MEASUREMENT OF FLOW THROUGH BRANCHED SYSTEMS USING EXTERNAL RADIATION DETECTORS

Stephen W. Thompson

University of New Mexico School of Medicine, Albuquerque, New Mexico

Time-dilution curves made after intravenous injection of a radioactive indicator and monitored by externally placed radiation detectors offer a simple means of studying circulation. A detector placed over the heart can monitor the rise and fall of radioactivity produced by the first passage through this organ of the entire amount of an intravenously injected dose of indicator. The area under the curve obtained is inversely proportional to cardiac output and can be used to measure this function (*1*). A detector placed over the periphery, on the other hand, can monitor only the first passage through the circulation of that portion of the indicator which passes through the peripheral region within its range. The resultant curve reflects certain quantitative aspects of blood flow through this region, but the relation is more complicated than in the case of the heart curve. Moreover, the areas under both the peripheral and the heart curve are inversely proportional to cardiac output regardless of the amount of the peripheral flow (*2*). Despite these problems, various methods of using this technique for studying peripheral blood flow have been described. Most of these studies have been concerned with cerebral circulation using curves produced by radiation detectors placed against the head (*3–6*).

One such method for measuring cerebral blood flow has been proposed by the author (*4,5*). This procedure is based on an analysis of factors determining the dimensions of a time-dilution curve made by continuously measuring the concentration of an indicator at a point in a branch channel situated downstream from the location of the injection.

The purposes of this paper are to discuss the theoretical analysis on which the method is based and to present the results of testing this hypothesis through curves produced by using a simple flow model.

THEORETICAL BACKGROUND

Consider that a radiation detector is placed against the side of a hollow tube containing flowing fluid. The tube bifurcates into two branches at a point downstream from this detector, and a second radiation detector is placed against one of these branches. A small amount of radioactive indicator, injected into the fluid in the main tube upstream to the first detector, will pass this detector contained within a segment of flowing fluid or bolus. When this bolus reaches the bifurcation, it divides and a portion of the original amount, or bolus portion, passes the second detector. Thus each detector monitors a rise and fall of radioactivity. Two different time-dilution curves can be constructed by plotting these changes on the vertical axis of a graph against time on the horizontal axis (Fig. 1).

Received Aug. 12, 1968; original accepted Feb. 28, 1969.

For reprints contact: Stephen W. Thompson, Dept. of Neurology, Univ. of New Mexico School of Medicine, 930 Stanford N.E., Albuquerque, N.M. 87106.

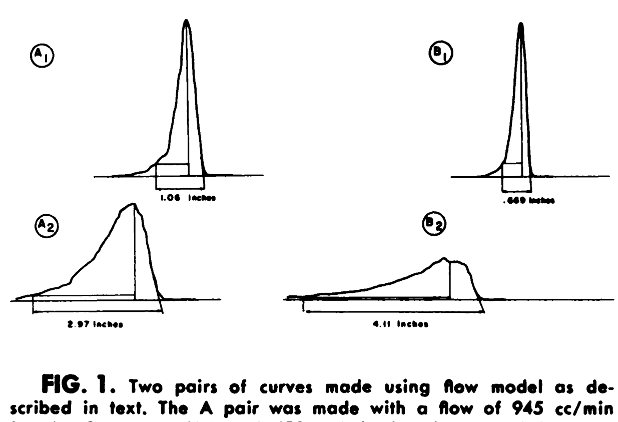

FIG. 1. Two pairs of curves made using flow model as described in text. The A pair was made with a flow of 945 cc/min for the first curve (A_1) and 490 cc/min for the second (A_2). For the B pair of curves the flow was 1,615 cc/min for the first (B_1) and 300 cc/min for the second (B_2).

The following postulates about these curves will be discussed:

1. The two time-dilution curves vary in length inversely with the respective mean concentrations of indicator which produced them, and any difference in length is determined only by this variable;
2. The area of each curve is inversely proportional to the flow rate through the main channel, and the area of the curve produced by the detector placed against the branch is not affected by flow rate through that branch; and
3. Flow rate through the branch is inversely proportional to the difference in length between the two curves.

Consider first the curve produced by the detector placed over the main channel of the tube and let subscript 1 denote expressions pertaining to this curve. The length of the curve (T_1) which represents the time required for the bolus to pass the detector is proportional to the bolus length (L_1) at the location of the detector and inversely proportional to the velocity (S_1) at which it is traveling at this location. Thus

$$T_1 = \frac{L_1}{S_1} t \qquad (1)$$

in which t is the factor converting units of time to linear units on the horizontal axis of the graph.

Curve height at any given point represents the amount of radioactive energy being detected at that instant. Thus the mean height of the curve (H_1) is proportional to the mean concentration of radioactive energy (C_1) within the bolus as it passes the detector. If the sensitivity of the detector system (K_1) is defined as the ratio of the deflection of the detector system to the concentration of radioactivity in the tube at the point where the detector is located, the mean height of the curve can be expressed by

$$H_1 = C_1K_1. \qquad (2)$$

The area of the curve (A_1) is T_1H_1 or

$$A_1 = \frac{L_1C_1K_1}{S_1} t \qquad (3)$$

If a_1 is the cross sectional area of the bolus at the location of the detector, the flow rate (F_1) is

$$F_1 = a_1S_1. \qquad (4)$$

Using this in the expression for A_1,

$$A_1 = \frac{a_1L_1C_1K_1}{F_1} t. \qquad (5)$$

It will be seen that a_1L_1 is the volume of the bolus at the time it passes the detector and that $a_1L_1C_1$ is the amount of radioactivity in the bolus and hence the dose of radioactive energy originally injected (d). Therefore

$$A_1 = \frac{dK_1}{F_1} t \qquad (6)$$

and

$$F_1 = \frac{dK_1}{A_1} t. \qquad (7)$$

Next, consider the curve produced by the detector placed against one of the branches from the main channel and let subscript 2 denote expressions pertaining to this curve. Then,

$$T_2 = \frac{L_2}{S_2} t, \qquad (8)$$

$$H_2 = C_2K_2 \qquad (9)$$

and

$$A_2 = \frac{L_2C_2K_2}{S_2} t \qquad (10)$$

as with the first curve.

L_2 and S_2 can be expressed differently. The fraction of the original bolus which traverses the branch to produce Curve 2 is considered to be equal to the fraction of the total flow which traverses the branch. Thus if M_1 is the volume of the bolus which produced the first curve and M_2 is that of the bolus portion which produced the second curve,

$$\frac{M_2}{M_1} = \frac{F_2}{F_1} \qquad (11)$$

and

$$M_2 = \frac{M_1F_2}{F_1}. \qquad (12)$$

However, any variation between the mean concentration (C_1) of indicator within the bolus which produced the first curve and that (C_2) within the bolus portion which produced the second would cause an inversely proportional effect on the respective volumes (M_1 and M_2) of the bolus and its portion. Therefore, the expression must be modified:

$$M_2 = \frac{M_1F_2C_1}{F_1C_2}. \qquad (13)$$

The volume of the bolus or of its portion at any given point along the tube or its branch can be expressed as the product of its cross sectional area and its length. Therefore

$$M_2 = a_2L_2 \qquad (14)$$

and

$$M_1 = a_1L_1. \qquad (15)$$

Substituting these in the expression for M_2,

$$a_2L_2 = \frac{a_1L_1F_2C_1}{F_1C_2} \qquad (16)$$

and

$$L_2 = \frac{a_1L_1F_2C_1}{a_2F_1C_2}. \qquad (17)$$

The velocity (S_2) of the bolus portion producing the second curve will vary with the velocity (S_1) of the bolus which produced the first. The velocities (S_2 and S_1) will vary directly with the ratio of the flow rates (F_2-to-F_1) and indirectly with the cross sectional areas (a_2-to-a_1).

$$S_2 = S_1 \frac{F_2 a_1}{F_1 a_2}. \tag{18}$$

Substituting these expressions for L_2 and S_2 in the original expression of T_2 and cancelling,

$$T_2 = \frac{L_1 C_1}{S_1 C_2} t. \tag{19}$$

Inasmuch as $T_1 = \frac{L_1}{S_1} t$ (Eq. 1), it is evident that

$$T_2 = T_1 \frac{C_1}{C_2}. \tag{20}$$

Therefore any difference between T_1 and T_2 depends on the difference between C_1 and C_2 and is independent of all other variables. This is the expression of Postulate 1.

The area of the second curve can now be expressed as

$$A_2 = \frac{L_1 C_1 K_2}{S_1} t \tag{21}$$

and, using the reasoning applied to the derivation of the area of the first curve,

$$A_2 = \frac{a_1 L_1 C_1 K_2}{F_1} t \tag{22}$$

or

$$A_2 = \frac{dK_2}{F_1} t \tag{23}$$

and

$$F_1 = \frac{dK_2}{A_2} t. \tag{24}$$

The area of the first curve, as previously noted (Eq. 6), can be expressed as $A_1 = (dK_1/F_1)t$. Therefore, A_1 and A_2 differ only as K_1 and K_2 differ, both are related in the same way to F_1, and A_2 is unaffected by F_2. This is the expression of Postulate 2.

In Fig. 1 it can be seen that the second curve is longer than the first. According to Postulate 1 this is because the mean concentration of the indicator in the bolus when recorded in the main channel by the first detector is greater than in the bolus portion recorded in the branch by the second detector. In other words, the portion of the bolus recorded by the second detector has become more dilute as it passed from the region monitored by the first detector.

This dilution is considered to be due to laminar flow which causes the indicator to spread into a constantly increasing volume of fluid vehicle as it moves through the tube. In this way, the portion of the bolus destined to be recorded by the second detector incorporates or acquires a volume of fluid vehicle as it travels through the tube from the region monitored by the first detector through that monitored by the second. It is this acquired volume that is responsible for the dilution referred to above.

The size of this acquired volume (I), which is considered the result of "spreading" of the indicator due to laminar flow, is independent of the volume of the incorporating bolus portion, but it is directly proportional to the volume of tubular lumen through which this bolus portion passes on its way from the first detector through the region monitored by the second. Thus the acquired volume would be the same for all curves made using the same tube system although it would be different for different systems.

To express the preceding statement quantitatively, T_2 can be considered as consisting of two parts: (1) that part which would be present if no dilution had occurred, and (2) that part for which the acquired volume is responsible. According to Postulate 1 (and Eq. 20), the former part, regardless of all other factors, is equal to the length of the first curve (T_1). Thus the part contributed by the acquired volume is always T_2–T_1.

Let x equal the fraction or percentage of the total flow (and of the original bolus) which passes through the branch. Then $F_2 = F_1 x$ and the acquired volume (I) can be expressed as

$$I = \frac{T_2 - T_1}{T_1} M_1 x \tag{25}$$

in which M_1 is the volume of the original bolus when it produced the first curve.

Solving for x in the above expression

$$x = \frac{I T_1}{M_1 (T_2 - T_1)}. \tag{26}$$

Inasmuch as $F_2 = F_1 x$,

$$F_2 = \frac{F_1 I T_1}{M_1 (T_2 - T_1)}. \tag{27}$$

Another expression for M_1 can be derived using the total flow (F_1) and the time (T_1) required for the original bolus to pass the first detector

$$M_1 = F_1 T_1. \tag{28}$$

Substituting this in the above expression for F_2

$$F_2 = \frac{I}{T_2 - T_1} \tag{29}$$

which is an expression of Postulate 3.

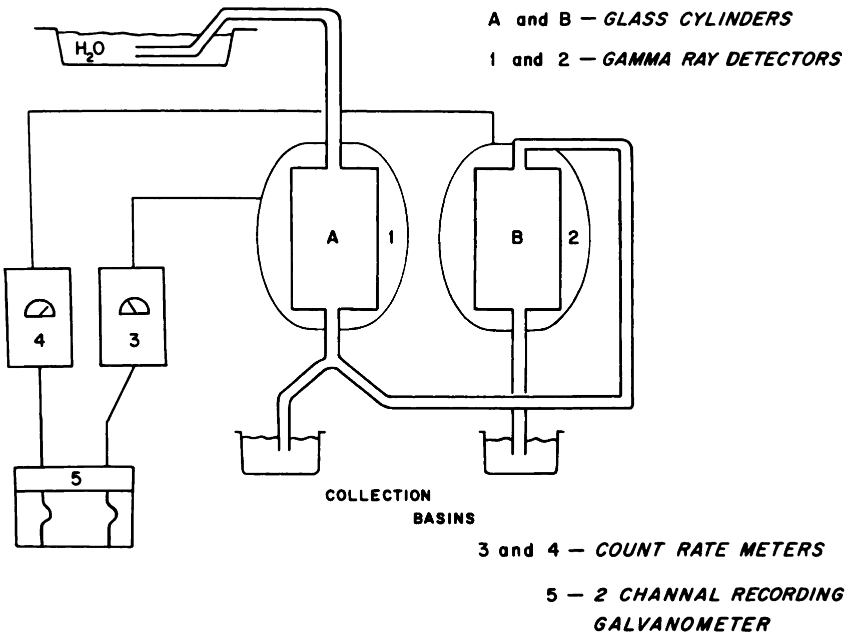

FIG. 2. Schematic diagram of flow model system used in experiments. Clamps were placed on tubing to regulate flow rate through first and second cylinders.

METHOD

A simple flow model was constructed using two glass cylinders interconnected with rubber tubing (Fig. 2). Water flowed through one tube and through the first cylinder and then into a bifurcated tube so that flow through one of the branches traversed the second cylinder. The flow rate through the first cylinder could be varied and the portion of this flow which reached the second cylinder also could be varied by clamps on the tubing. The flow rate through each of these cylinders was measured by making timed collections of the run-off from the system.

Each of the two cylinders was held in place against the end of a shielded gamma-ray detector which was connected through a count-rate meter to a recording galvanometer with a paper speed of 12 in./min.

Time-dilution curves were made with a rapid injection of radioiodinated diodrast (between 0.63 μCi and 2.7 μCi) into the tubing upstream to the first cylinder. A rise and fall of radioactivity in each of the cylinders resulted so that a curve was produced by each of the detectors on its respective recorder. Fifteen pairs of curves were made by using varying combinations of flow rates through the cylinders.

The sensitivity of each of the detectors (K_1 in Eq. 2 and K_2 in Eq. 9) was determined by filling each of the cylinders with a solution of radioiodinated diodrast of known concentration and measuring the deflection produced on each of the recorders. The result was 63.9 in./μCi/cc (K_1) for the first cylinder and its detector and 119.24 in./μCi/cc (K_2) for the second cylinder and its detector.

The total area of each curve was measured in square inches with a planimeter. Although irregularity of the down-slope frequently obscured the exact location of its union with the base line (Fig. 1), total-area measurements were considered accurate because of the close proximity of the down-slope to the base line near the end of the curve. Total length measurements, on the other hand, were often impossible because of inability to locate accurately the point of union between down-slope and base line. It was more practical to locate the point of intersection of the down-slope with a horizontal line 9% of the peak height of the curve above the base line. At this point the down-slope is steeper and the intersection relatively easily discerned. The length of each curve was measured in inches from its beginning to this point so that analogous portions of all curves were measured. These lengths were designated partial curve lengths. The areas of these same curve portions also were measured in square inches with a planimeter and designated partial curve areas.

RESULTS

The results are given in the tables where the curve pairs are numbered 1 through 15 in order of increasing difference in flow between the first and second cylinder.

Table 1 shows the actual flow rate in cc/min through each of the cylinders for each pair of curves and the flow rate through the first cylinder calculated from each of the curves using Eq. 7 for the first curve of each pair and Eq. 24 for the second curve in which $t = 12$, which is the paper speed of the recorder in in./min. A_1 and A_2 are the total curve areas.

Table 2 shows the total areas, A_1 and A_2, for each curve pair, the partial areas, A'_1 and A'_2, and the ratios A_1-to-A_2 and A'_1-to-A'_2.

In Table 3 the partial curve lengths are given in inches. The mean concentration of radioactivity which produced each curve is shown in the next column. This value is calculated by using Eq. 2 for the first curve of each pair and Eq. 9 for the second curve. H_1 and H_2, the mean heights of the curves, were derived by dividing the partial area of each curve by its partial length. Thus the mean concentrations are those for analogous parts of the curves rather than for the total curves. The last column shows the theoretical value of T_2 if derived from T_1 using Eq. 20.

Table 4 compares the actual flow rate (F_2) through the second cylinder for each curve pair with a factor (F'_2) which theoretically is propor-

TABLE 1. FLOW RATES

Curve pair number	True flow rate (cc/min)		Calculated flow rate for first cylinder (cc/min)	
	F_2 second cylinder	F_1 first cylinder	Using area of curve from first cylinder (Eq. 7)	Using area of curve from second cylinder (Eq. 24)
1	260	260	259	258
2	570	570	539	570
3	395	510	511	600
4	410	525	516	568
5	282	403	400	452
6	490	945	947	1,047
7	480	1,000	989	1,166
8	280	1,565	1,561	1,919
9	320	1,620	1,606	1,883
10	265	1,570	1,568	1,846
11	250	1,565	1,596	2,114
12	300	1,615	1,624	2,065
13	203	1,570	1,515	2,029
14	210	1,593	1,607	2,106
15	200	1,610	1,601	2,289

TABLE 2. CURVE AREAS

Curve pair number	Total curve areas (in.^{2})		Partial curve areas (in.^{2})		Ratio A_1-to-A_2	Ratio A'_1-to-A'_2
	A_1	A_2	A'_1	A'_2		
1	1.87	3.50	1.78	3.39	0.53	0.53
2	1.16	2.04	1.05	1.90	0.57	0.55
3	2.51	3.98	2.40	3.87	0.63	0.62
4	2.29	3.86	2.15	3.73	0.59	0.58
5	3.19	5.27	3.03	5.16	0.61	0.59
6	1.96	3.30	1.88	3.10	0.59	0.61
7	2.12	3.36	2.01	3.20	0.63	0.63
8	0.87	1.32	0.83	1.30	0.66	0.64
9	1.27	2.01	1.20	1.93	0.63	0.62
10	0.91	1.44	0.87	1.39	0.63	0.63
11	0.82	1.16	0.80	1.10	0.71	0.73
12	1.27	1.94	1.21	1.82	0.65	0.66
13	0.89	1.37	0.81	1.31	0.65	0.62
14	0.85	1.33	0.82	1.26	0.64	0.65
15	0.82	1.18	0.78	1.16	0.69	0.67

TABLE 3. RELATIONSHIP OF CONCENTRATION OF RADIOACTIVITY TO CURVE LENGTH

Curve pair number	Partial curve lengths (in.)		Mean concentration of radioactivity for each curve (μCi/cc)		Predicted value of T_2 based on Eq. 20
	T_1	T_2	C_1	C_2	
1	4.43	7.80	0.0063	0.0036	7.75
2	1.65	3.25	0.0099	0.0049	3.33
3	2.22	4.41	0.017	0.0074	5.10
4	1.97	4.49	0.017	0.0070	4.78
5	2.60	5.94	0.018	0.0073	6.41
6	1.06	2.97	0.028	0.0087	3.41
7	1.00	3.07	0.031	0.0087	3.56
8	0.689	4.23	0.019	0.0026	5.04
9	0.630	3.90	0.030	0.0041	4.61
10	0.669	4.37	0.020	0.0027	4.96
11	0.748	4.49	0.017	0.0020	6.36
12	0.669	4.11	0.028	0.0037	5.06
13	0.689	5.63	0.018	0.0020	6.20
14	0.669	5.37	0.019	0.0020	6.36
15	0.689	5.53	0.018	0.0018	6.89

TABLE 4. COMPARISON OF FLOW FACTOR WITH TRUE FLOW IN SECOND CYLINDER

Curve pair number	Flow rate, second cylinder (cc/min)	Factor proportional to F_2 based on Eq. 29	Ratio
	F_2	F'_2	F_2-to-F'_2
1	260	29.67	8.76
2	570	62.50	9.12
3	395	45.66	8.65
4	410	39.68	10.33
5	282	29.94	9.41
6	490	52.36	9.36
7	480	48.31	9.94
8	280	28.25	9.91
9	320	30.58	10.46
10	265	27.03	9.80
11	250	26.74	9.35
12	300	29.07	10.32
13	203	20.24	10.03
14	210	21.28	9.87
15	200	20.66	9.68

tional to this flow rate. This factor was derived using Eq. 29. Although I, as defined in the derivation of this equation, is not obtainable in absolute terms, it would be constant for all curve pairs made using the same flow model. Therefore, the factor F'_2 was obtained using the arbitrarily chosen number 100 for this constant. Thus, F'_2 is an index of flow expressed in arbitrary units. The last column of Table 4 shows the ratio of F_2-to-F'_2 for each of the pairs of curves. If F'_2 is exactly proportional to F_2, this ratio should be the same for each of the pairs of curves.

DISCUSSION

Calculations of flow rates through the first cylinder (main channel) using the areas of curves from this same cylinder (Eq. 7) gave accurate results (Table 1). According to Postulate 2, the areas of curves from the second or branched cylinder also could be used to calculate the flow rates through the first cylinder (Eq. 24). The correlation was reasonable although results from the second curves were a little high (Table 1); this tendency was more pronounced the greater the difference between the flows in the two cylinders. This result is best explained by considering that the curve areas used in Eq. 24 became relatively smaller as the difference in flow between the two cylinders became greater. The reason for this effect could be that, as the flow difference between the cylinders increased, the percentage of the total dose of radioactive indicator which traversed the second cylinder (to make the second curve) became increasingly less than the percentage of the total flow which traversed this cylinder. The assumption that these two percentages would be equal was made in the derivation of Eq. 24. Furthermore, the same assumption must be made when human cardiac output is measured using an intravenous injection of indicator and a time concentration curve is then obtained from the peripheral circulation (*2,7*). Van der Feer has shown that this assumption is reasonable when applied to the human circulation (*8*).

According to Postulate 2, the ratio of the areas of the first and second curve of each pair should be constant regardless of any difference in flow between the two cylinders. Table 2 supports this postulate although, again, the areas of curves from the second cylinder became relatively smaller as the difference in flow rates between the two cylinders increased.

A comparison of the ratio of the total curve areas A_1-to-A_2 with that of the partial curve areas A'_1-to-A'_2 for each curve pair shows good correlation (Table 2). Thus it seems reasonable to consider that analogous portions of the total curves are included in the partial curve areas.

The results of testing Postulate 1 are given in Table 3 which shows a fairly close correlation between the length of the second curve of each pair (T_2) and its predicted length (last column). These findings are based on the postulate that the first and second curves vary in length inversely with the respective mean concentrations of radioactivity which produced them as is expressed by Eq. 20. There is some tendency for the predicted value to be high. This result again seems to be more marked the greater the difference in flow between the two cylinders, suggesting that C_2 became relatively smaller as the difference in flow between the two cylinders became greater. If so, the probable explanation is the previously suggested disparity between the percentages of injected indicator and total flow which traversed the second cylinder.

Table 4 shows that the ratio of the true flow rate through the second cylinder (F_2) to the factor theoretically proportional to this flow rate (F'_2) does not vary greatly among all the curve pairs. For this reason, F'_2 is considered to be a quantitative expression of the flow rate through the second cylinder. The fact that the ratio F_2-to-F'_2 is not constant for all curve pairs means that F'_2 is not a precise value. The inequality suggested above between the percentages of injected indicator and total flow which went through the second cylinder cannot explain this inaccuracy inasmuch as this inequality tended to become more marked as the disparity in flow between the two cylinders became greater. Thus, the effect would have been to cause a larger inaccuracy as the flow differences between the two cylinders increased. The variation in the ratio F_2 to F'_2 does not seem to show such a trend. In addition, an inequality between the fraction of injected indicator and that of the total flow passing through the second cylinder would have less effect on the length of the second curve than on its area, and F'_2 does not depend on area as do the previously discussed results from which such an inequality was inferred. This inaccuracy probably is secondary to other, unexplained factors.

The quantitative expression of flow rate through the second (branched) cylinder gives a new dimension to the application of time-dilution curves to the measurement of flow through branched systems. The situation is analogous to that of a radioactive indicator injected intravenously (and thus into the heart) and a time-dilution curve is recorded by a detector placed over the heart (main channel) and another by a detector placed over a peripheral region (branch). The classical dilution principal using the area under either of these curves permitted measurement of the flow rate through the main channel only (*2,7*). The new concept described here allows quantitative analysis of the flow rate through the peripheral region, and its application to a method for measuring cerebral blood flow has been proposed (*4,5*).

SUMMARY

Time-dilution curves made by monitoring an intravenously injected radioisotope through externally placed radiation detectors provide a way of studying circulation. Attempts have been made to study the peripheral circulation using curves resulting from monitoring that portion of an injected indicator which passes through the peripheral region in question. The classical dilution principal, using the area under such a curve from the periphery, however, lets one measure only cardiac output and gives no information about peripheral flow.

This paper describes an analysis of time-dilution curves made with a branched tube through which fluid is flowing. If a radioactive tracer is injected into the main channel and its passage is monitored downstream by two externally placed detectors, one placed over the main channel and the other over one of the branches, the difference in length between the two resulting curves is inversely proportional to the flow rate through the branch. Thus a factor proportional to flow rate through the branch can be derived. The situation is analogous to that resulting when a radioactive indicator is injected intravenously and monitored by detectors placed over the heart and the periphery. A method for measuring cerebral blood flow based on this concept has been proposed previously.

Tests of this hypothesis using time-dilution curves made with a simple flow model are presented.

ACKNOWLEDGMENT

Supported in part by NIH Grant No. NB-03568-04.

REFERENCES

1. HUFF, R. L., FELLER, D. D., JUDD, O. J. AND BOGARDUS, G. M.: Cardiac output of men and dogs measured by in vivo analysis of iodinated (I^{131}) human serum albumin. *Circulation Res.* **3**:564, 1955.

2. VAN DER FEER, Y.: *The Determination of Cardiac Output by the Injection Method.* Excelsior, The Hague, 1958, p. 25.

3. OLDENDORF, W. H.: Measurement of the mean transit time of cerebral circulation by external detection of an intravenously injected radioisotope. *J. Nucl. Med.* **3**:382, 1962.

4. THOMPSON, S. W.: A radioisotope method for studying cerebral circulation. *Arch. Neurol.* **5**:580, 1961.

5. THOMPSON, S. W.: Cerebral blood flow assessment with a radioisotope method. *Arch. Neurol.* **10**:12, 1964.

6. BOHIM, E., ARONSON, G., HUGGOSSON, R., GRANGSJO, G., ULFENDAHL, H. R. AND WOLGAST, M.: Cerebral circulatory conditions in patients with ruptured aneurisms measured by an intravenous radioactive indicator technique. *Acta Neurol.* **44**:33, 1968.

7. HAMILTON, W. F., RILEY, R. L., ATTYAH, A. M., COURAND, A., FOWELL, D. M., HEMMELSTEIN, A., NOLDE, R. B. P., REMMINGTON, J. W., RICHARDS, D. W., WHEELER, N. C. AND WITHAM, A. C.: Comparison of the Fick and dye methods of measuring the cardiac output in man. *Am. J. Physiol.* **153**:309, 1948.

8. VAN DER FEER, Y.: *The Determination of Cardiac Output by the Injection Method.* Excelsior, The Hague, 1958, p. 40.