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☐ Review Article ☐

Detection of Physiological Events by Impedance

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The current emphasis on the acquisition of physiological data by noninvasive means for mass medical screening and patient monitoring has increased interest in the use of electrical impedance for the measurment of physiological events. The technique has gained some degree of acceptance for monitoring respiration (Baker & Geddes, 1970), and much interest has been displayed recently in use of the technique to measure cardiac output including studies by Kubicek et al. (1966) Judy et al. (1969), and Mohapatra (1981). Other applications using the impedance technique include thoracic fluid accumulation, peripheral blood flow, cerebral blood flow, muscle contraction, eye movement, and uterine contraction, etc. The purpose of this article is to introduce the various impedance techniques for the measurement of physiological variables.

Key Words: Impedance plenthysmography, noninvasiveness, stroke volume, cerebral and peripheral blood flow, respiration.

Nyboer (1944) passed a high-frequency current across the human chest from a constant-current sinusoidal generator and observed the changes in the throacic impedance which occurred with each heart beat. Nyboer subsequently applied the technique to the observation of the impedance change which occurs when a cylindrical volume of tissue is perfused with a pulsatile arterial flow of blood. During systole, blood flows into the segment under consideration and the electrical impedance of the segment will fall and then rise to the end-diastolic value as the blood flows out during diastole. The segment will also contain some pooled blood and the amount of this is a measure of the basal impedance Z_0 of the segment.

In impedance cardiography, four flexible metal band electrodes approximately 5 mm wide are placed to encircle the thorax as shown in Figure 1. A sinusoidal constant current (4 mA or less) in the frequency of 20 to 100 kHz is applied to the outer electrodes (1&4). Potential changes reflecting impedance change (ΔZ) accompanying cardiac activity are recorded between the two inner electrodes (2&3). An electronic differentiator is used to obtain the derivative of the impedance change, ΔZ. The derivative signal is designated dZ/dt. Figure 2 is a typical record from a dog showing ECG, ΔZ, dZ/dt, and aortic flow as measured by an electromagnetic flowmeter.

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The equation used to calculate stroke volume is based on the assumption that the thorax is equivalent electrically to a homogeneous cylinder of blood, the resistance of which is given by Ohm's law R=pL/A: where p is the resistivity of blood, L is the length of the cylinder and A is its cross-sectional area. If it is assumed that the diameter of the cylinder increases uniformly with ejection of blood from the heart, the expression R=pL/A can be mainpulated to give $dV=p(L/Z_0)^2dZ$, where dV is the volume (ml.) of blood ejected (stroke volume) and L(cm) is the distance between electrodes 2 and 3 in Figure 1. Z_0 is the basal value of thoracic impedance (Ω), and ΔZ is the change in the impedance of the cylinder (thorax) if the entire quantity of blood ejected were effective in producing the impedance change (*i.e.*, if no run-off blood from the thorax occurred). Thus, in order to estimate the change in impedance which could be expected without run-off, some investigators take the maximum rate of change of the ΔZ waveform, *i.e.*, $(dZ/dt)_{max}$ and multiply this latter quantity by the ejection time LVET. The complete equation for stroke volume, therefore, becomes $dV=p(L/Z_0)^2(dZ/dt)_{max}LVET$ (Geddes and Baker, 1975).

APPLICATION OF IMPEDANCE PLETHYSMOGRAPHY

Impedance Cardiography

The differentiated impedance cardiogram, dZ/dt

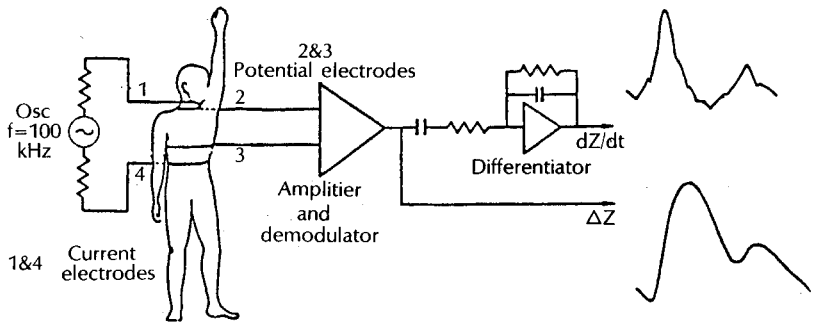


Fig. 1. *Schematic diagram of impedance cardiography.*

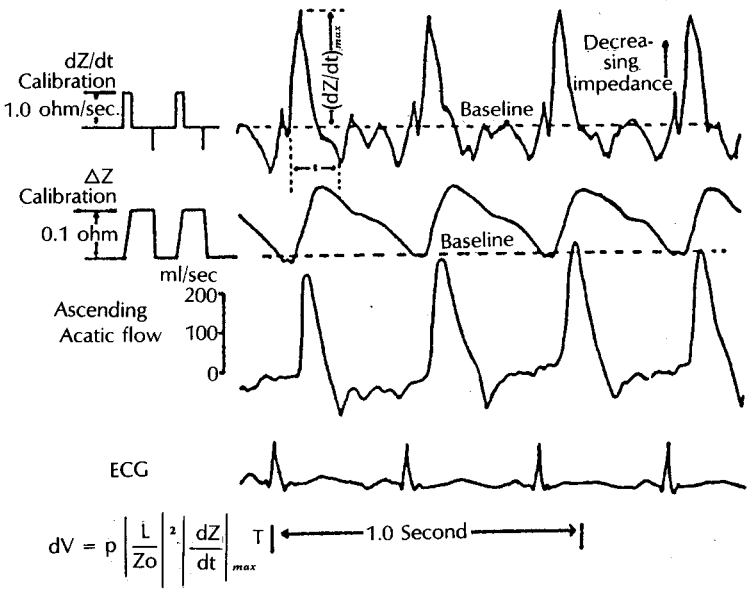


Fig. 2. *A typical record showing dZ/dt, ΔZ, aortic flow, and ECG in the dog.*

waveform, is a well-defined signal and contains valuable hemodynamic information including systolic time interval (pre-ejection period, ejection time), myocardial contractility,and ejection fraction (EF) as well as beat by beat stroke volume. The morphology of the first derivative thoracic impedance cardiogram is shown in Figure 3 (Lababidi *et al.* 1970; Mohapatra 1981). Decreasing rates of impedance change are recorded as upward deflections in the tracing. The "A" waveform corresponds to the atrial systole, and the "C" waveform corresponds to the ventricular systole and reflects the rate of change of speed of ejection or the pattern of ejection of blood from the ventricles. The "O" waveform corresponds to ventricular diastole and reflects the rate of change of volume of the atria and veins. Most of the O-wave occurs during the rapid filling phase and in some cases, the O-wave peak (if present) corresponds to mitral valve opening. The "B" point and "X" point appear immediately after the aortic valve opens and closes respectively. "B" point also coincides with the main portion of the first sound and "X" point coincides with the second heart sound. The peak C coincides with the peak flow time measured on the ascending aorta as shown in Figure 2.

Both carotid pulse and heart sound are necessary to measure the PEP and LVET, while an impedance cardiogram alone provides these. The ratio PEP/LVET has been shown by Weissler *et al.* (1961, 1969) to be

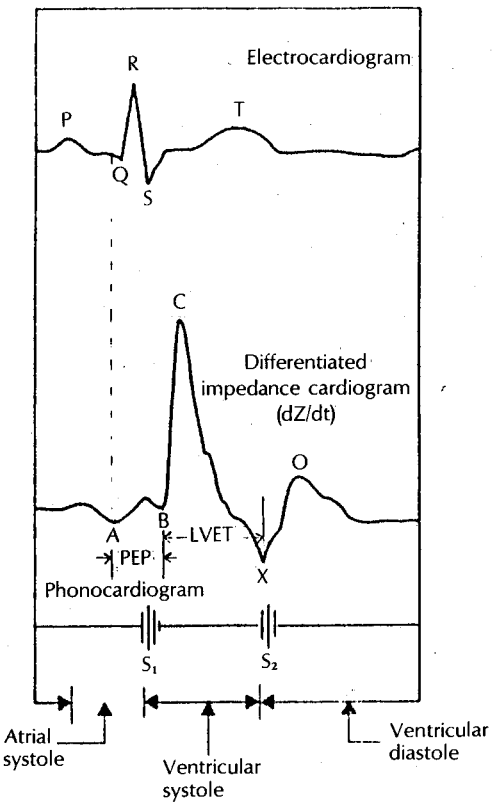


Fig. 3. *Schematic representation of the differentiated impedance cardiogram (dZ/dt) and its relationship to the cardiac cycle.*

almost independent of the heart rate and a valuable index of cardiac performance. As an index of cardiac contractility, Dr. Loren Heather has proposed the Heather Index which is defined as dZ/dt_{max} in Ω/sec divided by the Q-Z interval in seconds. The time interval is measured from the commencement of the preceding Q-wave to the top of the dZ/dt_{max} wave peak. The dZ/dt_{max} and Q-Z interval are equivalent to the maximum ejection velocity and a time delay from the beginning of depolarization to maximum ejection velocity, respectively. Thus the shorter the Q-Z interval, the stronger the cardiac muscle. As the unit of Heather Index is equivalent to ml/sec^2, it indicates ejection acceleration.

The fact that this impedance cardiography is a beat-by-beat method must lead to some difficulties when it is compared with indicator dilution methods which measure a cardiac output averaged over several beats. However, in 20 children without shunts or valvular insufficiency, Lababidi *et al.* (1971) found a 5.5% mean difference between the impedance and dye cardiac output values in 53 sequential estimates, the correlation coefficient being 0.97. Costeloe *et al.* (1977) have found, in babies carefully selected to avoid shunting, a correlation of 0.94 between the impedance and nitrous oxide uptake methods for cardiac output at hematocrits greater than 30%. Smith *et al.* (1970) found a correlation of 0.87 between the impedance and dye methods with 35 simultaneous comparisons in 8 normal subjects, and this was increased to 0.95 when corrections were made using the respective impedance-dye ratios for individual subjects. Hill and Thompson (1975) found a correlation of 0.88 between the impedance and radioisotope cardiac outputs with hematocrits ranging from 20 to 48%.

A correlation coefficient of 0.89 was obtained by simultaneous measurement of cardiac output using the impedance and thermodilution techniques from 7 patients with mitral stenosis by Kim *et al.* (1988). This value is thought to be quite high considering the fact that the accuracy of cardiac output of patients with valvular diseases or shunts measured by both methods is low. However, it was found that measurement of cardiac output by impedance cardiography is not accurate in cases of severe atrial fibrillation. In general, the impedance cardiac outputs are higher (5 to 20%) than the corresponding dye values.

Impedance cardiography has a particular value for the assessment of stroke volume, and hence cardiac output during exercise, because of its noninvasive nature. The accuracy and reproducibility of the stroke volume derived by the impedance method are shown to be reliable in comparison with other standard techniques such as the CO_2 rebreathing method (Miyamoto *et al.* 1981; Miles *et al.* 1981) and dilution method (Takada *et al.* 1981). The rebreathing method, however, requires that the subject learn a specific breathing technique, have a normal ventilation/perfusion ratio, and be in a metabolic steady state. The dilution method is invasive and its use is very restricted during exercise. On the other hand, impedance cardiography is noninvasive, easy to measure, reliable, and inexpensive. However, it is difficult to measure stroke volume during severe exercise due to the motion artifact resulting from excessive body movement and extreme breathing. To reduce the motion artifact, measurements were made immediately after exercise and bicycle ergometers were used instead of treadmills (Kobayashi, 1978; Hatcher, 1986).

Cardiac functions of humans were measured during exercise without pause using impedance cardiography with an ensemble averaging technique to reduce the motion artifact by Gollan *et al.* (1978) and

Miyamoto *et al.* (1981). Miyamoto and his associates found a good correlation coefficient of 0.94 between oxygen uptake and cardiac output. Kim successively measured cardiac output for work loads up to 200 W using a bicycle ergometer with a newly devised electrode configuration made of elastic band for minimum motion artifact (Hwang *et al.* 1989). They found the above correlation coefficients of 0.69 and 0.76 for 13 athletes and 6 nonathletes, respectively.

The value of Z_0 is markedly dependent upon the presence of fluid within the thorax. Van de Water *et al.* (1971) found that in a 60-year-old man with a left pleural effusion, Z_0 rose from 25 to 26.8 Ω when 850 ml of fluid was removed from the pleural space. In a woman, Z_0 fell from a post-operative value of 21.5 Ω to 14 Ω just prior to death. At post mortem, 750 ml of blood was found in the pleural space and at least 500 ml within the chest wall. Hill (1975) observed an increase from 12 Ω to 20 Ω in a woman who had inhaled vomit and was then ventilated with a positive end-expiratory pressure. It would appear that the simple monitoring of changes in Z_0 may have a real clinical value.

Peripheral Blood Flow

A reduction in blood flow to the extremities occurs in many types of cardiovascular diseases. Accordingly, to assist in the diagnosis of peripheral vascular diseases and in evaluating the effect of therapeutic measures, considerable effort has been directed toward the development of quantitative methods to measure peripheral blood flow. The only accurate method available (venous-occlusion plethysmography) is cumbersome to apply, and clinicans have almost abandonded it. The impedance method, however, is much easier to use and therefore offers attractive clinical possibilities. It has not seen extensive use because of difficulties in relating the impedance change, which is measured in ohms, to units of blood flow, namely, milliliters per minute. Excellent accounts of the history and development of the impedance method are to be found in Nyboer's two monographs (1959, 1970).

When electrodes are applied to the finger within a closed chamber, as in Figure 4, the pulsatile impedance change is strikingly similar to the pulsatile pressure change in the air within the chamber. This fact has been well documented with bipolar and tetrapolar electrode systems; an example of the latter from Nyboer's studies (1970) is illustrated in Figure 4. Therefore, it would seem that the two recordings reflect the same event, and it ought to be a straightforward task to verify the volume flow obtained by use of the impedance method with that determined by venous-occlusion plethysmography.

The end-systolic (backslope) graphical construction has been applied to both the pneumatic and impedance recordings illustrated in Figure 4. The volume of blood entering the region within the finger-surrounding capsule amounts to 0.00735 ml per heart beat for the pneumatic recording. For the impedance recording, the basal impedance (Z_0) between the potential measuring electrodes, 3.1 cm apart and at the edges of the capsule, is 214.4 Ω, and the extrapolated value for the impedance change (ΔZ) is 0.24 Ω. Using a typical value of 150 Ω-cm for the resistivity of blood, the predicted volume entering the body segment is

$$\Delta V = p(L/Z_0)^2\Delta Z = 150 \times (3.1/214.4)^2 \times 0.24 = 0.00753 \text{ ml}$$

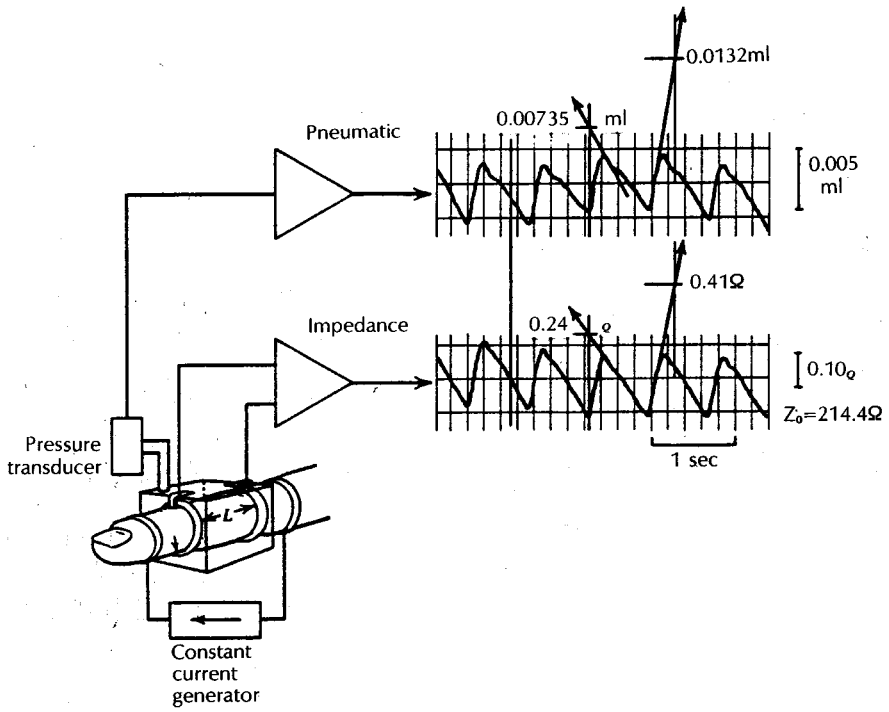
The forward extrapolation technique has been applied to both the pneumatic and impedance recordings appearing in Figure 4. The pneumatic recording indicates a flow of 0.0132 ml per heart beat. The extrapolated impedance change (ΔZ) amounts to 0.41 Ω and using the same values for L and Z_0, the volume obtained by the impedance method is

$$\Delta V = p(L/Z_0)^2\Delta Z = 150 \times (3.1/214.4)^2 \times 0.41 = 0.0128 \text{ ml}$$

Cerebral Blood Flow

Measurement of cerebral blood flow is extremely difficult. The only reliable method of determining the amount of blood that flows through the brain per minute was described by Kety and Schmidt (1945, 1948). With this technique, the subject inhales nitorus oxide (N_2O, 15%) and exhales to the atmosphere for a period of 10 min, the time necessary for cerebral venous blood to reach equilibrium with the tension of N_2O in the brain tissue. During the 10-min period, 5 paired samples of arterial and jugular-vein blood are drawn and graphs are plotted of the arterial and venous blood concentrations of N_2O. From these data and using the dilution formula, cerebral blood flow per 100 grams of brain tissue can be calculated. Typically in man, the flow amounts to about 55 ml/min per 100 grams of brain tissue.

Clearly, measurement of cerebral blood flow is difficult, and any noninvasive, nonhazardous method for obtaining information on cerebral circulation is extremely attractive to neurologists, the neurosurgeon, and the vascular surgeon. Probably for this reason, Polzer and Schuhfried (1950) investigated the value



Heart Rate = 75/min; Volume of Digit = 14.5 ml; Length, L = 3.1 cm

Extrapolation Technique	Flow (ml/heart beat)	
	Pneumatic	Impedance
Backward	0.00735	0.00753
Forward	0.0132	0.0128
	Flow [ml/(min)/(100 ml of digit)]	
Backward	3.80	3.89
Forward	6.83	6.62

Fig. 4. *Pneumatic and impedance plethysmography of the digit.*

of the impedance method to estimate cerebral blood flow. They placed a pair of electrodes on the head of a patient having an occlusion of one carotid artery and measured the 20 kHz pulsatile impedance change, first on one side of the head and then on the other. On the affected side, the height of the pulsatile impedance change was diminished, thereby indicating a possible relationship with cerebral blood flow. Since that time, numerous studies have been carried out; one book has been published (Jenkner, 1962), and three international symposia have been held on the subject (Martin and Lechner 1963; Lechner *et al.* 1969; Markovich 1979). Review papers have been presented by Lifshitz (1963), Geddes (1964), McHenry (1965), Perez-Borja and Meyer (1964), and Hadijev (1972). Although not all these reviewers are laudatory of the method, there is considerable interest in the potential of rheoencephalography (REG), and several instruments are available commercially. There is undeniable evidence that useful qualitative information regarding cerebral perfusion can be obtained by rheoencephalography, but there is no agreement on the optimum electrode placement or instrumentation technique. Therefore, the results obtained must be evaluated in view of the type of recording technique employed.

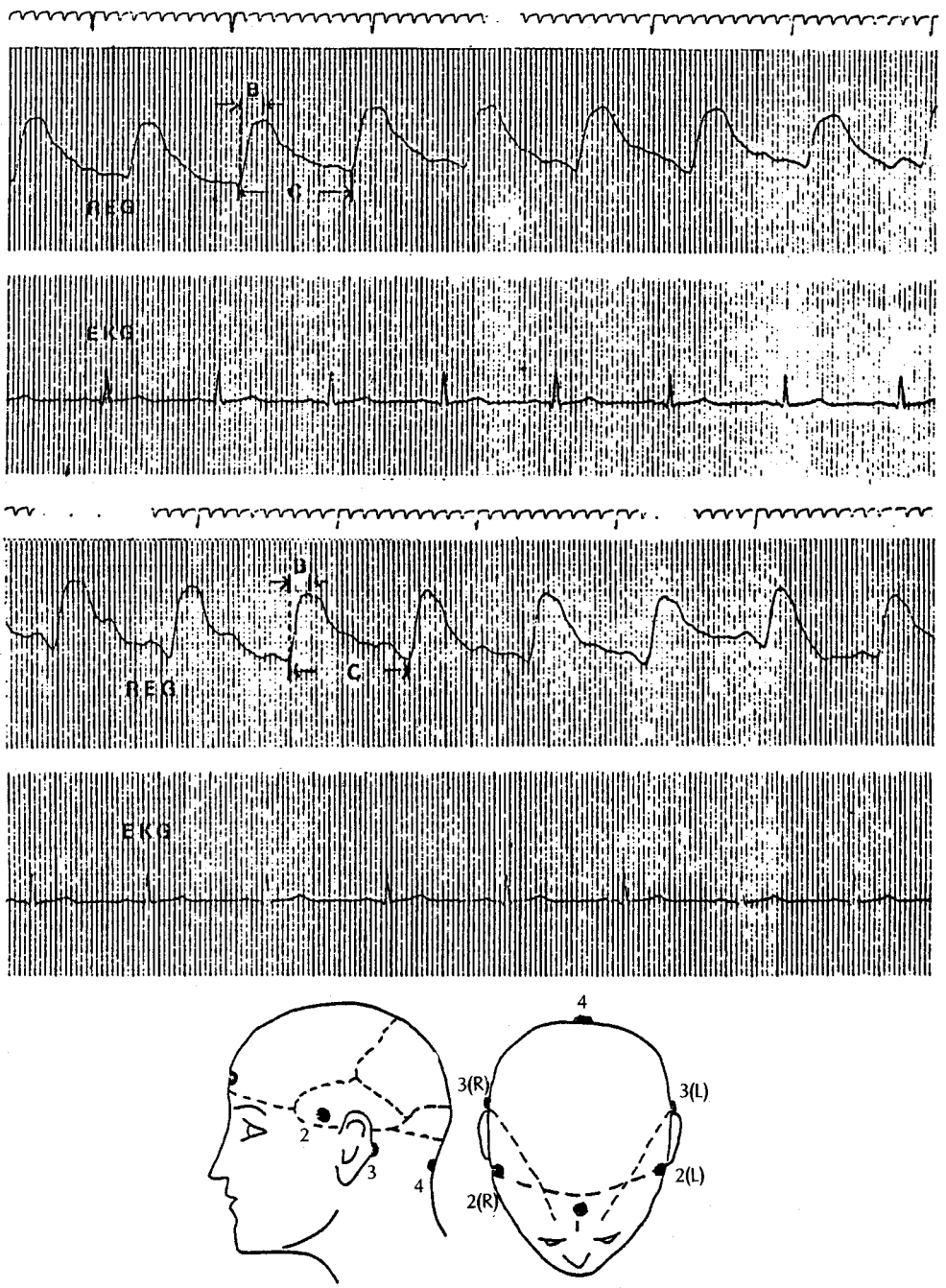


Fig. 5. *Rheoencephalogram (channel 1:left and 3:right) and the ECG (channel 2 and 4). A decrease in impedance is shown upward.*

A typical tetrapolar (four) recording of REG from a normal subject appears in Figure 5 using an instrument developed in our department. The electrodes were arrayed as shown, and the impedance changes were measured at 100 kHz using 1 mA. the constant current is applied to the outer pair of EEG electrodes

(1&4) and the resistance change is picked up from the inner ones (2&3). In this record it was observed that the REGs from the right and the left sides are slightly different in waveform. It was also noticed that the peak amplitude of the REG in supine position was about twice as large as that in sitting position. The pulse transmission time from the heart to the head is evident from the relationship between the R wave of the ECG and the onset of the impedance pulse. This interval is often described as the appearance time. It is customary to measure the peak amplitude (usually 20-200 mΩ) and the rate of rise of the impedance pulse (Ω/sec), B/C, as shown in Figure 5. Often the time from the oneset to the peak is also measured. Alterations in these quantities accompanies cerebrovascular disease.

For current to gain access to the brain by means of scalp electrodes and the brain, it must transverse the scalp and the scull, entering the brain through the cerebrospinal fluid. The resistivity of the scalp is much lower than that of the bony cranium, and the cerebrospinal fluid has a resistivity even lower than that of blood (Radvan-Ziemnowicz *et al.* 1964). Thus low-frequency current can easily pass between the electrodes through scalp tissue, and only a small fraction will pass through the high-resistivity calvarium to enter the brain. If the frequency is high enough, the reactance of the path constituted by the scalp-calvarium and brain substance will be low, and current will gain easier access to the brain.

Although it is well known that the pulsatile impedance change detected by scalp electrodes is a reflection of pulsatile blood flow, there is no agreement on the relative contributions of the extracranial and intracranial circulations. However, the relative contributions of each can be demonstrated by the simple technique of placing a tight band caudal to the electrodes to cut off the extracranial blood flow. When this is done, there is a significant reduction in pulsatile amplitude with some electrode arrays and circuits.

The clinical value of the various rheoencephalographic methods has not been established. Progress is slow because there are so many different techniques in use. Hadijev's review (1972) describes the clinical evaluations established to date. The really attractive feature of the REG is its noninvasive and painless nature. A second attribute is its continuous recording aspect and ability to indicate immediate changes in response to stimuli (carotid and jugular occlusion, hyperventilation, etc.), Although there is no method available at present for converting the pulsatile impedance change to pulsatile flow, the potential for correlating REG changes with cerebrovascular disease exists and, with the passage of time, useful correlations will be established. Its use

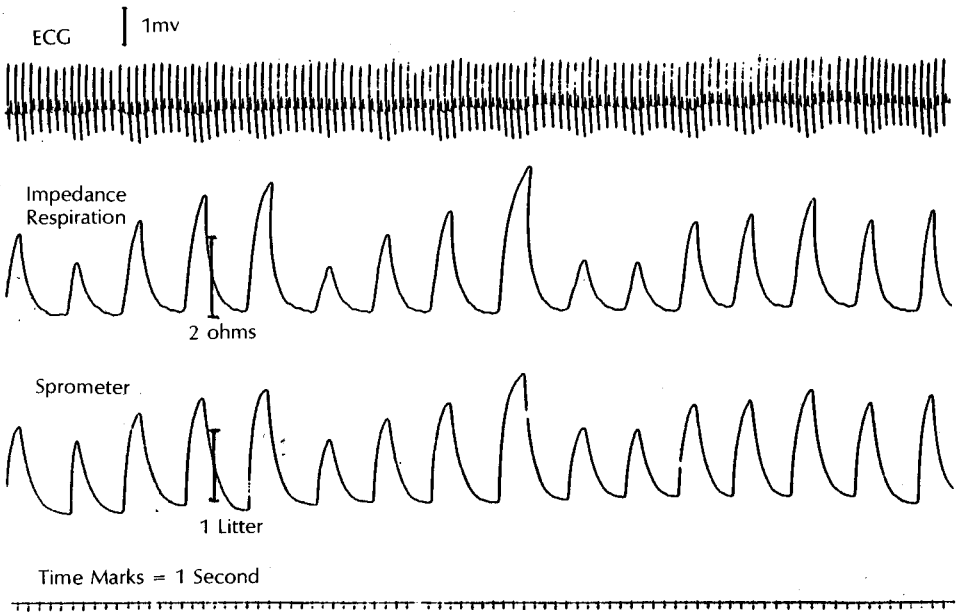


Fig. 6. *The electrocardiogram, impedance pneumogram, and spirogram.*

as a safe screening technique may well be its most valuable contribution.

Respiration

The use of electrical impedance to measure respiration is based upon the close correlation found experimentally between changes in the respired volume and changes in transthoracic impedance. The method is elegant in its simplicity, requiring only the application of two or four electrodes to the surface of the thorax. This technique does not require direct contact with the air stream, and hence does not impose any restriction on breathing; neither does it impose restrictions on body movements as do many volume-determining devices such as spirometers and pneumotachometers.

Figure 6 is a typical three-channel record of an electrocaridogram, an impedance pneumogram, and a spirogram in a human subject made with electrodes at the level of the xiphoid process and along the midaxillary lines. While the recording was being made, the subject was asked to vary his depth of respiration. The impedance and ECG recordings were made from the same pair of electrodes (Geddes *et al.* 1962).

The impedance-volume relationship has been investigated by McNally (1963), Kubicek (1964), Kinnen (1963), Allison (1964), and Baker (1965, 1967). The method has been applied to recording respiration in space flights and to patient monitoring (Geddes, 1964) and on unrestrained animals (Geddes 1962) and man during anesthesia (Farman, 1967; Baker, 1969; Noe, 1969).

Uterine contraction

Kornmesser and Nyboer (1962) developed an interesting noninvasive method of recording uterine contractions during labor in the pregnant human female. The method employed is sketched in Figure 7. Four silver electrodes were mounted in a band that maintained the electrodes against the abdomen in the position shown in Figure 7.a. A low intensity current (100 kHz) was admitted by the two outer electrodes (I_1, I_2), and the voltage that is proportional to the impedance between the potential-measuring electordes (E_1, E_2) was continuously recorded after amplification and demodulation.

The record of the impedance change between the two potential measuring electrodes was called an impedance hysterogram (IHG). A typical example of uterine contraction from a pregnant human female appears in Figure 7.b, along with the electrohysterogram (EHG), which is a recording of the slow

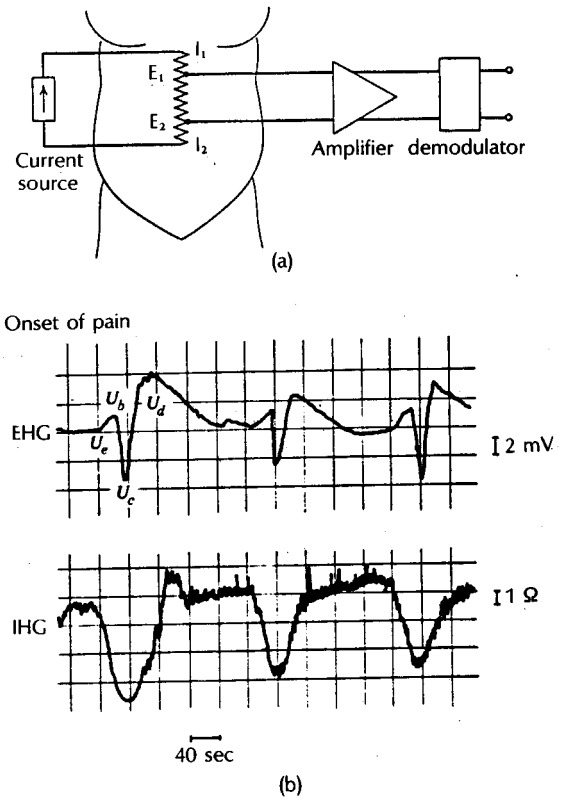


Fig. 7. *Arrangement of equipment for recording uterine contraction by impedance change, a record of which is called the impedance hysterogram (IHG). Also shown is electrohysterogram (EHG), the voltage change that accompanies uterine contractions, detectable with electrodes placed on the abdomen.*

changes in potential detected by electrodes on the abdomen (Larks 1960).

On the basis of clinical observations, Kornmesser and Nyboer suggested that the recorded impedance changes were related to mechanical displacement of the uterus during contraction. Such a suggestion is not without good foundation because during contraction the uterine contents (fetus and amniotic fluid) were displaced in a direction away from the potential-measuring electrodes. Amniotic fluid and uterine have the lowest resistivities of all biological fluids (Geddes and Baker 1967), and it is not surprising that displacement of this highly conducting mass is detectable with abdominal electrodes. An impedance hysterogram would appear to be a safe, practical method for recording the frequency of uterine contraction with pro-

perly placed electrodes, but little use has been made of this technique.

DISCUSSION

Impedance cardiography has been used extensively for monitoring cardiac function because it is noninvasive, has good reproducibility, gives beat-by-beat information, and is simple. However, the sources of the measured impedance change and their relative contributions to the thoracic impedance change are incompletely understood even though the values of cardiac output measured simultaneously by impedance cardiography and invasive clinical methods such as thermodilution correlate highly. Due to this lack of scientific basis for impedance cardiography, it has not been widely accepted by clinicians despite the advantages described above.

Though all the changes of volume, conductivity, and location of the organs in the thorax contribute to the impedance change measured by the potential electrodes, several origins have been though to be dominant (Mohapatra, 1981). These are: 1) decrease of the blood volume in the ventricles. 2) increase of the blood volume by aortic expansion. 3) decrease of the lung resistivity due to the blood perfusion in the lungs, and 4) decrease of the blood resistivity due to the orientation of the erythrocytes in the arteries during systole.

There have been numerous empirical studies using animals to identify the sources and their contributions to the impedance change. However, it is very difficult to identify the sources of the impedance change in animal experiments since there are so many physiological changes during a cardiac cycle and it is almost impossible to control these physiological changes.

Another promising approach to identifying the sources of the impedance change is through computer simulation of a three-dimensional model of the thorax (Silvest *et al.* 1974; Demers *et al.* 1976; Sakamoto *et al.* 1979; Kim, 1986; Kim *et al.* 1988). Kim et al. found that the blood volume changes in the aorta were roughly linear with the impedance change, which is one of the main assumptions of impedance cardiography.

CONCLUSION

The flexibility of the impedance method to detect a wide variety of physiological events is its chief attribute. Its chief drawback is the difficulty encountered in calibrating the impedance in true physiological terms. At present, many studies are underway to establish the relationship between impedance values and physiological events.

The impedance method is subject to the limitations inherent in many indirect techniques. Since frequently the signal is obtained at a distance from the phenomenon, resolution is compromised. However, signals that cannot be calibrated but directly reflect a physiological event can have considerable value for monitoring changes under a variety of experimentally controlled conditions.

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