 and 4 and the impedance was measured between the other two electrodes. C: Longitudinal spot electrode array. Standard disposable ECG electrodes were applied to the thorax as shown. A constant sinusoidal current was applied to electrodes 1 and 6, and impedance changes between electrodes 2,3 ($Z_1$ - right hemithorax) and 4,5 ($Z_2$ - left hemithorax) were recorded. An array designated $Z_3$ was also used in which electrodes 2 and 4 were connected together as were electrodes 3 and 5, and the impedance between the two sets was recorded.

Fig. 2 The change in thoracic impedance (ΔZ, ohms) measured using the band and the 2415 spot electrode arrays as a function of the time course of development of pulmonary edema induced with alloxan in six dogs.

Fig. 3 Mean change in thoracic impedance (ΔZ) measured during the time course of development of pulmonary edema of the left lung induced with sucrose. A: Mean ΔZ measured using the band and $Z_3$ longitudinal electrode arrays. B: Mean ΔZ measured using the $Z_1$ and $Z_2$ longitudinal electrode arrays. Regression lines determined from data points through 35 min. t = time (min). r = correlation coefficient. P = significance level. n = number of animals. N = number of x, y pairs. Data adjusted to initial starting impedance of 5 ohms instead of 0 ohms for regression analysis.

Fig. 4 Thoracic impedance measured using the band (A) and 2415 (B) electrode arrays vs. volume (ml) of blood, saline, or plasma infused into the left hemithorax or plasma infused into the left lung. Data from individual animal. Plasma-L = plasma infused in left lung. Saline-T = saline infused in left hemithorax. Blood-T = blood infused in left hemithorax. Plasma-T = plasma infused in left hemithorax.

Fig. 5 Electrical model of the thorax. A: Cross section of thorax showing the partitioning of the "thoracic cylinder" into electrical resistance zones ($R_{RL}$ = resistance of the right lung; $R_{LL}$ = resistance of the left lung; and $R_S$ = shunting resistance of thoracic muscle and blood). B: Current distribution with the band electrode array. C: Lumped resistance model of the thorax when using the band electrode array. $R_{RL} = R_1 + R_2 + R_3$; $R_{LL} = R_1' + R_2' + R_3'$; and $R_S = R_{S-B}$. D: Current distribution for the 2415 spot electrode array. E: Lumped resistance model of the thorax using the 2415 spot electrode array. $R_{RL} = R_4$; $R_{LL} = R_4'$; and $R_S = R_{S-S}$.

## REFERENCES


1. Achauer, B. M., P. A. Allyn, D. W. Furnas, and R. H. Bartlett. Pulmonary complications of burns: the major threat to the burn patient. Ann. Surg. 177: 311-319, 1973.
2. Aviado, D. M. and C. F. Schmidt. Pathogenesis of pulmonary edema by alloxan. Circulation Res. 5: 180-186, 1957.
3. Benfield, J. R., R. Coon, and E. M. Cree. Canine bronchospirometry: the development of a reliable catheter. J. Thorac. Cardiovas. Surg. 52: 882-892, 1966.
4. Burford, J. H. and B. Burbank. Traumatic wet lung. J. Thorac. Surg. 14: 415-424, 1945.
5. Calderwood, H. W., J. H. Modell, B. C. Ruiz, J. E. Brogdon, and C. I. Hood. Pulmonary lavage with liquid fluorocarbon in a model of pulmonary edema. Anesthesiology 38: 141-144, 1973.
6. Chinard, F. P. The permeability characteristics of the pulmonary blood-gas barrier. In: *Advances in Respiratory Physiology*, edited by C. G. Caro. London: Edward Arnold, 1966, p. 106-147.
7. Denniston, J. C. and L. E. Baker. Measurement of pleural effusion by electrical impedance. J. Appl. Physiol. 38: 851-857, 1975.
8. Dove, G. B., J. M. Van De Water, and R. W. Borst. The application of impedance to the intensive care unit patient: a look toward continuous computer monitoring. Proc. San Diego Biomed. Symp. 10: 161-166, 1971.
9. Frank, E. D. The hazard of interstitial pulmonary edema. Ann. Surg. 169: 641, 1969 (editorial).

10. Fraser, R. G. and J. A. Pare. *Diagnosis of Diseases of the Chest.* An integrated study based on the abnormal roentgenogram. Philadelphia: W. B. Saunders Co., 1970, vol. 1 & 2, 1388 p.

11. Geddes, L. A. Measurement of electrolytic resistivity and electrode-electrolyte impedance with a variable-length conductivity cell. Chem. Instrum. 4: 157-168, 1973.

12. Gump, F. E., Y. Mashima, A. Ferenczy, and J. M. Kinney. Pre- and postmortem studies of lung fluids and electrolytes. J. Trauma 11: 474-482, 1971.

13. Hultgren, H. N. and M. D. Flamm. Pulmonary edema. Mod. Concepts Cardiovas. Dis. 38: 1-6, 1969.

14. Kubicek, W. G., J. N. Karengis, R. P. Patterson, D. A. Witsoe, and R. H. Mattson. Development and evaluation of an impedance cardiac output system. Aerospace Med. 37: 1208-1212, 1966.

15. Levine, O. R., R. B. Mellins, and A. P. Fishman. Quantitative assessment of pulmonary edema. Circulation Res. 17: 414-426, 1965.

16. Luepker, R. V., J. R. Michael, and J. R. Warbasse. Transthoracic electrical impedance: quantitative evaluation of a noninvasive measure of thoracic fluid volume. Am. Heart J. 85: 83-93, 1973.

17. McCredie, M. Measurement of pulmonary edema in valvular heart disease. Circulation 36: 381-386, 1967.

18. Moore, F. D., J. H. Lyons, E. C. Peirce, A. P. Morgan, P. A. Drinker, J. D. MacArthur, and G. Dammin. *Post-traumatic Pulmonary Insufficiency.* Philadelphia: W. B. Saunders Co., 1969, 116 p.

19. Pearce, M. L., J. Yamashita, and J. Beazell. Measurement of pulmonary edema. Circulation Res. 16: 482-488, 1965.

20. Philipps, E. and F. G. Fleischner. Pulmonary edema in the course of a blood transfusion without overloading the circulation. Dis. Chest 50: 619-623, 1966.

21. Pomerantz, M., R. Baumgartner, J. Lauridson, and B. Eiseman. Transthoracic electrical impedance for the early detection of pulmonary edema. Surgery 66: 260-268, 1969.

22. Pomerantz, M., F. Delgado, and B. E. Eiseman. Clinical evaluation of transthoracic electrical impedance as a guide to intrathoracic fluid volumes. Ann. Surg. 171: 686-694, 1970.

23. Severinghaus, J. W. Electrical measurement of pulmonary edema with a focusing conductivity bridge. J. Physiol. 215: 53P-55P, 1971.

24. Simmons, R. L., C. A. Heisterkamp, J. A. Collins, C. E. Bredenburg, and A. M. Martin. Acute pulmonary edema in battle casualties. J. Trauma 9: 760-775, 1969.

25. Staub, N. C., H. Nagano, and M. L. Pearce. Pulmonary edema in dogs, especially the sequence of fluid accumulation in lungs. J. Appl. Physiol. 22: 227-240, 1967.

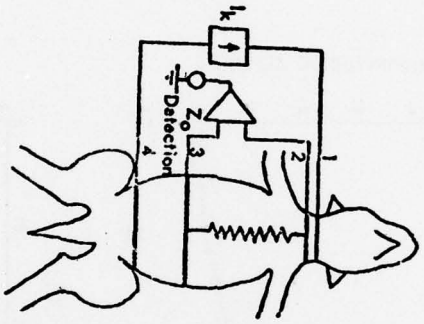
26. Taylor, A. E. and K. A. Gaar. Estimation of equivalent pore radii of pulmonary capillary and alveolar membranes. Am. J. Physiol. 218: 1133-1140, 1970.

27. Van De Water, J. M., I. T. Miller, E. N. C. Milne, E. L. Hanson, G. F. Sheldon, and K. S. Kagey. Impedance plethysmography. A noninvasive means of monitoring the thoracic surgery patient. J. Thor. Cardiovas. Surg. 60: 641-647, 1970.

28. Van De Water, J. M., P. A. Philips, L. G. Thouin, L. S. Watanabe, and R. S. Lappen. Bioelectric impedance. New developments and clinical application. Arch. Surg. 102: 541-547, 1971.

## FOOTNOTE

This investigation was supported by NIH research grant HL 15454 from the National Heart and Lung Institute and was conducted in the Department of Physiology, Baylor College of Medicine, Houston, Texas.

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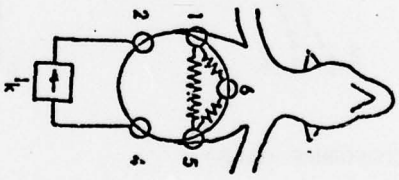


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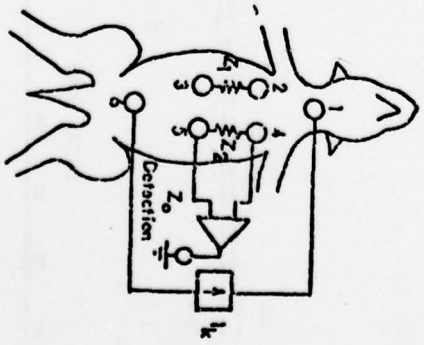


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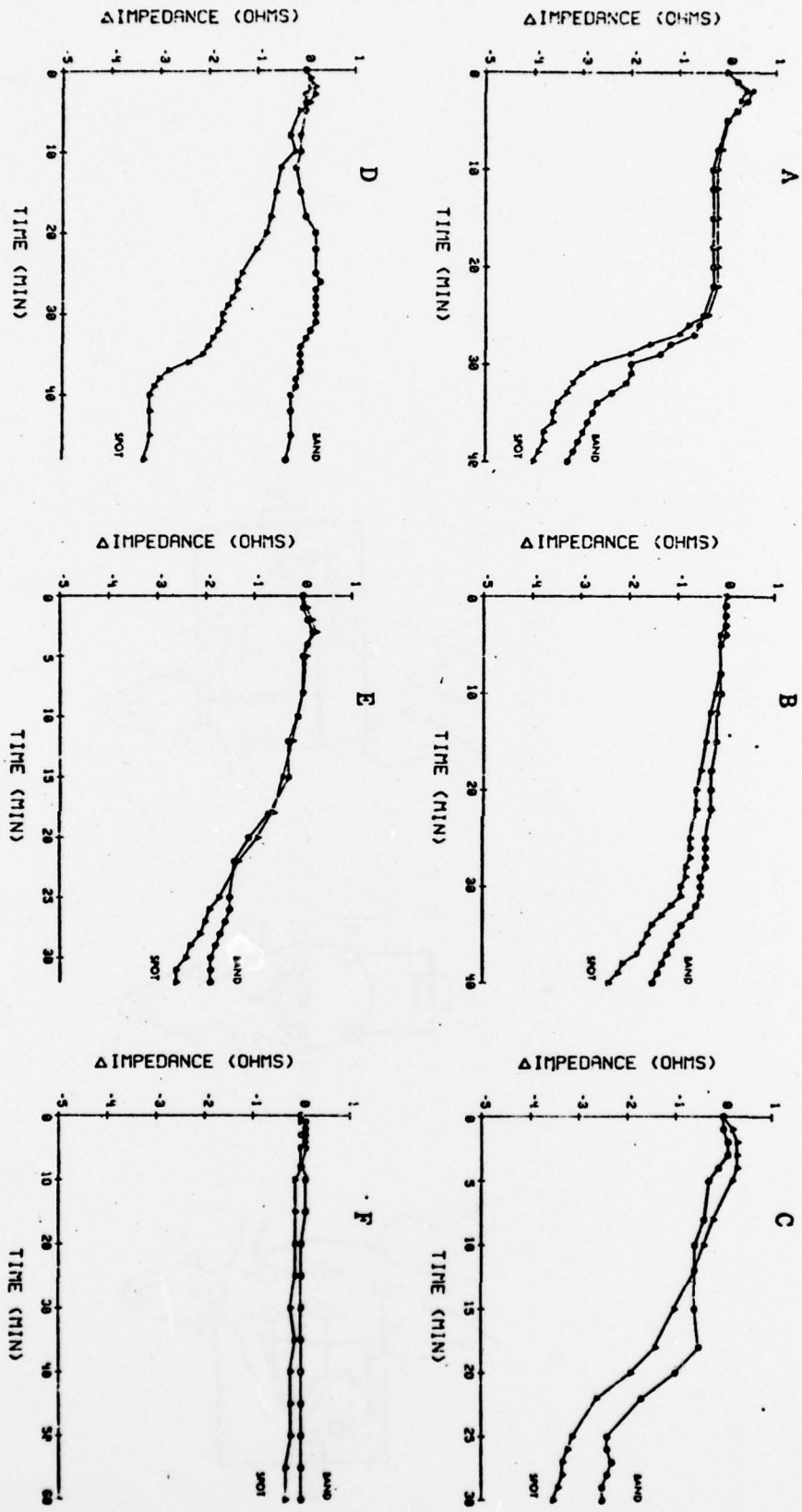
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SPOT
BAND
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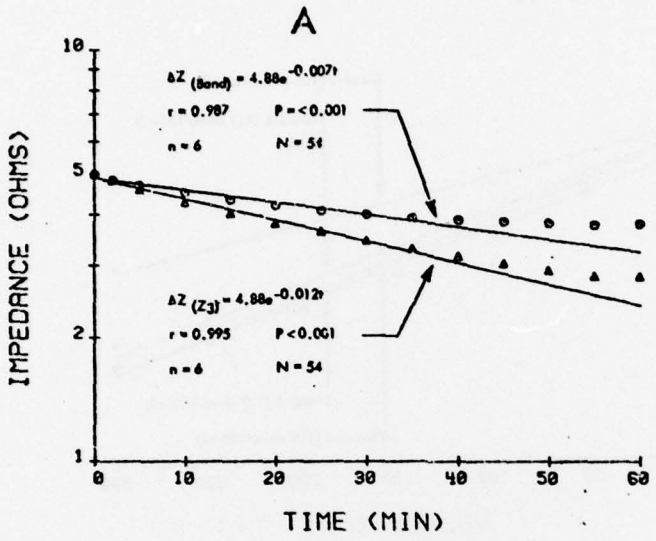
B
C
D
E
F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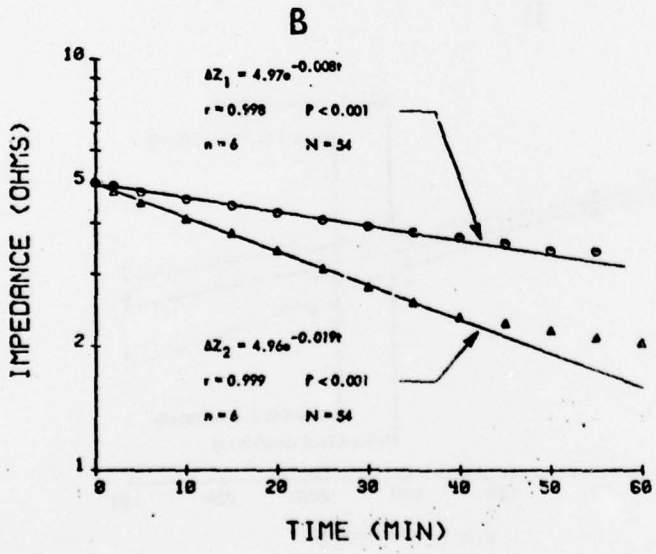
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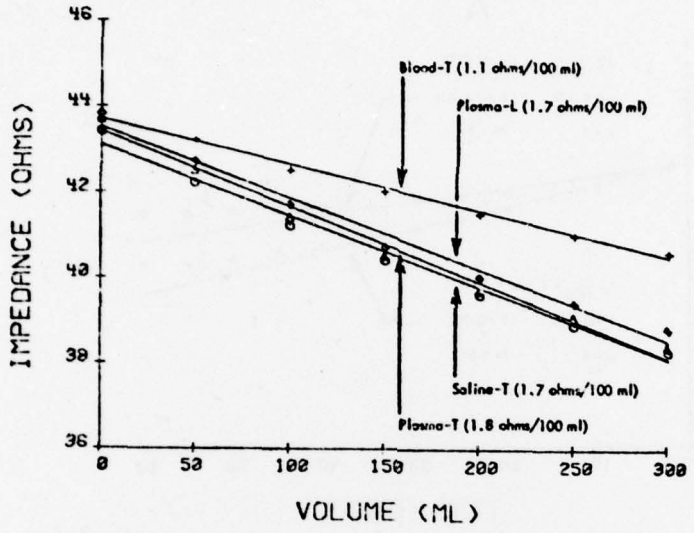
A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Saline-T (1.7 ohms/100 ml)
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200
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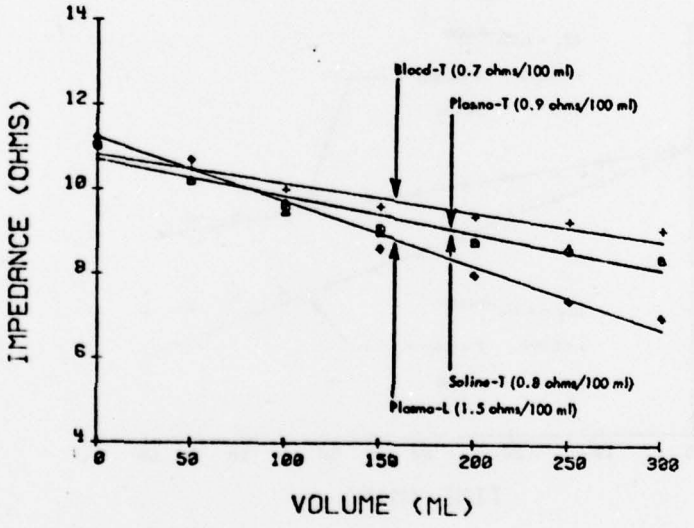
VOLUME (ML)

B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Blood-T (0.7 ohms/100 ml)
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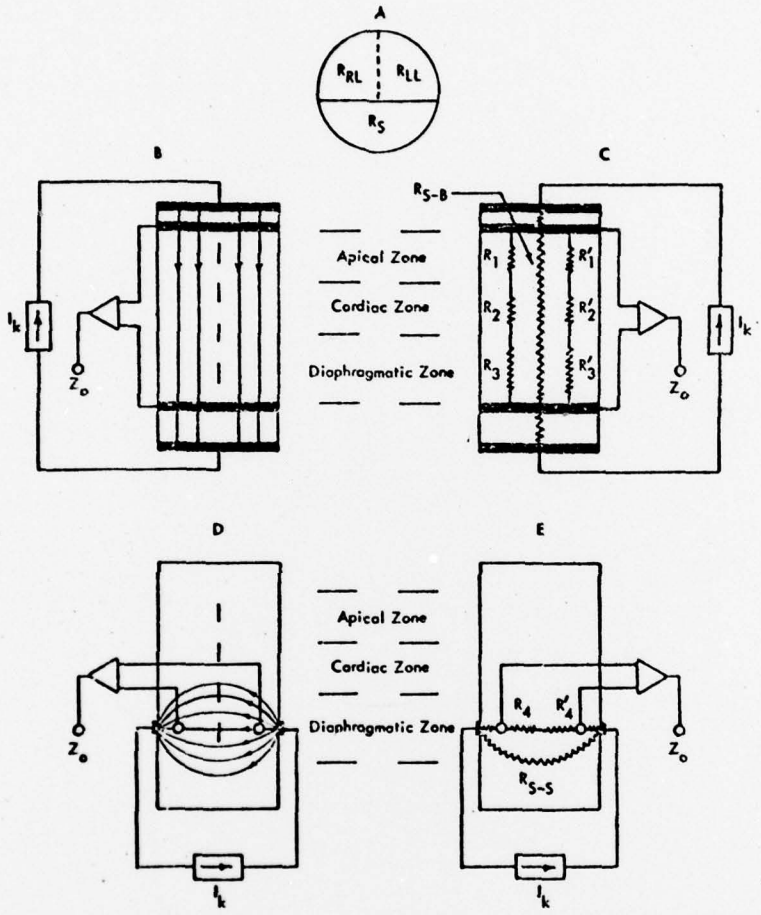
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C
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Apical Zone
Cardiac Zone
Diaphragmatic Zone
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$R_3$
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Apical Zone
Cardiac Zone
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| 4. TITLE (and Subtitle): The Detection of Pulmonary Edema by Means of Electrical Impedance, | 5. TYPE OF REPORT & PERIOD COVERED |
| | 6. PERFORMING ORG. REPORT NUMBER |
| 7. AUTHOR(s): W.C. Denniston, J.E. Baker, Joseph Lee | 8. CONTRACT OR GRANT NUMBER(s): 12 38p. |
| 9. PERFORMING ORGANIZATION NAME AND ADDRESS: US Army Research Institute of Environmental Medicine, Natick, MA 01760 | 10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS |
| 11. CONTROLLING OFFICE NAME AND ADDRESS: US Army Medical Research and Development Command, Washington, DC | 12. REPORT DATE: Oct [redacted]75 |
| | 13. NUMBER OF PAGES: 35 |
| 14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): NA | 15. SECURITY CLASS. (of this report): Unclassified |
| | 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE |

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18. SUPPLEMENTARY NOTES

To be published in Journal of Applied Physiology.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Electrical impedance, pulmonary edema, noninvasive technique, electrode arrays.

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The detection, localization, and quantification of pulmonary edema by electrical impedance were investigated using band, circumferential, and longitudinal electrode arrays in a series of four studies utilizing 35 dogs. Pulmonary edema was induced with alloxan, sucrose, and saline lavage. The ability of the various electrode arrays to distinguish between pulmonary edema and pleural effusion was also investigated. The largest absolute changes in impedance were detected by the band electrodes, although larger percent changes in impedance were.

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measured using the circumferential arrays. The circumferential arrays indicated the possibility of differentiating between pleural effusion and pulmonary edema. The longitudinal array had essentially the same characteristics as the band array, although it permitted localization of either edema or effusion to one hemithorax. The impedance method provides a reliable quantitative index of pulmonary edema in carefully controlled experiments in dogs.