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Measurement of the Regional Distribution of Arterial Blood Flow in the Human Forearm and Hand[1]

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INTRODUCTION

In measuring the perfusion of an organ or region of the body, it is important to consider the distribution of blood flow within the organ or region as well as the total blood flow. Information about the distribution of blood flow in an arm or leg might be helpful in the characterization of pathological states associated with vascular insufficiency, or in testing the response of the extremity to drug therapy, or in estimating the effects of procedures such as sympathectomy. Although there are techniques for measuring both total and regional blood flow, most studies in the past have been concerned with the determination of total blood flow (1, 2).

The recent development of macroaggregated albumin labeled with ^{131}I (MAA-^{131}I) for measuring regional pulmonary arterial blood flow has been the first of a series of potential applications of the particle distribution principle to the measurement of regional blood flow (3, 4, 5). The labeled MAA particles that have an average size of 15 μ lodge in the arterioles and capillaries of the first vascular bed they encounter; in the case of an intravenous injection, this is the lung. After lodging in the capillary bed, the particles break down several hours after injection, and the radioactivity gradually disappears from the initial sites of deposition. Clearance studies after femoral artery injection have demonstrated that the biological half-life of ^{131}I-labeled MAA in the thigh is three hours and the half-life in the calf and foot is five hours (6).

In using the particle distribution technique to measure regional blood flow, two assumptions have been made. It is assumed that complete mixing of the aggregates takes place in the injected artery and that the regional capillary beds are uniformly efficient in extracting the aggregates from the blood.

This report describes the use of the particle distribution technique to measure the regional blood flow of the forearm and hand in: a) patients with no evidence of peripheral circulatory disorders and b) in several patients with clubbing of the fingers or with Raynaud's phenomenon.

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MATERIALS AND METHODS

Macroaggregated human serum albumin labeled with ^{131}I is the agent ordinarily used for lung scanning. It is prepared by controlled heating, with pH and concentration adjusted to yield particles that range in diameter between 10 and 70 micra with a median size of 15 μ as determined in the Coulter counter (5).

To study the distribution of blood flow in the forearm and hand, a dose of 300 μC of MAA-^{131}I in a 0.5 – 1.0 cc volume was injected in a cephalad direction into the brachial artery, through a #20 or #18 (Cournand) needle. The upstream injection was used to promote uniform mixing by creating local turbulence in the arterial flow. All injections were made with the patients at rest in air-conditioned laboratories under relatively constant room temperature (22 – 24°C). On the day prior to injection and on each of three consecutive days, the patients were given 10 drops of Lugol's solution to drink to prevent uptake of the free ^{131}I by the thyroid gland after metabolism of the iodinated particles.

Within one to two hours after the injection of the particles, the distribution of radioactivity within the forearm and hand was determined by scanning the ventral aspect with an eight-inch thallium-activated NaI crystal scintillation detector. In addition to obtaining the scanning image, counts were accumulated over regions delineated by four points: (1) midway between olecranon process and ulnar styloid; (2) ulnar styloid; (3) metacarpophalangeal joints; and (4) the ends of the fingers. These four points divided the lower arm into three segments: the forearm, the hand (except for fingers) and the fingers. The distal two segments of the thumb were excluded from the detector by means of lead shield, in order to avoid its contribution to the hand segment.

The counting rates used for quantification were obtained with a scaler and

TABLE IA

PER CENT OF TOTAL FLOW PER SEGMENT IN 11 NORMAL SUBJECTS

Subject	*Forearm*	*Hand*	*Fingers*
(1) E.C.	82	17	1
(2) C.B.	67	29	4
(3) F.C.	50	35	15
(4) F.F.	76	17	7
(5) J.L.	55	35	10
(6) J.S.	56	29	15
(7) G.R.	69	26	5
(8) J.G.	67	32	1
(9) C.B.	50	36	14
(10) T.K.	58	26	16
(11) G.R.	68	27	5
Mean $\bar{X}$	63	28	8
Standard deviation	±10	±7	±6

the only data processing was gamma-ray spectrometry to record the pulses around a 360 keV photopeak. The scaler counts were obtained independently of the data-processing subsystem of the scanner. The scanning image was obtained with minimum contrast enhancement, to provide the truest image of the distribution of the radioactivity.

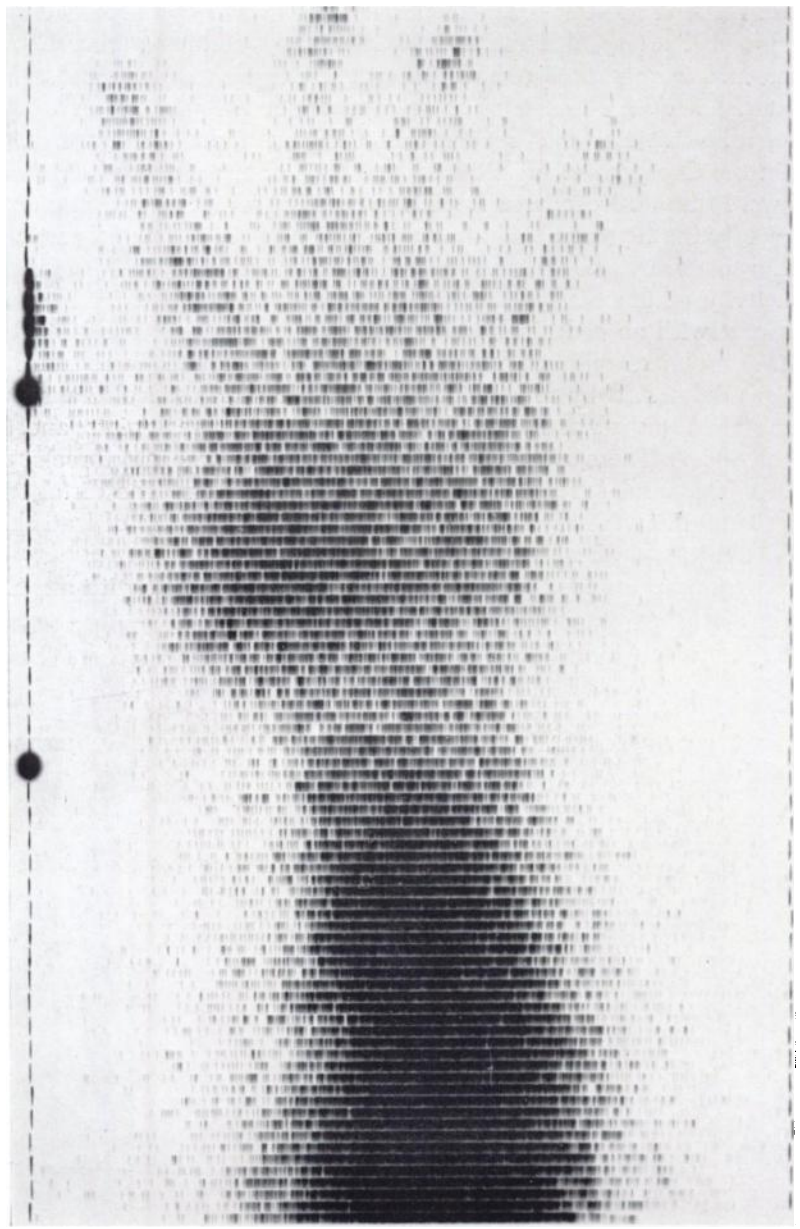

Fig. 1a. Arm scan of normal subject, T. K.

To obtain the distribution of blood flow per unit volume of tissue within a given segment, the volumes of each segment were measured by immersing the patient's hand and arm vertically downward into a specially-built container and recording the volumes of water displaced by successive segments.

The total radioactivity from midforearm to fingertips was taken as 100 per cent. Counts per segment were divided by total radioactivity in the entire region from the midforearm distally to obtain the fraction of blood flow per segment. The theoretical basis of the particle distribution method and evidence that the concentration of radioactivity is proportional to regional blood flow have been presented (5). The fractional flow/volume of segment was obtained by dividing the fractional flow of a segment by the volume of the segment.

Arm scans were performed in 11 subjects who were without known peripheral circulatory disorders, in three patients with moderate or marked clubbing of the fingers, and in three patients with Raynaud's phenomenon.

Data on the clearance of MAA-^{131}I from the forearm, hand and fingers in normal subjects were obtained by placing the segment to be measured directly over a well scintillation counter.

RESULTS

Typical arm scans from two normal subjects are shown in Figures 1a and 1c. Characteristically, the radioactivity was greatest in the distal half of the forearm and at the thenar eminence. A smaller amount of activity was present in the wrist, in the ulnar half of the hand and in the fingers. Patches of increased activity were sometimes seen at the tips of the fingers.

The percentage flow in each segment and the percentage flow per unit volume of each segment in 11 normal subjects are shown in Tables IA and IB. Results in three patients with clubbing of the fingers and three patients with Ray-

TABLE IB

PER CENT FLOW PER UNIT VOLUME OF EACH SEGMENT IN 11 NORMAL SUBJECTS

Subject	*Forearm*	*Hand*	*Fingers*
(1) E. C.	0.13	0.13	0.07
(2) C. B.	0.21	0.09	0.04
(3) F. C.	0.12	0.10	0.05
(4) F. F.	0.14	0.05	0.04
(5) J. L.	0.12	0.14	0.05
(6) J. S.	0.16	0.10	0.10
(7) G. R.	0.11	0.10	0.08
(8) J. G.	0.21	0.12	0.01
(9) C. B.	0.09	0.10	0.12
(10) T. K.	0.21	0.11	0.12
(11) G. R.	0.22	0.11	0.04
Mean $\bar{X}$	0.16	0.10	0.06
Standard deviation	±0.05	±0.02	±0.04

naud's phenomenon are shown in Tables IIA and IIB. It can be seen that there was no significant difference in the distribution of blood flow through vessels with an average diameter of less than 15 μ in the six patients when compared with the 11 control subjects.

The half-life of ^{131}I-MAA was 5⅝ hours in the forearm, 6 – 7 hours in the hand and 6½ – 7 hours in the fingers.

The only untoward reaction noted in any patient was a localized dermatitis at the site of arterial injection in one of the control patients, J.S. This condition was believed to be due to sensitivity to topical medication or adhesive tape and it disappeared after one week.

DISCUSSION

The distribution of radioactivity in the normal arm after the injection of labeled MAA was similar to our previous finding in the leg after femoral artery injection (7). In that study, the greatest activity was found in the thigh and calf and a decreased activity was noted in the knee and ankle. In both the upper and lower extremity, the greatest flow was to the muscle masses. The distribution of the blood flow per unit volume could be explained by the fact that the relative amounts of muscle per volume of segment decreases progressively from the forearm to the fingers. The patches of activity seen at the tips of the fingers may reflect a somewhat increased flow in these regions (8).

Data on regional blood flow in the hand obtained by the present method differ significantly from the results of plethysmographic studies. Greenfield found

TABLE IIA

PER CENT OF TOTAL FLOW PER SEGMENT IN 6 PATIENTS

Subject	Forearm	Hand	Fingers
A. *Raynaud's Phenomenon*[1]			
(1) H. H. (right)	79	21	0
H. H. (left)	66	26	7
(2) K. R.	56	38	6
(3) S. R.	70	25	4
Mean $\bar{X}$	68	27	4
B. *Clubbing*			
(1) R. C.	83	13	3
(2) A. J.	54	35	10
(3) L. L.	89	8	2
Mean $\bar{X}$	75	19	5

[1]In patient H.H., Raynaud's phenomenon was unassociated with physical changes in fingers or with secondary disease. K. R. had malignancy of stomach, but no objective changes in fingers. S. R. had undiagnosed connective-tissue disease with atrophic changes in finger tips.

that 46 to 82% (average 69%) of the total hand flow was to the fingers when the subject was normally dressed in a room at 20 – 29°C (1). Using our method, if we calculate the contribution of the fingers to the whole hand we obtain a value of 23% for the flow in the fingers. The discrepancy between 69 and 23% may be explained by two factors. Plethysmography estimates the total blood flow, including both shunted and nutritional flow. The particle distribution method indicates

Fig. 1b. Soft-tissue radiograph of forearm and hand in same subject, T. K.

primarily the distribution of blood flow through vessels that have an average diameter of less than 15μ. Another difference between the present experiment and that of Greenfield is that the thumb was excluded in our study; therefore, the fraction of total hand flow that is due to the four fingers would be expected to be smaller.

The values obtained for segmental blood flow and percentage flow/unit volume in the patients with clubbing or with Raynaud's phenomenon did not

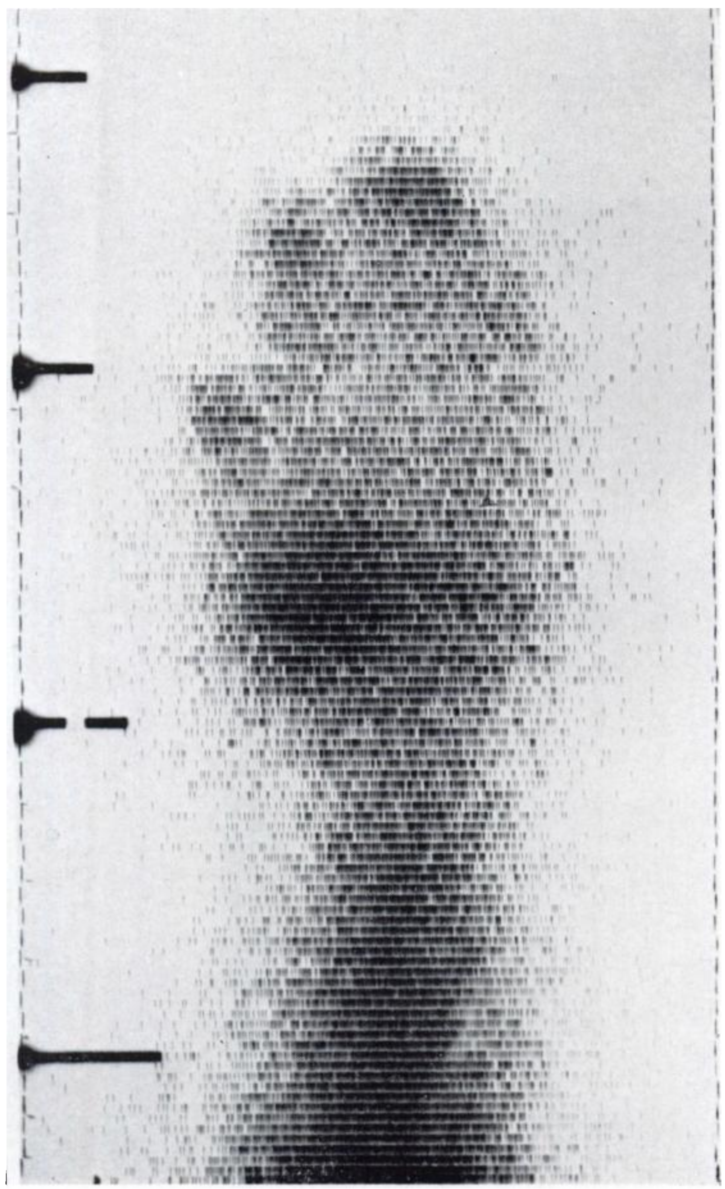

Fig. 1c. Arm scan of normal subject, C.B.

differ significantly from the values of the normal group. Although the size of the experimental groups and the wide variance do not permit any firm conclusions, these observations indicated that in both Raynaud's phenomenon and clubbing, there may be a normal distribution of blood flow through vessels 15 micra in size or less. The findings in the patients with clubbing are in accord with the recent report by Price, who (using plethysmography) found that blood flow is normal in the clubbed finger (9). Perhaps clubbing does not lead to abnormalities in the digital blood vessels with a diameter of 15 micra or less.

After the intravenous injection of 300 μC of MAA labeled with ^{131}I, the total body dose is below 0.1 rad. The radiation dose to the upper extremity in the present experiment is less than 1 rad. Experience with more than 2000 lung scans has shown that labeled MAA in these doses is a satisfactory and safe radiopharmaceutical. No hemodynamic or immunologic toxicity has been observed.

The particle distribution technique cannot be readily compared to other methods of measuring blood flow. It has already been noted that ^{131}I-MAA is distributed chiefly to the muscle masses. Thus, a technique using ^{131}I-MAA would mainly measure the muscle blood flow. The calf plethysmograph does not provide a suitable means of comparison because it measures total blood flow. Blood flow to muscle can be measured by studying the clearance of ^{133}Xe or ^{85}Kr or ^{24}Na after intramuscular injection. The major disadvantage of the clearance methods is that they measure blood flow at a few selected points and do not adequately reflect perfusion throughout the entire muscle. Muscle blood flow can also be measured by determining the thermal conductivity of intramuscular electrodes, but this method is a painful procedure and also does not reflect the circulation through the whole muscle.

In the absence of comparable techniques, the validity of the particle distribution method can only be established by long-term experience. In the future, it may

TABLE IIB

PER CENT FLOW PER UNIT VOLUME OF EACH SEGMENT IN 6 PATIENTS

Subject	*Forearm*	*Hand*	*Fingers*
	A. *Raynaud's Phenomenon*		
(1) H. H. (right)	0.22	0.15	0.00
H. H. (left)	0.28	0.13	0.07
(2) K. R.	0.22	0.11	0.06
(3) S. R.	0.23	0.13	0.05
Mean $\bar{X}$	0.24	0.13	0.04
	B. *Clubbing*		
(1) R. C.	0.17	0.04	0.02
(2) A. J.	0.11	0.10	0.05
(3) L. L.	0.22	0.03	0.02
Mean $\bar{X}$	0.17	0.06	0.03

be possible to improve the characteristics of the particle by using ^{113m}In-tagged iron hydroxide in place of ^{131}I-MAA. This compound would offer the advantage of lowering the radiation dose to the patient because of its short half-life of 1.7 hours. In addition, the ^{113m}In labeled particles have a smaller range of size (20 to 40 micra) and a greater uniformity than the ^{131}I-MAA particles.

SUMMARY

The regional distribution of blood flow through vessels less than about 15 micra in diameter in the forearm, hand, and finger was measured by radioisotope scanning after intra-arterial injection of 300 μC of ^{131}I labeled macroaggregated albumin. The blood flow was distributed primarily to the muscle masses. In 11 selected control subjects, plus three patients with clubbing of the fingers and three patients with Raynaud's phenomenon, the regional distribution of blood flow in the forearm, hands and fingers was essentially the same.

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