Forearm Blood Flow Measurements Using Technetium-99m Human Serum Albumin Following Brachial Arteriotomy

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A simple, low cost method for measuring forearm blood flow during reactive hyperemia has been developed. Subjects are seated with hands and forearms over a large field-of-view gamma camera. Blood pressure cuffs inflated above the elbows isolate the blood in the forearms and hands and induce a hyperemic response. The remaining blood pool is labeled with technetium. The rate of increase of activity following release of the cuffs is measured from the gradient of time-activity curves and is calibrated for flow by counting a venous blood sample. The technique has been applied to a group of normal controls and to symptomatic and asymptomatic patients following right brachial arteriotomy. Forearm blood flow in normal subjects was 32.9 ± 6.4 ml/100 ml/min and for subjects with occlusion of the brachial artery was 6.4 ± 2.1 ml/100 ml/min. The method is simple, widely available, and reproducible. The good signal to noise ratio allows it to be used in cases of very low flow either as an aid to diagnosis or to measure treatment response.

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Retrograde catheterization of the coronary arteries and left ventricle via brachial arteriotomy has been an accepted technique in evaluating coronary heart disease for over 30 years (*1*). This procedure is associated with a small proportion of serious complications. Ischemia of the forearm is the main potential hazard and several investigations (*2–5*) have reported the incidence of impaired peripheral blood flow varying from between 0.9% (*5*) to 24% (*3*). Indirect methods were used to assess peripheral perfusion in these studies including subjective grading of radial artery pulsation and blood pressure differences between the two arms.

According to Machleder (*3*), a weakened or absent radial pulse was a frequent outcome following brachial artery catheterization. The significance of this is uncertain. In some patients the extremities of the limbs appeared to be warm with no other symptoms of ischemia, whereas in other cases abnormal pulse was associated with severe claudication.

Venous occlusion plethysmography (*6*) has been used to measure blood flow in limbs, but it has a poor signal to noise ratio, uses equipment which is not widely available, and has poor reproducibility at low flow rates. Doppler ultrasound flow detection is a simple and noninvasive technique that can be used to aid diagnosis but it is difficult to produce quantitative flow measurements from flow velocity and only gives information about a single vessel (*7*).

An accurate and sensitive measurement of the forearm blood flow under conditions of hyperemia induced by either exercise or arterial occlusion is needed to assess the significance of changes in radial pulse and to quantify the reduction in blood flow in symptomatic and asymptomatic subjects.

Radionuclides have been used previously to study blood flow in patients with peripheral vascular disease by measuring clearance rates of technetium-99m (^{99m}Tc) following an intramuscular injection (*8*) and by first-pass radionuclide arteriography (*9*). Both methods have proved sensitive in detecting peripheral vascular disease, but they do not lend themselves to absolute measurements of flow. Muscle clearance of xenon-133 (^{133}Xe) has the potential to give absolute values of flow

Measured flow ml/min

+ R = 0.99
--- p < 0.001
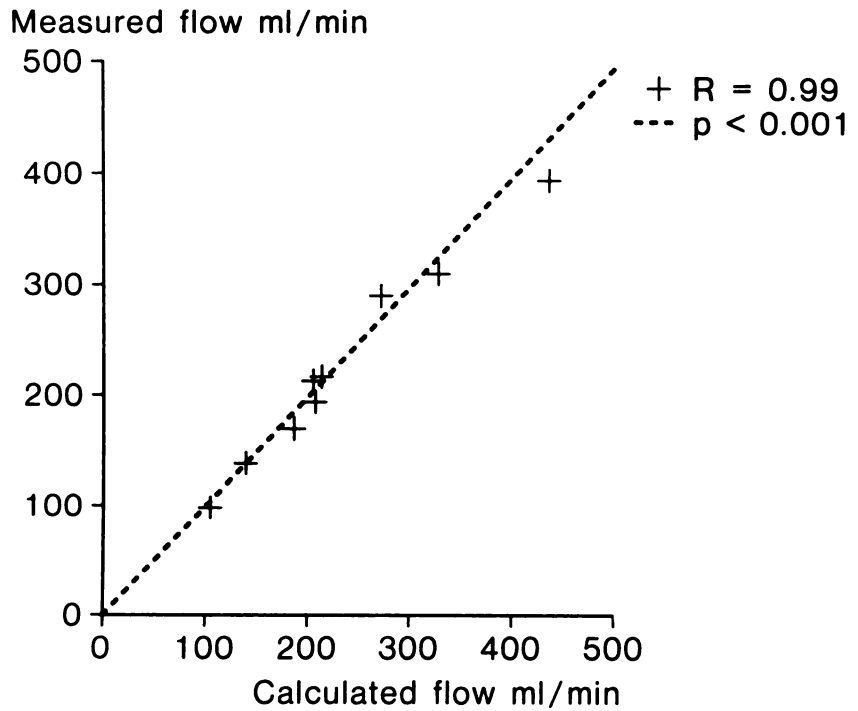
FIGURE 1
Flow measurements from limb phantom.

Calculated flow ml/min

per unit volume (*10*) but this is only to a small volume of tissue around the injection site and is subject to errors due to retention of tracer by fat and local inflammation following injection.

A simple noninvasive method of measuring blood flow in the legs during reactive hyperemia has been described previously (*11*). Subjects are positioned supine with legs and feet over a large field-of-view gamma

camera. Blood pressure cuffs inflated below the knees isolate the blood in the legs and induce a hyperemic response while the remaining blood pool is labeled with technetium. The rate of increase of activity in the limbs following the release of the cuffs is measured from the gradient of time-activity curves and these are calibrated for flow by counting a venous blood sample from the patient. Studies using a tissue equivalent leg phantom
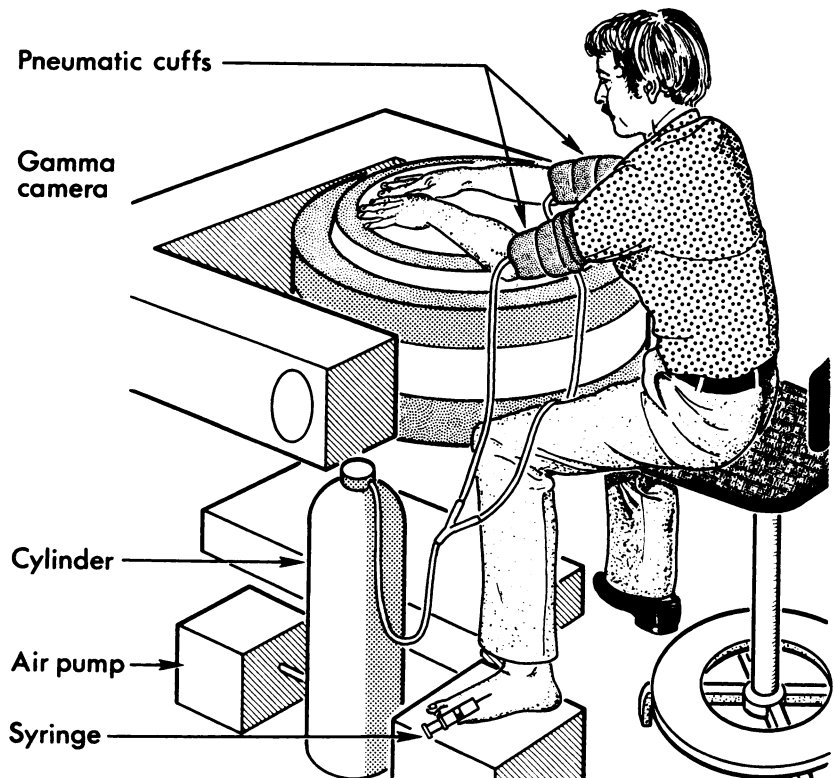

Pneumatic cuffs

Gamma camera

Cylinder

Air pump

FIGURE 2
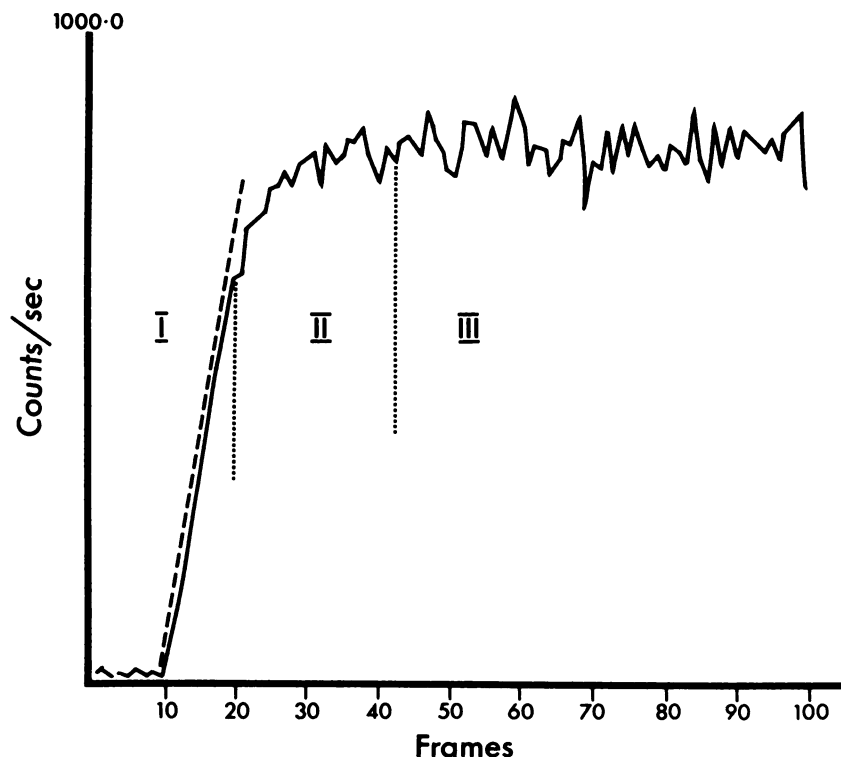Patient positioning for blood flow measurements.

Syringe

FIGURE 3
Time-activity curve from a normal subject.

connected to a peristaltic pump have shown this method to give an accurate measurement of flow (*11*). The phantom was placed on the gamma camera and connected to a reservoir containing ^{99m}Tc which was thoroughly mixed. The outflow from the phantom was collected in a measuring cylinder so that absolute flow could be determined. The calculated flow in ml/min obtained from the gradient of the time-activity curve and from counting a sample of reservoir liquid was found to differ from measured flows by < 6% over a wide range of pump speeds (Fig. 1).

In the present study, this technique has been adapted to measure flow in the upper limbs. A group of normal controls has been studied to establish a normal range. Reproducibility has been assessed by repeating the measurements in 13 subjects (15 limbs).

TABLE 1
Forearm Blood Flow in Normal Subjects (ml/100 ml/min)

Subject	R arm	L arm
1	22.4	25.1
2	39.4	32.0
3	24.6	30.0
4	37.1	33.1
5	46.5	44.9
6	29.6	32.3
7	34.8	32.4
8	29.8	32.5

Mean = 32.9
Standard deviation = 6.4

Results are reported for a group of patients undergoing catheterization of the right brachial artery and for five patients presenting with claudication of the right forearm following catheterization and closure of the arteriotomy with a purse string suture.

METHOD

Eight healthy male volunteers age 25–64 yr with no history of peripheral vascular disease were studied to establish a normal range.

Eight patients (two female) age 41–65 yr were studied before and after brachial arteriotomy. They were suffering from coronary artery disease (*5*), valvular heart disease (*2*), and presumed coronary artery spasm (*1*). None of these patients had ischemic symptoms related to the right forearm before or after brachial arteriotomy and there were no significant differences in the volume of the radial pulse or blood pressure in each arm. Five additional patients (two female) age 40–52 yr with forearm claudication were examined after brachial arteriotomy. Only one patient had pain at rest and this was the only subject with a noticeably paler right forearm. The brachial and radial pulses were absent in the right arm in all five patients.

To assess the reproducibility, two of the normal controls and three patients undergoing right cervical sympathectomy were studied on two occasions. The left arms of the three sympathectomy patients and the eight pre- and post-catheter patients were used giving a total of 15 limbs.

Subjects are rested at an ambient temperature of 25°C and are then seated in front of a large field-of-view gamma camera fitted with a high sensitivity collimator. The hands and forearms are placed in contact with the collimator (Fig. 2) and the limit of the field of view is marked on the skin with a pen. Blood pressure cuffs are wrapped around the arms immedi-
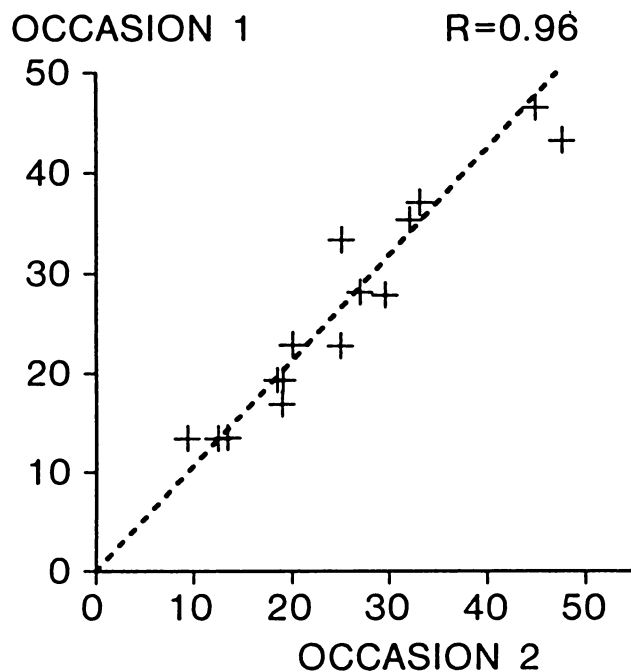
FIGURE 4
Reproducibility of arm blood flow measurements in ml/100 ml/min.

ately above the elbow and are rapidly inflated to 300 mmHg. The purpose of the cuffs is to isolate the blood in the arms from the rest of the pool and to induce a hyperemic response. The occlusion time must be sufficiently long to induce a reproducible hyperemic response and to allow complete mixing of tracer in the blood pool. It must also be tolerable for the patient and must not risk occluding in situ grafts. To determine the time necessary for complete mixing of our tracer in the blood pool, 14 subjects for limb blood flow measurements were given 400 MBq of tracer into an antecubital vein and serial blood samples were taken from the opposite arm and counted. Our results showed that complete mixing of the tracer had occurred by 3 min (12). Measurements of hyperemic flow in the legs have been shown to vary with the period of occlusion (13) with a maximum response being obtained after 5 min of occlusion. It was found in practice that 5 min of occlusion was not tolerable in all patients so a compromise was reached using 4 min of occlu-

TABLE 2
Forearm Blood Flow (ml/100 ml/min) in Asymptomatic Subjects

Subject	Pre-catheter		Postcatheter	
	Right	Left	Right	Left
1	19.7	16.9	20.0	19.0
2	22.0	19.3	18.8	18.1
3	25.2	22.9	20.0	20.1
4	16.6	13.4	14.9	12.5
5	33.2	33.4	30.1	25.1
6	10.2	13.4	12.5	9.4
7	29.4	28.2	25.0	27.0
8	30.0	22.8	26.8	25.0

sion but asking subjects to exercise the hands for 2 min by squeezing rubber balls, during occlusion.

After inflating the cuffs, 400 MBq of ^{99m}Tc-labeled human serum albumin is given into a dorsal foot vein and flushed with 20 ml of saline. This tracer has been shown to remain in the vascular compartment with negligible clearance for 5 min (14,12).

Following the injection, subjects are requested to flex the foot for 1 min to aid mixing. After 3 min 55 sec of occlusion, data acquisition is begun in 1 sec-frames for 100 sec and stored using an on-line mini computer. The cuffs are released after 4 min (the 5-sec lead time is to ensure that no labeled blood has leaked past the cuffs into the isolated forearm segments before their release). At the end of the dynamic acquisition, a 10-ml blood sample is taken from an antecubital vein and counted on the camera for 2 min. A background measurement is also made for 2 min. Finally the limb volumes are measured using water displacement. The arms are submerged up to the skin marks (delineating the field of view of the camera). The volume of water displaced is measured and this figure is used in the calculation of flow per unit volume of tissue.

The stored dynamic data is processed by drawing a region of interest around the whole of each limb within the camera field of view and generating time-activity curves (Fig. 3). Three characteristic phases can be seen in the curves:

1. *Linear phase.* Activity is entering the arm at a constant rate and displacing only nonactive blood.

2. *Exponential phase.* After mixing of tracer in the arm a constant fraction of the activity is replaced by an equal volume of blood from the pool having a higher specific activity (the curve continues to rise but no longer linearly as we are losing activity by venous return).

3. *Equilibrium phase.* Complete mixing has occurred and the activity per unit time flowing out of the arms is equal to that flowing in.

The least squares gradient is calculated over the linear phase. This represents the rate of arrival of tracer and is proportional to flow. The gradient of the curve also depends on the specific activity of tracer in the blood, since a more active tracer will produce a steeper curve for the same flow. The blood sample count is used to calibrate the gradient for flow.

If G cts/sec/sec = least squares gradient of the linear phase

C cts/sec/ml = specific activity of the blood sample (corrected for background)

then Flow F = $\frac{G}{C}$ ml/sec.

The tracer will record a higher count in the 10-ml syringe than the arm because of differences in self-attenuation between the two. A correction factor is needed to allow for these differences. To determine this factor, a tissue equivalent arm phantom was constructed: An arm cavity was vacuum formed from PVC sheets using a cast taken from a volunteer. The cavity was filled with tissue equivalent pellets and the remaining air space filled with water. Transmission profiles obtained using a photon absorptiometer showed the attenuation characteristics of the arm phantom to be within 10% of the human arm. A 10-ml aliquot of tracer was counted in a syringe on the gamma camera. This was injected into the arm phantom
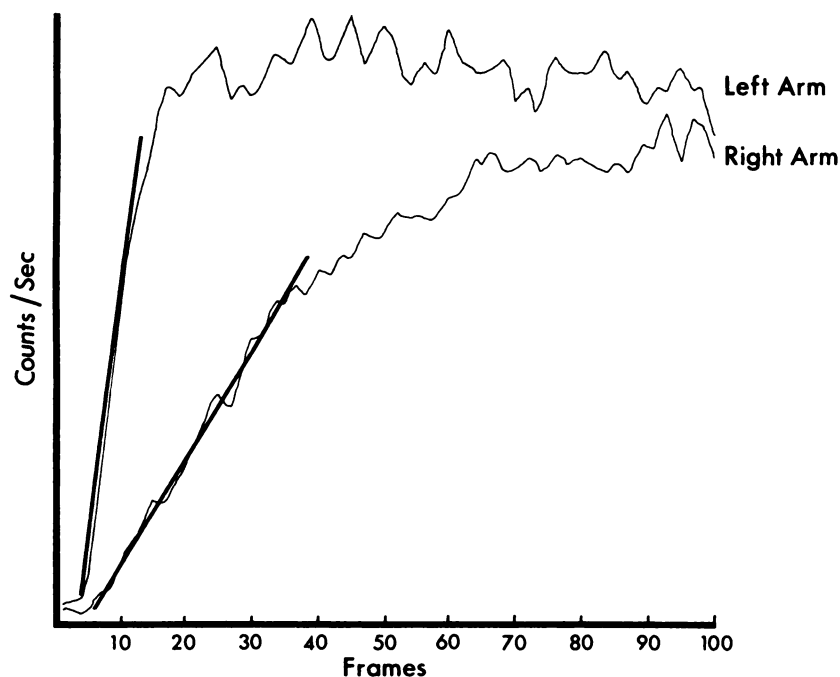
FIGURE 5
Time-activity curves from a patient with right forearm claudication (Subject 1, Table 3).

and thoroughly mixed. The phantom was then counted for the same time on the camera and the attenuation correction factor calculated from the ratio of these counts. It was found to be 1.1. The least squares gradient G is therefore scaled in each case by this factor before calculating the flow. Flow per unit volume in ml/100 ml tissue/min is obtained by dividing the flow value by the limb volume obtained using water displacement.

RESULTS

Results for the eight healthy male volunteers are shown in Table 1. The mean value was found to be 32.9 ± 6.4 ml/100 ml/min. This is significantly higher than the leg blood flow following 3 min of occlusion which was found to be 15.6 ml/100 ml/min (*12*).

To assess the reproducibility eight patients undergoing right brachial artery catheterization, three patients undergoing right cervical sympathectomy and two normal controls were studied on two occasions. The left

TABLE 3
Forearm Blood Flow (ml/100 ml/min) in Patients with Claudication

Subject	Right	Left
1	5.6	19.3
2	8.4	28.8
3	6.9	20.0
4	7.7	20.6
5	3.2	25.9

arm of the patients and both arms of the controls were used for reproducibility giving a total of 15 limbs. An overall correlation coefficient of 0.96 was obtained between the two readings with a gradient of 1.02 (Fig. 4) illustrating that the technique is reproducible over a wide range of flows. Table 2 summarizes the flow measurements in eight patients before and after right brachial arteriotomy. None of the patients had symptoms or clinical evidence of right brachial artery damage following catheterization and this was supported by the right forearm blood flow measurements, none of which show gross reduction. There is, however, a small but significant reduction in right arm flow ($p < 0.05$) in six out of eight subjects, the largest change being 21% in Patient 3. This might be expected after a longitudinal incision and purse string repair. No significant change was noted in the flows to the left arms (paired t-test).

Figure 5 shows the time-activity curves of a patient with severe right arm claudication following catheterization. The reduction in the gradient over the linear phase of the right arm is clearly seen. Table 3 summarizes the results in five patients who were investigated for claudication of the right forearm following catheterization. All five patients had absent radial pulses. Arteriography in four of these showed complete occlusion of the right brachial artery. In the fifth case the patient complained of rest pain and an occlusion of the right brachial artery was discovered at operation.

Limb blood flow measurements show gross reduction in flow in all these cases. The difference between left and right arm flow varies from 63% to 88% whereas in our normal controls the maximum difference was 18%.

DISCUSSION

Any new technique for investigating patients must either provide new information or have some advantages over existing methods in terms of time, cost, patient discomfort, or availability. This method has distinct advantages over other methods (6,7) in that it gives an absolute measurement of flow or flow per unit volume and takes account of any collateral vessels. The signal-to-noise ratio is excellent since the starting activity is zero and we measure the rate of increase from the gradient of a time-activity curve. Because of this, and the high reproducibility, the technique can be applied with confidence in a situation of very low flow. One disadvantage of the method is that complete occlusion of the circulation is essential and any leakage of tracer past the cuffs invalidates the measurement. For this reason, we ensure that the cuffs are inflated to 300 mm Hg in every case.

Rapid inflation is needed to prevent arterial inflow continuing when the venous system is occluded. This would lead to limb engorgement.

If serial measurements are to be made to monitor treatment response, care must be taken to ensure that the arms are accurately repositioned since any change in this will lead to a different amount of forearm muscle being imaged and an apparent change in flow.

Our interpretation of the linear phase of the time-activity curves as indicating a constant inflow with no loss of activity via venous return has been confirmed experimentally. Continuous venous blood sampling has been carried out from the time of release of the cuffs in four subjects. No activity appears in the blood until the end of the linear phase in all the subjects tested.

The correction factor for self attenuation was found to be 1.1. Variation of this factor between individuals was assessed by measuring the attenuation of a point source of cobalt-57 through the thickest part of the forearm within the camera field of view. The factor was found to be relatively constant between individuals and a figure of 1.1 can be used in all cases without appreciable error.

The method described is simple, low cost, and widely available. It can be used as an initial screening procedure to confirm the diagnosis and to assess the degree of impaired flow. It can also provide baseline and subsequent measurements of treatment response.

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