Measurement of Intramyocardial Phasic Blood Flow Using Impedance Plethysmography

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SUMMARY

Impedance plethysmography was applied for the measurement of intramyocardial phasic blood flow. In the region of the left circumflex artery M-shaped blood flow curve was obtained in the outer and middle layer. This pattern did not resemble that of the inner layer. At the time of reactive hyperemia, increase in blood volume was seen within the myocardium.

Additional Indexing Words :

Reactive hyperemia Specific resistance Urethane coated electrode

COMplete method of measurement of intramyocardial phasic blood flow has never been settled up, though some aimed at it by indirect method in dog experiments.¹⁾ Although N₂O method,²⁾ isotope clearance method using ⁸⁶Rb³⁾ or ¹³¹I⁴⁾ and indicator dilution method⁵⁾ might give information on coronary flow, they are not informative on its phasic change. On the other hand, an electromagnetic flowmeter can measure phasic coronary flow, but it is limited to measure blood flow of comparatively large coronary artery exposed on the surface of the heart. In this study, in order to measure intramyocardial phasic blood flow, the impedance plethysmography with divided electrodes was applied.

PRINCIPLES AND METHODS

The impedance (Z_c) in ohm of a rectangular myocardial segment is determined by its specific resistance (ρ_c) expressed in ohm centimeter and its dimensions, length (l) in centimeter, and cross section (s) in square centimeter, according to the following formula :^{6),7)}

$$Z_c = \rho_c \cdot \frac{l}{s} \quad (1)$$

Since any fraction remains unchanged if multiplied or divided by a value which equals one, equation (1) may be expressed as :

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$$Z_c = \rho_c \cdot \frac{l}{s} \cdot \frac{l}{l} \quad (2)$$

As the product $s \cdot l$ is equal to volume (V_c), equation (2) may be rewritten as :

$$Z_c = \rho_c \cdot \frac{l^2}{V_c} \quad (3)$$

If the length of the rectangular myocardial segment is constant and the volume is increased by the change in blood volume (ΔV_b), likewise the impedance of only increased blood volume (Z_b) becomes as follows :

$$Z_b = \rho_b \cdot \frac{l^2}{\Delta V_b} \quad (4)$$

where ρ_b equals the specific resistance of blood.

When Z_b acts in parallel anatomically and electrically as a parallel impedance to Z_c , the change in impedance of Z_c (ΔZ_c) is written as follows as a result of the increased blood volume :

$$\Delta Z_c = \frac{1}{1/Z_b + 1/Z_c} - Z_c = - \frac{Z_c^2}{Z_b + Z_c} \quad (5)$$

and furthermore Z_b is much greater than Z_c , therefore ΔZ_c is approximately given by :

$$\Delta Z_c = - \frac{Z_c^2}{Z_b + Z_c} \simeq - \frac{Z_c^2}{Z_b} \quad (6)$$

By substituting equation (3) and (4) into equation (6), equation (6) is rearranged as :

$$\frac{\Delta V_b}{V_c} = - \frac{\rho_b}{\rho_c} \cdot \frac{\Delta Z_c}{Z_c} \quad (7)$$

Equation (7) means that the product of the fractional specific resistance of blood to cardiac muscle multiplied by the fractional change in impedance, approximately equals the fractional change in blood volume within the segment. The negative sign on the right side of equation (7) indicates that a small increase in volume brings about a decrease in electrical impedance. An increase or decrease of impedance is therefore produced by the blood being reduced or added to the segment respectively. Thus, if the fractional specific resistance of blood to cardiac muscle and the fractional change of Z_c are measurable, one should be able to calculate the fractional blood volume per unit mass of the myocardium.

Ten mongrel dogs weighing 16 to 21 Kg were subjected to the series of experiments. They were anesthetized with sodium pentobarbital (25 to 50 mg/Kg, iv) and the chest was opened in the 4th left intercostal space under artificial respiration. The heart was exposed by making longitudinal incision through the pericardium to approach the left coronary artery and the free wall of the left ventricle. A diagram of set-up of apparatus and preparation is shown in Fig. 1. An electromagnetic flowmeter probe (Nihon Kohden Kogyo Co, Tokyo, Japan) was placed

Fig. 1. Schematic representation of the apparatus for the measurement of intramyocardial phasic blood flow. EMF, electromagnetic flowmeter; HFA, high frequency amplifier; LFA, low frequency amplifier.

on the left circumflex artery to measure the coronary flow and close to the distal side of the probe a constrictor was placed around the coronary artery to occlude the coronary flow for several seconds. A catheter connected to a pressure transducer (Nihon Kohden) was inserted into the left ventricle via the left atrium to measure left ventricular pressure. A pair of urethane coated electrodes ($200\ \mu$ in diameter) which had small uncoated parts ($5\text{ mm} \times 1/3$ of circumference) were inserted face to face at the site of measurement. Each uncoated part was placed approximately 8 mm apart at the same depth. Near the electrodes a strain-gauge was located for observing a change in myocardial segment length around the electrodes before and during occlusion. A block diagram of the impedance plethysmograph (Nihon Kohden), whose frequency characteristics is DC to 100Hz, is shown in Fig. 1. Between the paired electrodes a 50kHz, 200 microampere constant current was supplied and impedance changes were continuously detected as voltage changes with a high-frequency amplifier. Detected impedance changes after dealing with a rectifier and low-frequency amplifier circuit were divided into 2 kinds of signals, one is DC component (Z_{DC}) which is limited above some reference level by a clipping circuit and the other is the impedance consisting of AC component (Z_{AC}).

After the recording a control state, the impedance was recorded during several second occlusion of the left circumflex artery (Nihon Kohden, Polygraph RM-1000). Fractional change in impedance was obtained by dividing the maximum difference of Z_{DC} before and during occlusion (ΔZ), by the impedance at end-diastolic phase before occlusion (Z_{ED}). Changes in impedance caused only by cardiac movement is canceled by the procedure of subtracting the impedance during occlusion from that before occlusion, providing that the heart has the same movement before and during occlusion. After the foregoing procedures were over, the

specific resistance of blood and cardiac muscle was measured by the same impedance plethysmograph in the free wall of the left ventricle and blood contained in the left ventricular cavity respectively, immediately after induced ventricular fibrillation. The depth of electrodes was measured in a manner perpendicular to the epicardium with cutting the ventricular free wall as close as possible to the electrodes and designated as a relative depth to wall thickness.

RESULTS

Fig. 2 shows one of the recordings illustrating a method for obtaining intramyocardial phasic blood flow depicted on the bottom tracing. In this case a pair of electrodes was inserted into the inner layer at depth of 8 mm from the epicardium (wall thickness 10 mm). In 2 sec after occluding the left circumflex artery, Z_{ED} was increased from 590 to 630 ohms as a result of the reduction of blood and at that time Z_{AC} changed from a control state. The left ventricular pressure and the segment length remain approximately unchanged. The postmortem fractional specific resistance of blood to

Fig. 2. Representative recording showing methods for obtaining intramyocardial phasic blood flow. Relative myocardial depth 0.8. From top to bottom; time scale, left ventricular pressure, segment length, impedance Z_{DC} , impedance Z_{AC} , and measured intramyocardial phasic blood flow (a solid line connecting the values successively). Z_{DC} was increased about 40 Ω at end-diastolic phase 2 sec after occluding the left circumflex artery. Z_{AC} changed from a control state. L. V. pressure and segment length remain approximately unchanged.

cardiac muscle was measured 0.29. Thus, the product of the fractional specific resistance 0.29 multiplied by the whole quantity the difference of Z_{DC} at each equivalent point of a cardiac cycle before and during occlusion divided by Z_{ED} (590 ohms), leads to the intramyocardial phasic blood flow contours as depicted on the bottom tracing in Fig. 2.

In a manner as stated above, observations were performed in the region of the left circumflex artery in each layer. The results are shown in Fig. 3 illustrating the average blood flow at the same depth of the myocardium. The numerals denoted by d , express the average depth of 2 electrodes in pair. When the depth of the 2 electrodes in pair differed more than 2.5 mm, the data were excluded out of evaluation. In the outer and middle layer, M-shaped blood flow curve was obtained. The first peak was coincident with isovolumetric contraction period and the second one was located in diastole.

Fig. 3. Intramyocardial blood flow curves in the outer, middle and inner layers. In the outer and middle layer, M-shaped blood flow curve was seen, while that in the inner layer was not clear M-shaped.

Fig. 4. Comparison of increase in blood volume during reactive hyperemia between the electromagnetic flowmeter and the impedance method. Relative myocardial depth 0.4. During occlusion Z_{DC} increased, while EMF showed zero flow. Following a 4.0 sec occlusion, Z_{DC} gradually decreased down and finally reached below control level, and EMF showed reactive hyperemia.

Fig. 5. Percent ratio of increase in blood volume at the time of reactive hyperemia in each layer. Discussed in text.

Fig. 6. Effect of occlusion of the anterior descending artery on flow in the region of the left circumflex artery. During occlusion, EMF mean flow on the left circumflex artery slightly increased and coincidentally small decrease in impedance was seen.

Fig. 7. Linear correlation between ratio of the specific resistance of blood to cardiac muscle and hematocrit.

While in the inner layer the flow curve was not clear M-shaped and rather has a tendency to be monophasic. The peak in diastole appeared earlier in the outer layer. The average blood flow was 0.0114, 0.0113, and 0.0150 in the outer, middle and inner layer respectively. Blood flow in the inner layer was greater than any other layers. In all observations the impedance (Z_{DC}) was always maintained at higher level several seconds after occlusion.

Increased values of blood volume during reactive hyperemia was observed both by the electromagnetic flowmeter and in the impedance method for the purpose of comparison. It is shown in Fig. 4. Immediately after the occlusion the electromagnetic flowmeter showed zero flow whereas the impedance Z_{DC} was increased a little later. The electromagnetic flowmeter showed reactive hyperemia which took place after 4.0 sec occlusion, while the impedance Z_{DC} decreased down little by little and finally reached below control level. This phenomenon implies that at this time blood volume was more abundant than that in a control state. It is concluded that at the time of reactive hyperemia the increase in blood volume took place also within the myocardium.

Ratio of increased blood volume to fractional blood volume at the time of reactive hyperemia are shown in percentage in Fig. 5. Average values of percent change in blood volume in middle and outer layer are 60.0% (s.d. 12.4) and 69.0% (s.d. 14.5) respectively, while that in the inner layer is 35.5% (s.d. 8.0). This may indicate that the capacity of the coronary vascular reserve is poor in the inner layer in comparison with that in the outer layer.

Fig. 6 shows the effect of occlusion of the anterior descending artery on the flow in the region of the left circumflex artery. When the anterior descending artery was occluded, the electromagnetic mean flow on the left circumflex artery slightly increased and coincidentally small decrease in impedance was seen as a result of increase in blood volume in the region of the left circumflex artery. Similar observation, an increase in coronary blood flow in vessels adjacent to the occluded arteries, was made by Herzberg et al.⁸⁾

The ratio of the specific resistance of blood to that of cardiac muscle is plotted as a function of hematocrit in Fig. 7. A significant correlation ($r=0.941$) was found between them. The linear regression equation for ρ_b/ρ_c as a function of hematocrit was calculated to be $Y=0.00889X+0.0441$.

DISCUSSION

The fundamental equation already mentioned in the foregoing chapter becomes available only when the movement of the myocardium at the site of electrodes should have the same way before and during occlusion. If it is

altered, some errors might intervene the results because it is impossible to avoid impedance changes caused by cardiac movement. Relative errors of the impedance (Z) on the left side in equation (1), equals the sum of those of ρ , l , and s . Therefore, suppose the distance between the paired electrodes is settled at 8 mm, ± 0.8 mm change in cardiac movement caused by occlusion gives $\pm 10\%$ relative errors of Z under the condition of constant ρ and s . This value is also equivalent to relative errors of fractional blood volume on the left side in equation (7). In all observations of this study, errors caused only by the change in cardiac movement before and during occlusion were less than several percents.

The surface areas of electrodes used in this experiment were small as compared with the distance between paired electrodes, therefore under these conditions the current flux distribution would be curved outside of a straight line between the electrodes. But it is supposed that the current flows dominantly in the straight course between the electrodes, so the experimental results could be estimated to be the changes only in the localized parts of the myocardium where electrodes were inserted.

The absolute values of the impedance obtained in this series of experiments are smaller than the values calculated theoretically by substituting the known numerals into the formula $Z = \rho \cdot l / s$. This must be due to the traumatic bleeding caused by the insertion of the electrodes. By this traumatic injury, shortening of the distance between paired electrodes and enlargement of the effective surface area of the electrodes took place. Accordingly, the former gave smaller value to l and the latter gave larger one to s than those expected theoretically.

Thinking over the electrical impedance in biological materials, behavior of tissue and fluid in a time-varying field should at first be taken into consideration. Referring to Kraus' criteria⁹⁾ for classification whether the medium behaves as a conductive, semiconductive or dielectric, sea water can be substitutive for cardiac muscle. Therefore, the following speculation is to be done on sea water in stead of cardiac muscle. Here cardiac muscle is thought to be almost perfect conductor at 50 kHz. It is concluded that the change in impedance measured in this experiment was produced essentially by a resistive change.

When the left circumflex artery is occluded, it is estimated that all blood contained in the arterioles, capillaries, and venules is squeezed into the venous side by myocardial contraction. Therefore, the intramyocardial blood flow obtained in this experiment can be thought to be total blood flow in situ. However, this is pretty lower than that of Gibson et al.¹⁰⁾ They used isotope techniques in order to determine the blood volume in coronary arterioles,

capillaries, and venules in cardiac arrest, and obtained 6.6 ml/100 Gm cardiac muscle in average (fractional blood volume ; 0.066, if the specific gravity of cardiac muscle is 1.0). The reason why the mean values in this method was considerably different from the data of Gibson et al¹⁰⁾ might probably due to the fact that blood contained in the coronary vessels was not completely squeezed out.

The peak which appeared in isovolumetric contraction period is coincident with so called early systolic backflow observed in the electromagnetic flowmeter tracing of the left circumflex artery. The impedance plethysmography cannot differentiate forward flow from backward. Therefore, the first peak appeared inversely to that of the electromagnetic flowmeter.

The second peak appearing in the outer and middle layer must be identical with the forward larger flow in diastole observed in the electromagnetic flowmeter on the left circumflex artery. In the middle layer the second peak was seen later than that in the outer layer. This mechanism is not clear, but it might be due mainly to the difference of the intramyocardial pressure.

It has been pointed out that myocardial blood flow in the endocardial side of the left ventricle is larger than that in the epicardial side.^{4), 11), 12)} In this study mean flow in the inner layer was larger than that in other layers. Myers and Honig¹³⁾ studied number of intramyocardial capillaries and its distribution, and concluded that a vascularity gradient increasing from epicardium to endocardium exists throughout the ventricular myocardium.

The monophasic tendency of phasic flow in the inner layer could be explained by the anatomical characteristics of the inner layer of the left ventricle. Some investigators^{14)–16)} have found that intramyocardial tissue pressure in the endocardial side is much larger than that in the epicardial side during systole and even exceeds left ventricular pressure. Accordingly, the pressure condition surrounding the vessels in the inner layer must fluctuate in a wide range. It is obvious that there should be a wide fluctuations in the blood flow in a same way. In this view there is some conflict in findings in Fig. 3 in which the flow curve in the inner layer tends to be monophasic. The inner layer of the left ventricle has some anatomical drainage to the ventricular cavity.¹⁷⁾ Therefore, it can be supposed that during occlusion by-passed blood will be, to some extent, left there. This remaining blood lessens the difference between the impedance before and during occlusion, consequently the fluctuation of the flow curve is calculated much smaller than as it is. The mean flow in the inner layer shown in Fig. 3 also seems to be much smaller in appearance. Moir and Debra¹⁸⁾ suggest that in the experiment in RI clearance method there may be isotope uptake of endocardial side directly from the ventricular cavity.

According to Kinnen et al.¹⁹⁾ the specific resistance of cardiac muscle and blood of a dog at body temperature and 100 kHz are $456 \Omega \cdot \text{cm}$ and $108 \Omega \cdot \text{cm}$ (29% hematocrit) to $153 \Omega \cdot \text{cm}$ (47% hematocrit) respectively. The results shown in Fig. 7 took generally a little larger value compared with the values calculated from the data by Kinnen et al.¹⁹⁾ This might be caused by the difference of frequency used in the measuring device or size and type of electrodes. The specific resistance of blood is also dependent on hematocrit and a nearly linear relationship between blood and hematocrit is obtained. In order to keep a linear relationship between ρ_b/ρ_c and hematocrit shown in Fig. 7, ρ_c should be independent of hematocrit, therefore the data suggest that the blood volume contained in the myocardium is a little.

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REFERENCES

1. Eckstein RW, Moir TW, Driscoll TE: Phasic and mean blood flow in the canine septal artery and an estimate of systolic resistance in deep myocardial vessels. *Circulat Res* **12**: 203, 1963
2. Eckenhooff JE, Hafkenschiel JH, Harmel MH, Goodale WT, Lubin M, Bing RJ, Kety SS: Measurement of coronary blood flow by the nitrous method. *Am J Physiol* **152**: 356, 1948
3. Love WD, Romney RB, Burch GE: Comparison of distribution of potassium and exchangeable rubidium in organs of dog, using rubidium⁸⁶. *Circulat Res* **2**: 112, 1954
4. Griggs DM, Jr, Nakamura Y: Effect of coronary constriction on myocardial distribution of iodoantipyrine-¹³¹I. *Am J Physiol* **215**: 1082, 1968
5. Sevelius G, Johnson PC: Myocardial blood flow determined by surface counting and ratio formula. *J Lab Clin Med* **54**: 669, 1959
6. Nyboer J: Electrical Impedance Plethysmography. CC Thomas, Springfield, Ill, 7, 1959
7. Allison RD, Holmes EL, Nyboer J: Volumetric dynamics of respiration as measured by electrical impedance plethysmography. *J Appl Physiol* **19**: 166, 1964
8. Herzberg RM, Rubio R, Berne RM: Coronary occlusion and embolism: effect on blood flow in adjacent arteries. *Am J Physiol* **210**: 169, 1966
9. Kraus JD: Electromagnetics. McGraw-Hill Book Co, New York, 120, 1953
10. Gibson JG, Seligman AM, Peacock WC, Aub JC, Fine J, Evans RD: The distribution of red cells and plasma in large and minute vessels of the normal dog, determined by radioactive isotopes of iron and iodine. *J Clin Invest* **25**: 848, 1946
11. Love WD, Tyler MD: Effect of hypoxemia and hypercapnia on regional distribution of myocardial blood flow. *Am J Physiol* **208**: 1211, 1965
12. Moir TW, Debra DW: Effect of left ventricular hypertension, ischemia and vasoactive drugs on the myocardial distribution of coronary flow. *Circulat Res* **21**: 65, 1967
13. Myers WW, Honig CR: Number and distribution of capillaries as determinants of myocardial oxygen tension. *Am J Physiol* **207**: 653, 1964

14. Johnson JR, Di Palma JR: Intramyocardial pressure and its relation to aortic blood pressure. *Am J Physiol* **125**: 234, 1939
15. Gregg DE, Eckstein RW: Measurements of intramyocardial pressure. *Am J Physiol* **132**: 781, 1941
16. Kirk ES, Honig CR: An experimental and theoretical analysis of myocardial tissue pressure. *Am J Physiol* **207**: 361, 1964
17. Bartelstone HJ, Scherlag BJ, Cranefield PF, Hoffman BF: Partition of canine coronary blood flow. *Bull New York Acad Med* **42**: 951, 1966
18. Moir TW, Debra DW: Measurement of the endocardial distribution of left ventricular coronary blood flow by Rb⁸⁶ chloride. *Am Heart J* **69**: 795, 1965
19. Kinnen E, Kubicek W, Hill P, Turton G: Thoracic cage impedance measurements. (Tissue resistivity in vivo and transthoracic impedance at 100 kc/s.) USAF School of Aerospace Medicine technical documentary report SAM-TDR-64-5, Brooks Air Force Base, Texas, 1, 1964