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Coronary Flow. Method of Returning Coronary Bolus

CARLOS A. LEGUIZAMÓN

Biomatemática, Area de Protección y Seguridad, Comisión Nacional de Energía Atómica, and Departamento de Matemática, Facultad de Ciencias Exactas y Naturales, UBA. Buenos Aires, Argentina

ELMA A. A. TENREYRO

Biomatemática, Area de Protección y Seguridad, Comisión Nacional de Energía Atómica, Buenos Aires, Argentina

AND

VICTORIO PECORINI

Departamento de Biología Nuclear Aplicada, Area de Radioisótopos y Radiaciones, Comisión Nacional de Energía Atómica, Buenos Aires, Argentina

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This paper presents a mathematical procedure in order to obtain the coronary flow. The analysis is accomplished by considering an intravascular tracer and its detection in the right ventricle at the beginning and end of the ventricular phase of expulsion.

1. Introduction

The present work introduces a mathematical method of analysis of the parameters involved in the detection of the passage of an intravascular tracer through the right ventricle, in order to calculate the coronary flow. Information is essentially derived from registers of the tracer's return from the coronary circulation towards that chamber.

In order to simplify the statement of the mathematical procedure involved, reference is made to a radioactive bolus, detected externally by means of usual radiocardiographic techniques. However, this method is also applicable to other techniques adopted, provided that they satisfy the conditions which will be mentioned below.

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The mathematical analysis of the passage of a tracer bolus through cardiac circulation follows the general pattern described in earlier papers (Betti, Tenreyro & Leguizamón, 1973*a*, *b*; Leguizamón, Betti & Tenreyro, 1972; Tenreyro *et al.*, 1973).

2. General Conditions

Though in this paper we make reference to the radiocardiographic technique as a means of obtaining the mathematical expressions, the method described can be generally applied to other techniques provided they meet with prescribed conditions. This technique is based on the assumption that a dose of tracer X_0 is injected into a peripheric vein close to the right ventricle. (Fig. 1 shows a diagram of the blood circulation). This shot of

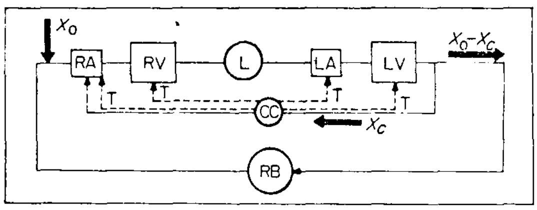

FIG. 1. Diagram of blood circulation. *RA:* right auricle, *RV:* right ventricle. *L:* lungs. *LA:* left auricle. *LV:* left ventricle. *CC:* coronary circulation. *RB*: blood circulation through the rest of the body. *T:* Thebesian coronary circulation.

tracer is transformed into a radioactive bolus, which must be retained intravascularly throughout the experiment. As this bolus flows through the blood stream there is a continuous distribution of radioactive concentrations, which tend to decrease in time due to successive mixing of the bolus with the blood stream, until complete and uniform mixing is attained (radioactive concentration C_p). This occurs after the experimental method referred to is completed. The tracer bolus passes successively through the right auricle (RA), right ventricle (RV), lung beds (L), left auricle (LA) and left ventricle (LV). After this chamber, the original bolus is divided between the coronary circulation (CC) (to which it supplies a dose X_c), and the remainder of the total blood circulation (RB) (dose $X_0 - X_c$), passing onward through the aorta and subsequent vessels. The fraction of the original bolus which entered the coronary circulation is divided between a principal return going to the right auricle again and subsidiary pathways such as the Thebesian veins, so that through these a negligible flow will pass directly to the left and right chambers (lines marked T in Fig. 1). As this flow is negligible, and as the flow which passes to the left chambers is the only unregistered fraction, it is assumed that the dose X_c entering the coronary circulation will be the same as that going to the right auricle by the main returning route. Thus, this radioactive bolus is termed "returning coronary bolus", and will again pass through the right ventricle, lung beds, left auricle, left ventricle, and so on.

As regards the original injection, it should be noted that it must be made suddenly and with the greatest amount of tracer which were possible, during only one diastole into the right ventricle. These requirements arise from the need, for statistical reasons, to eliminate noise corresponding to small fractional doses from the register. Moreover a sudden shot should also enable a better detection only in the right ventricle, then, if radiocardiographic method were applied, the register in this chamber should not be modified by the contribution of counting rates originated in other chambers. This can be achieved through perfect collimation by means of a regular scintillation crystal, which can also be aided by use of the Anger camera. With it a shot of gaseous radioactive product injected next to the right ventricle will facilitate the location of this chamber during the whole cardiac cycles. This gaseous product will be eliminated through lungs, after which, with inhalation of a new gaseous radioactive product, this will pass through the left chambers, and consequently their position relative to the right ventricle will be obtained. By this method the sites where the right ventricle can be "seen alone" are readily determined (selective radiocardiography). The selection of these sites are obtained by the analysis of different positions of the detector respect to the heart. It must be stressed that for the cases of uniform concentration of the tracer into the ventricle, the sites "seen alone" may cover only a part of the right ventricle. So, if the statistic is good, it shall be easier to place the detector. Using a similar method, a better statistic is obtained if registers of the right ventricle are made with a common detector capable of good collimation, as was noted above (Tenreyro *et al.*, 1970, 1973). The counting rates (H) will be proportional to the amount of tracer contained in the right ventricle, being related by the corresponding efficiency E_v.

By means of Fig. 2 it is possible to recognize the cardiac cycle where the three different bolus initiate and terminate their entrance to the right ventricle. Thus we have:

$i = 1$: first cycle in which the original bolus (X_0) enters the right ventricle

$i = n_r$: first cycle in which the returning coronary bolus (X_c) enters the right ventricle.

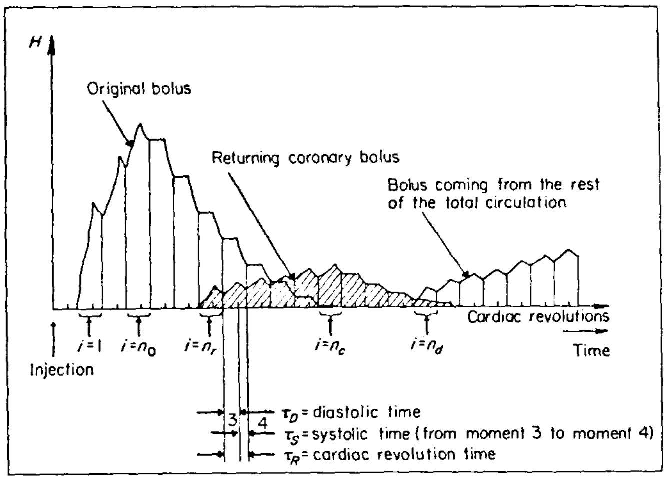

FIG. 2. Right ventricle registrations. Each radioactive bolus is considered as isolated.

$i = n_0$: last cycle in which the originary bolus (X_0) enters the right ventricle.

$i = n_c$: last cycle in which the returning coronary bolus (X_c) enters the right ventricle.

$i = n_d$: first cycle in which the bolus coming from the remainder of the total circulation enters the right ventricle.

It is considered that:

$$n_0 + 1 < n_r \tag{1}$$

$$n_c + 1 < n_d \tag{2}$$

as may be recognized from Fig. 2.

As is shown in this figure, detection of activity in the right ventricle cannot be negligible when cycle n_r is produced. This can be the case when the last fraction of the original bolus (X_0) is in the right ventricle, and its first fraction, which passed on to the aorta, was distributed between the first part of the returning coronary bolus (appearing at n_r) and the first part of the bolus going to the rest of the total circulation. In this instance, the component of the returning coronary bolus is obtained by deducting the values corresponding to the remainder of the original bolus from the total register. These values can be obtained by extrapolation, as this remnant of the original bolus follows an exponential function during the cycles n_0+1, $n_0+2, \ldots$, for the same physiological moments (for instance when the diastole is initiated).

It must be added that condition (1) is satisfied provided that the dose X_0 is injected suddenly, and into or very close to the right ventricle.

This is also useful to satisfy condition (2). If this one is not satisfied, that is, if the bolus coming from the remainder of the total body circulation enters the right ventricle during the cyles when the returning coronary bolus is still entering this chamber, then the foregoing mathematical procedure is no longer valid. In this case, and only with reference to radioactive methods, a combination of the previous method with injection of a different radionucleide into the left ventricle may be attempted, so the condition (2) could be performed in many more cases due to the fact of a more sudden radioactive output from the left ventricle when the shot is made in it. Thus, discrimination of the two different radioactive tracers registered in the right ventricle, will give the counting rate corresponding to the returning coronary bolus of the radionucleide injected into the left ventricle, which is independent of the counting rates due to the radionucleide injected next to the right ventricle. Injection of the first radionucleide into the right ventricle is used to calculate the efficiency of the detection of the second radionucleide.

The previous analysis of conditions (1) and (2) by means of Fig. 2, it is useful for considering the moments of possible contributions of counting rates from lungs, right atrium, left heart and coronary bed. Thus, if the right ventricle cannot be "seen alone", then a convenient design may reduce strange contributions and it may give an approximate value of coronary flow by the present method.

In order to obtain this, the detector must be located in such a manner that the radioactivity of lungs be discarded and the radioactivity of right atrium and left heart "seen" by a detector be a minimum. This can be resolved by a good collimation (Tenreyro *et al.*, 1970).

As the next expressions (20) and (21) are used to get the coronary flow, it is interesting to analyse the influence of contributions from right auricle, left heart and coronary bed. The difference of counting rates into the systolic time of expression (21) during the first cycles up to n_0, is only influenced by the variation of contribution from the beginning to the end of the ventricular systole, coming from right atrium. In order to obtain this only contribution, the bolus X_0 must enter to the left heart after the cycle n_0+1. From this, it is also null the contribution of the coronary bed.

Concerning to the counting rate at the moment of cycle n_0+1 [expression (21)] there are no influences from any chamber, if the bolus X_0 goes into the left heart as before. Similar instants for the expression (20) have other alternatives. Thus, the difference of counting rates during the beginning and end of the ventricular systolic time may be influenced from contributions coming from right auricle and left heart, and this is the principal reason for locating the detector for a minimum of contribution coming from these chambers. Respect to the coronary bed, it has no influence on results because the radioactivity in it may be considered the same at both moments of measure.

In the same expression (20) the counting rate at the instant n_c+1 is not theoretically affected by any chamber or coronary bed. This is true when the first part of the returning coronary bolus (that passed between n_r and n_c through the right ventricle) have not again arrived to left heart (and coronary bed and right auricle, of course). In spite of this fact may be possible, the analysis cannot be followed because it is depending on other factors, as experimental conditions, statistic reasons, noises, and so on; which are out of the present mathematical development. The previous analysis indicates that other chambers and coronary bed may only partially affect the validity of expressions (20) and (21), in the case of right ventricle cannot be detected alone. Thus, also in this case, the method may be useful for approximative values of coronary flow.

From a strictly experimental point of view, it is stressed that the method requires sufficient quantity of tracer and change in volume, that the difference in the registers between systole and diastole of right ventricle can be statistically worked, out of those given by noise.

3. Relations Between Flow and Dose

The injected dose X_0 is forced out from the left ventricle during successive ventricular systoles. In each of these, the left ventricle ejects a systolic flow ϕ_{s_j} during the j systolic time interval $\mathscr{T}_{s_j}$, and with a concentration of activity C_j which is assumed to be uniform. We then have:

$$X_0 = \sum_{j=1}^{\infty} \phi_{s_j} \cdot \mathscr{T}_{s_j} \cdot C_j. \tag{3}$$

This expression can be obtained in terms of the total flow ϕ_{T_j}, considered for each cycle j during the time interval $\mathscr{T}_{R_j}$. Thus, we have:

$$\phi_{s_j} \cdot \mathscr{T}_{s_j} = \phi_{T_j} \cdot \mathscr{T}_{R_j}$$

such that:

$$X_0 = \sum_{j=1}^{\infty} \phi_{T_j} \; \mathscr{T}_{R_j} \; C_j. \tag{4}$$

The mean aortic flow $\bar{\phi}_T$, which corresponds to the flow in the aortic root is defined during the cycles $j = 1, 2, \ldots,$ by:

$$\bar{\phi}_T = \frac{\sum_{j=1}^{\infty} \phi_{T_j} \cdot \mathscr{T}_{R_j} \cdot C_j.}{\sum_{j=1}^{\infty} \mathscr{T}_{R_j} \cdot C_j} \tag{5}$$

From equations (4) and (5) it follows that:

$$X_0 = \bar{\phi}_T \cdot \sum_{j=1}^{\infty} \mathscr{T}_{R_j} \cdot C_j. \tag{6}$$

The bolus entering the coronary circulation carries a total dose X_c determined mathematically by the sum of the coronary flow ϕ_{c_k} produced during each cardiac cycle $\mathscr{T}_{R_k}$, with a concentration of activity C_k^c. Thus, we have:

$$X_c = \sum_{k=1}^{\infty} \phi_{C_k} \cdot \mathscr{T}_{R_k} \cdot C_k^c. \tag{7}$$

The mean coronary flow $\bar{\phi}_c$ is defined by the expression:

$$\bar{\phi}_c = \frac{\sum_{k=1}^{\infty} \phi_{C_k} \cdot \mathscr{T}_{R_k} \cdot C_k^c.}{\sum_{k=1}^{\infty} \mathscr{T}_{R_k} \cdot C_k^c} \tag{8}$$

From equations (7) and (8) we obtain

$$X_c = \bar{\phi}_c \cdot \sum_{k=1}^{\infty} \mathscr{T}_{R_k} \cdot C_k^c \tag{9}$$

and from equations (6) and (9) we have:

$$\bar{\phi}_c = \bar{\phi}_T \cdot \frac{X_c}{X_o} \cdot \frac{\sum_{j=1}^{\infty} \mathscr{T}_{R_j} \cdot C_j}{\sum_{k=1}^{\infty} \mathscr{T}_{R_k} \cdot C_k^c} \tag{10}$$

In this equation, the subindex j indicates the cardiac revolutions during which the original bolus is ejected from the left ventricle, while the subindex k indicates those cycles during which the inflow of the radioactive coronary bolus is at the entrance of its bed.

In practice, both subindexes may be equated: the first inflow of activity into the coronary bed takes place during the same cardiac cycle as the first outflow of activity from the left ventricle. Then:

$$\frac{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j}{\sum_{k=1}^{\infty} \mathscr{C}_{R_k} \cdot C_k^c} \simeq \frac{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j}{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j^c} \tag{11}$$

The mean concentration at the root of the aorta is defined by:

$$\bar{C} = \frac{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j}{\sum_{j=1}^{\infty} \mathscr{C}_{R_j}} . \tag{12}$$

The mean concentration of the inflow to the coronary bed is defined by:

$$\bar{C}^c = \frac{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j^c}{\sum_{j=1}^{\infty} \mathscr{C}_{R_j}} . \tag{13}$$

From equations (11) and (13) it follows that:

$$\frac{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j}{\sum_{k=1}^{\infty} \mathscr{C}_{R_k} \cdot C_k^c} \simeq \frac{\bar{C}}{\bar{C}^c} . \tag{14}$$

The ratio of the sums indicated in equation (14) is approximately equal to that of the mean concentrations of the outflow from the left ventricle and the inflow to the coronary bed, defined according to equations (12) and (13), throughout the total number of cycles during which the expulsion of the radioactive bolus from the left ventricle takes place. If these mean concentrations are considered to be approximately equal in an average, which is acceptable from the experimental viewpoint and from the anatomic features involved, it will follow that:

$$\frac{\sum_{j=1}^{\infty} \mathscr{C}_{R_j} \cdot C_j}{\sum_{k=1}^{\infty} \mathscr{C}_{R_k} \cdot C_k^c} \simeq 1 \tag{15}$$

then:

$$\bar{\Phi}_c \simeq \bar{\Phi}_T \cdot \frac{X_c}{X_0} \tag{16}$$

according to which the doses are distributed in relation to flows (Maseri, Kushnir, Duce, Pesola & Donato, 1969; Sheppard, 1962).

4. Calculation of the Dose returning by Way of Coronary Circulation

The dose of radioactivity which returns from the coronary circulation to the right chambers of the heart and which is detected in the right ventricle, is assumed to be equal to that entering the coronary circulation from the aorta. Thus, the dose X_c ejected during successive systoles of the right ventricle will be determined between moments 3 and 4 when the ventricular systole begins and ends respectively. The dose X_c will be registrable starting from revolution n_r, so that

$$X_c = \sum_{i=n_r}^{\infty} d^r_{34_i} = \sum_{i=n_r}^{n_c} d^r_{34_i} + \sum_{i=n_c+1}^{\infty} d^r_{34_i}, \tag{17}$$

where $d^r_{34_i}$ is the fraction of the dose of returning coronary bolus ejected from the right ventricle during moments 3 and 4 of the ith systole.

From equation (17) the expression

$$\sum_{i=n_r}^{n_c} d^r_{34_i}$$

may be given by:

$$\sum_{i=n_r}^{n_c} d^r_{34_i} = \frac{1}{E_v}\sum_{i=n_r}^{n_c} (H^r_{4_i} - H^r_{3_i}) = \frac{1}{E_v}\sum_{i=n_r}^{n_c} \Delta H^r_{34_i} \tag{18}$$

and the expression

$$\sum_{i=n_c+1}^{\infty} d^r_{34_i}$$

denotes the dose present in the right ventricle at the begining of the n_c+1 ventricular systole. It can be expressed in terms of the counting rate as:

$$\sum_{i=n_c+1}^{\infty} d^r_{34_i} = \frac{1}{E_v} H^r_{3\,(n_c+1)} \tag{19}$$

From equations (17), (18) and (19), we get:

$$X_c = \frac{1}{E_v}\left[\sum_{i=n_r}^{n_c} \Delta H^r_{34_i} + H^r_{3\,(n_c+1)}\right]. \tag{20}$$

The efficiency E_v is obtained from the passage of the original bolus through the right ventricle (Betti, 1973*b*) by means of:

$$E_v = \frac{1}{X_0}\left[\sum_{i=1}^{n_o} \Delta H_{34_i} + H_{3\,(n_o+1)}\right] \tag{21}$$

From equations (20) and (21) we get:

$$X_c = X_0 \frac{\sum_{i=n_r}^{n_c} \Delta H^r_{34_i} + H^r_{3\,(n_c+1)}}{\sum_{i=1}^{n_o} \Delta H_{34_i} + H_{3\,(n_o+1)}} \tag{22}$$

5. Coronary Flow Calculation

Equations (16) and (22) enable us to obtain an expression for coronary flow in terms of the counting rates registered in the right ventricle, and the total flow:

$$\bar{\Phi}_c \simeq \bar{\Phi}_T \frac{\sum_{i=n_r}^{n_c} \Delta H^r_{34_i} + H^r_{3\,(n_c+1)}}{\sum_{i=1}^{n_o} \Delta H_{34_i} + H_{3\,(n_o+1)}} \tag{23}$$

The mean aortic flow $\bar{\Phi}_T$ can be obtained from the expression:

$$\bar{\Phi}_T = \frac{\mathrm{f} \cdot \overline{\Delta H}^p_{34}}{C_p \cdot E_v} \tag{24}$$

which can be derived from the new radiocardiographic technique termed "total mixing zone" (Leguizamón *et al.*, 1972). This method uses the registers obtained once the tracer has been uniformly distributed throughout the blood stream. In equation (24) f denotes the frequency, C_p the concentration of tracer uniformly distributed in the blood stream, $\overline{\Delta H}^p_{34}$ the mean value of ΔH^p_{34} which is the difference between the counting rates registered at the beginning (moment 3) and at the end (moment 4) of the ventricular systole, both counting rates being registered during the interval of total mixing xone. E_v can be obtained from equation (21).

ΔH^p_{34} can be obtained from

$$\Delta H^p_{34} = d^p_{34} \cdot E_v, \tag{25}$$

where d^p_{34} denotes the dose ejected by the right ventricle during the systole at the total mixing zone. This dose can be expressed in terms of C_p and the ejected blood volume (v) during the systole. Thus,

$$d^p_{34} = C_p \cdot v \tag{26}$$

and

$$\Delta H^p_{34} = C_p \cdot v \cdot E_v \tag{27}$$

The mean $\bar{\Delta}\bar{H}^{p}_{34}$ is obtained directly from a given number of systoles, by averaging the different systolic blood volumes ejected for a concentration C_p which is assumed to be constant.

Thus

$$\bar{\Delta}\bar{H}^{p}_{34} = C_p \cdot E_v \cdot \bar{V}, \tag{28}$$

where $\bar{V}$ is the mean ventricular systolic volume.

Moreover, we have the expression

$$\bar{\Phi}_T = f \cdot \bar{v} \tag{29}$$

Thus, from equations (28) and (29), we can readily derive expression (24). As regards $\bar{\Phi}_T$, it can be obtained by applying other experimental techniques, such as those described in earlier papers (Leguizamón *et al.*, 1972, Tenreyro *et al.*, 1974).

6. Discussion

The present work furnished a simple mathematical development used to calculate coronary flow, which involves the nutritional flow and that passing directly from arterioles to veins. The Thebesian coronary flow is only partially considered, that is, the fraction of this flow which goes to the left chamber of the heart, is neglected. It must be stressed that this method is not exclusively applicable to radiocardiographic techniques.

Note

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