MAPPING MYOCARDIAL MASS AND REGIONAL CORONARY BLOOD FLOW BY EXTERNAL MONITORING OF ^{42}K OR ^{86}Rb CLEARANCE

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Previous studies have shown that there is a close relationship between the rate at which the myocardium clears ^{86}Rb from arterial blood and the simultaneous rate of coronary blood flow (*1*). In a group of 56 dogs the rate of coronary blood flow could be predicted from the rate of ^{86}Rb clearance with a mean error of 7.8% (*2*). Because of the problems resulting from the 1.08-MeV gamma emission of ^{86}Rb, conventional scanning apparatus has not given satisfactory results (*3*). New external counting techniques have been developed for mapping ^{86}Rb and ^{42}K content of the hearts of dogs and man *in situ*. Because of a 20-fold concentration that occurs in the myocardium relative to the plasma, these elements outline the size and location of the ventricular myocardium very effectively. This is of potential usefulness in the detection of pericardial effusion and ventricular hypertrophy and possibly also in locating tumors.

Since areas of healed myocardial infarction are associated with fibrosis and reduced potassium content, it is reasonable to expect that such areas will also be visualized. However, probably the most promising area of application is in the detection and localization of areas of the human myocardium in which the coronary vascular reserve has been reduced by disease of the coronary arteries. Such areas could be demonstrated because they would exhibit a reduced rate of regional isotope uptake during stress. The present report describes preliminary results using these new methods in dogs and man.

METHODS

Choice of ^{86}Rb or ^{42}K. Documentation of the relationship of isotope clearance and coronary blood flow has been based almost exclusively on studies done with ^{86}Rb. However, since rubidium and potassium exhibit similar biological behavior in the myocardium, it is likely that isotopes of potassium will serve as well or better than those of rubidium. Recent studies have confirmed this assumption (*4*). Rubidium-86 is suitable for use in dogs, where the radiation absorbed by the animal is not a consideration. Its low cost and half-life of 18.7 days are convenient. For studies in man, ^{42}K is preferred to ^{86}Rb because the short physical half-life of 12.4 hr results in a dose of only 1–1.3 rads to the critical organ and the skeletal muscle for each millicurie administered (*5,6*). The 1.51-MeV gamma of ^{42}K is sufficiently energetic to allow its separation from that of ^{86}Rb by pulse-height discrimination. Therefore, a dog which has received ^{86}Rb can be immediately studied again with ^{42}K. Although isotopes of cesium achieve a degree of concentration in the myocardium that is similar to that of potassium and rubidium, the relationship between coronary blood flow and isotope clearance is not nearly so close (*4*).

Shielding and collimation. Since ^{86}Rb and ^{42}K emit very energetic gamma rays, it was necessary to design special shields and collimators to reduce the interference from tracer present in the organs adjacent to the heart, particularly the liver. The use of 5 in. of lead shielding on the side of the crystal together with collimators 8.5 in. thick has been found to give satisfactory results. This requires shields that weigh approximately 1,100 lb. Dual-shielded probes with 5.25 × 3.00-in. NaI(Tl) crystals above and below the supine subject were accommodated by a slightly modified Ohio–Nuclear rectilinear scanner (Fig. 1.). Design and characteristics of the collimators have been described in detail elsewhere (*7*).

Digital data recording. A rectangular area of the precordium overlying the ventricles was selected using 6-ft anterior-posterior and lateral radiographs made while the subject was supine on the scanning table and breathing normally during a 28-sec exposure period. The probes moved at speeds up to 1.4 in./sec. Maximum scanning time was 60 min.

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A minimum of 3 min was required to scan a 6 × 6-in. area with 3/16 in. between scan lines. Each scintillation with a pulse height corresponding to absorption of an emission with peak energy was recorded in the pulse mode on magnetic tape. A buffer-storage interface was constructed to eliminate losses of counts due to coincidence caused by an additional count being detected while the previous one was being recorded (*8*). Data from the upper and lower probes were recorded separately on two channels. Pulses generated photoelectrically by each 0.1 in. of head movement and by the beginning and end of scan lines were recorded on two additional channels. The results were either punched in cards by playing the tape through an interface (Dymec 2540) to an IBM 026 printing card punch or were directly entered into an IBM 1401 digital computer through a specially constructed interface (*9*). The rate of conversion for computer entry was limited to one 10-digit entry per second in the first instance but could be increased 16-fold by use of direct entry.

Computation. The exchange of ^{86}Rb and ^{42}K between the blood and myocardium is a continuous process. Therefore, the radioactivity of each area is constantly changing. The changes in distribution which can occur during the time which elapses between the beginning and end of a ½-hr study are very significant. The isotope content of areas scanned first cannot be directly compared with those scanned last when the time elapsed between the two measurements is more than a few minutes. Time averaging can be achieved by making several rapid scans and summing the counts recorded at each location. However, a residual difference equal to the amount taken up in one scan period still remains between the first and last points.

The intravenous infusion of the tracer in these studies was given at a gradually decreasing rate to maintain a plateau level in arterial blood (*1,10*). There was an immediate rise in radioactivity in the circulating blood and other areas which equilibrate rapidly with it. Thereafter the tracer content of these areas remained at a plateau while the more slowly exchanging areas progressively accumulated isotope by exchange with the plasma and extracellular fluid. Although the slow rise in radioactivity is actually exponential, it can be regarded as linear during the early period before significant tracer has returned from the cells.

The first and last entries in each scan line were discarded because the detector could not reach full scanning speed immediately. The resulting matrix of 500–1,500 numbers was "bounded" in some cases by replacing entries which varied by more than 2 s.d. from the mean of the eight surrounding it with this mean ± 1 s.d. The results were then smoothed one or more times by averaging each entry with the eight surrounding it. In some instances, four to seven serial scans were made during a 20–30-min intravenous infusion of the tracer.

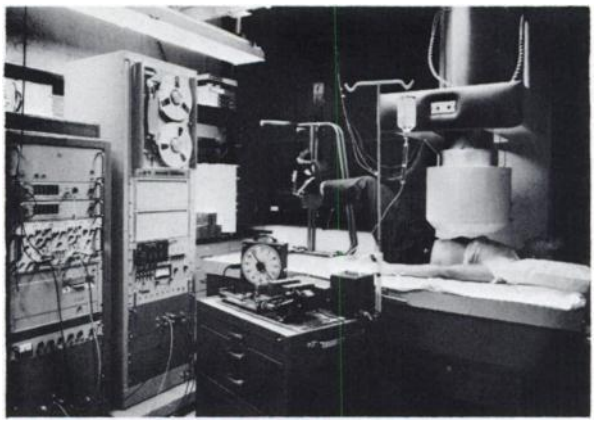

FIG. 1. View of modified scanner and associated equipment.

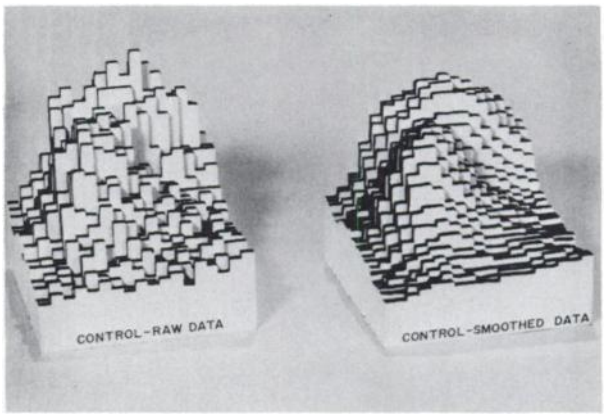

FIG. 2. Three-dimensional models showing effects of computer smoothing of data.

To determine the concentration in all areas at one instant, the linear regression equations for all locations were solved for the same time, e.g., the end of the last scan made during the infusion. During some studies in dogs, the radioactivity of arterial blood in an exteriorized loop was continuously monitored.

Three-dimensional models of results. Since the scanning procedures are in a developmental phase, a very sensitive and reliable method of evaluating the results was needed to minimize the likelihood of overlooking positive findings. The line printer output of the IBM 1401 computer was used to produce a histogram representing the results in each scan line. The individual histograms were glued to balsa wood panels of the same thickness as the distance between

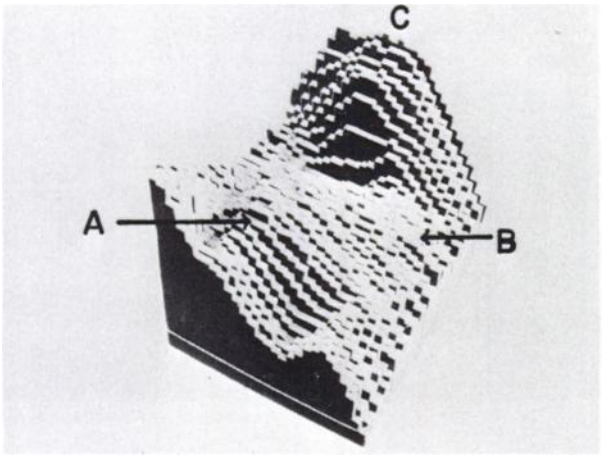

FIG. 3. Model of human transmission scan. A is base of heart, B is apex and C is liver.

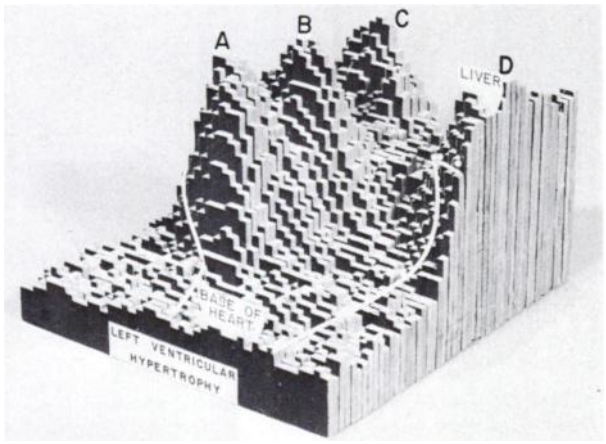

FIG. 4. Model made from data obtained from patient with left ventricular hypertrophy. A and B are two peaks of enlarged mass of ventricular muscle. C corresponds to intra-abdominal organ and D to liver.

scan lines. When cut out with a saw, these provided a set of laminae which were assembled to make a three-dimensional map of the results (Fig. 2.).

Effect of combining counts from two probes. In most instances the counts detected by the opposing pair of probes have been combined for analysis with the concept that the result is the same as would be obtained with a single counter with an essentially depth-independent and symmetrical focus (*11*). In some cases the results from the upper and lower probes have been processed separately, and the results compared with those obtained with combination analysis. In most instances the models made from data from the upper and lower probes have been very similar. However, on occasion there were significant differences.

Transmission scanning. Kuhl, Hale and Eaton have recently described "transmission scanning" as an aid in interpreting conventional emission scans (*12*). In this procedure a narrow beam of gamma rays is obtained by mounting a sealed isotope source within the collimator of one probe. The beam is detected through a small aperture in the opposing probe after having passed through the region of the body being scanned. Since the amount of radiation detected is inversely related to the mass of tissue through which the beam passed, an outline of the position of the heart, liver and chest wall is obtained (Fig. 3.). This is used to supplement the x-rays to establish the exact position of the heart within the areas scanned. Recently, this approach has been applied during studies with ^{42}K by using ^{137}Cs as the source. Since absorption of the radiation from ^{137}Cs is logarithmically related to the mass of tissue encountered, the height at each area in the model representation is proportional to the logarithm of the number of counts which were absorbed.

RESULTS

Left ventricular hypertrophy. Figure 4 shows the results of a single scan done 25 min after intravenous administration of 2.64 mCi ^{42}K in a patient with left ventricular hypertrophy caused by luetic aortic insufficiency. The outline of the heart shadow from the x-ray is shown by white lines. Note elevations corresponding to the enlarged mass of ventricular muscle consisting of two peaks (A) and (B), another intra-abdominal organ (C) and the liver (D). The myocardial elevation has been found to have a similar contour in other cases of left ventricular hypertrophy. On some occasions, the existence of concentric hypertrophy has seemed to be more evident from the contour of the ^{42}K scan than from the ECG or chest film.

Pericardial effusion. Outlining the myocardial mass with ^{42}K scanning offers another method for establishing the presence of pericardial effusion. This approach would be expected to be effective chiefly in demonstrating fluid on the left, where the blood pool which is demonstrated in ^{131}I-albumin studies is normally separated from the heart border by the ventricular wall. The findings in a patient with pericardial effusion and systemic lupus erythematosus are shown in Fig. 5.

Effect of occlusion of coronary arteries in dogs. Figure 6A shows the results of a single scan done on a dog 15 min after 5 mCi ^{86}Rb was given intravenously. The animal was lying on its left side, the ventral surface being to the left. The elevation corresponding to the myocardium is smooth and ovoid.

Figure 6B shows the results in a similar study made immediately after the anterior coronary artery had been occluded by tightening a ligature brought out through the closed chest wall. The area supplied by the anterior coronary artery is outlined in white. It is convex in the normal dog, but concave and "scooped-out" in the presence of coronary occlusion. Figures 7A and B are from a similar study in which the posterior coronary artery was ligated in one dog and the anterior coronary artery in the other. A difference in the location of the counting peaks is apparent in the two models. Figure 8 shows the defect produced by ligation of three small arteries supplying a small part of the anterior wall of the heart in a dog. In all dog studies involving occlusion of selected arteries, except in the one in Fig. 6A, infusion and scanning were started immediately after ligation was accomplished.

Myocardial infarction in man. Figure 9A shows a single scan in a normal man 6 min after 2 mCi ^{42}K was given intravenously. The myocardial elevation (a), the liver, and an intra-abdominal organ (b) are identified. Figure 9B is a similar scan from a subject with posterior myocardial infarction, established by clinical findings and electrocardiography. An area of reduced uptake corresponding to the anatomic location of the infarct is indicated in white.

Visualizing changes in the rate of isotope clearance. In the study shown in Fig. 10 the scanning heads went back and forth over the same area of canine precordium during an 18-min infusion of ^{86}Rb. The passage of time is therefore represented along one axis of the model. At the point indicated, 10 mg dipyridamole was given intravenously. This resulted in a sharp rise in the rate of isotope clearance over the heart but not over the adjacent lung and chest wall. Arterial ^{86}Rb concentration which was monitored in an external loop did not change. The same approach has been applied to the whole heart by making complete scans at 3-min intervals.

DISCUSSION

Results with these techniques to date have been much more satisfactory in dogs than in man. This is caused by the more favorable anatomical location of the heart, by the ability to achieve high counting rates without consideration of the radiation load and by the ease with which known changes in regional coronary blood flow can be produced in dogs. Scans of the myocardium in human subjects without known cardiovascular disease have shown a wide variety of shapes so that detection of a localized lesion at present on the basis of a defect in the contour is at best uncertain. Frequently it is difficult to separate the inferior portion of the heart from the adjacent abdominal organs. In any case a localized defect in uptake might be caused by reduced blood flow or by replacement of muscle by scar tissue.

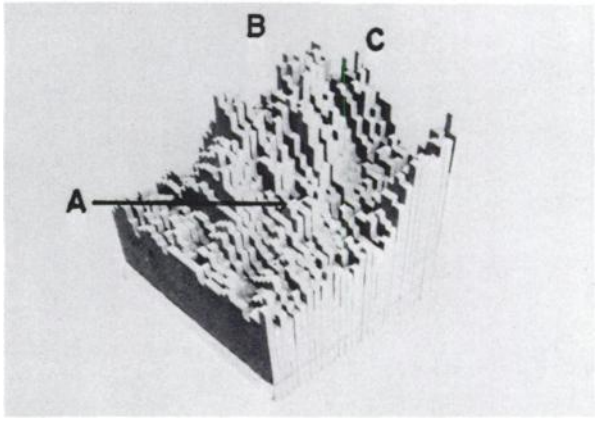

FIG. 5. Data from patient with pericardial effusion and systemic lupus erythematosus produced this model. A is base, B is mass of ventricular muscle and C is liver.

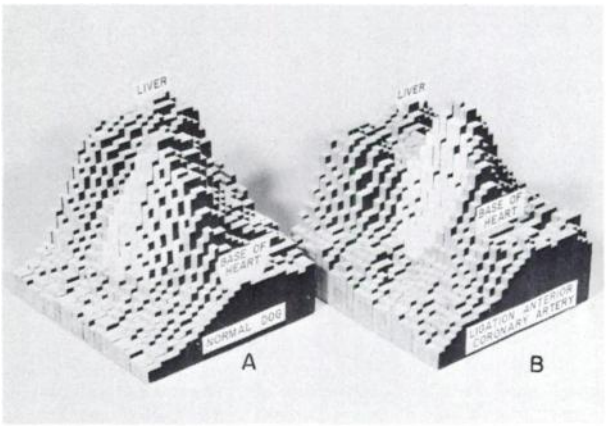

FIG. 6. Concave area in white in "B" model resulted from ligation of anterior coronary artery.

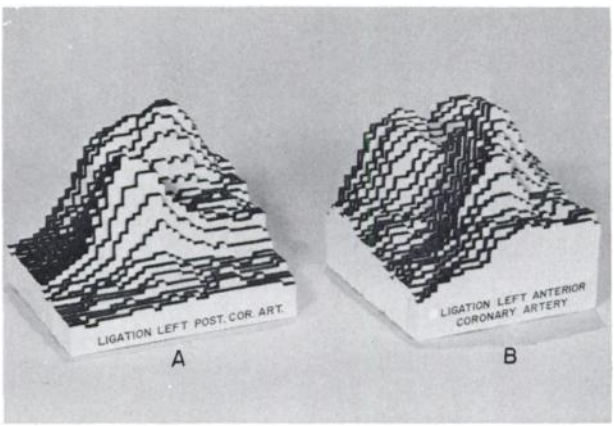

FIG. 7. Two models which show shift in myocardial peaks resulting from ligating two different coronary arteries.

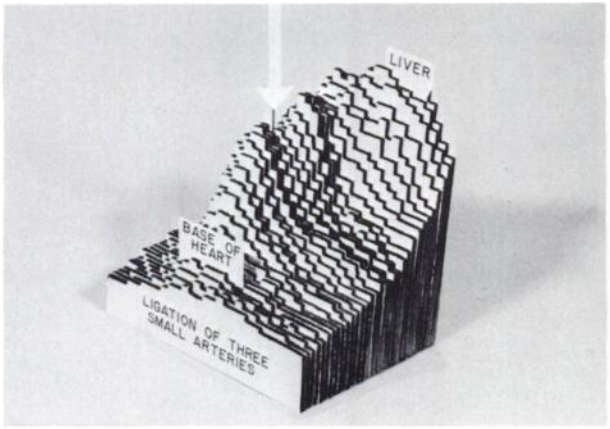

FIG. 8. Ligation of three small arteries produced defect pointed out by arrow.

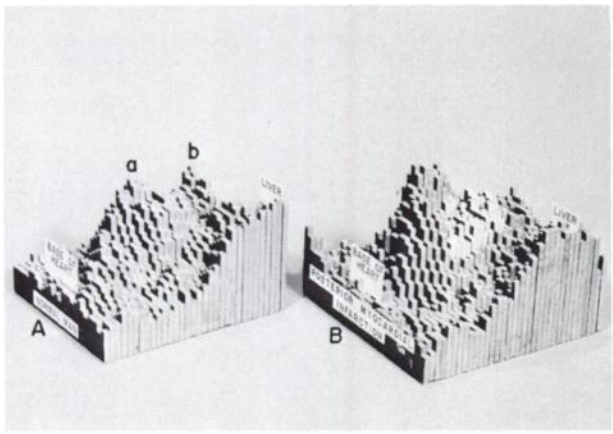

FIG. 9. Model of normal man is on left with myocardial elevation under "a", and intra-abdominal organ under "b". Model on right reveals area of reduced uptake in white which corresponds to location of infarct.

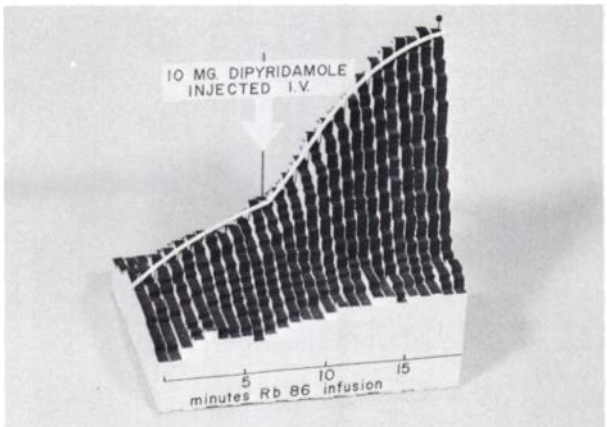

FIG. 10. Scanning back and forth on same line during infusion of ^{86}Rb produced data for this model. Point of injection of drug is indicated by arrow. Resulting increase in isotope clearance over heart but not over adjacent lung and chest wall is shown.

Clues to the differentiation of these possibilities, as well as to the separation of organs and the quantitation of uptake, are to be found in the relationships of regional uptake rates to the content of the area at equilibrium. This will require extension and elaboration of approaches used previously (*13*). Although this will mean increasing the already considerable amount of computation required, it is not unreasonable to assume that sizeable computer facilities will be available to all medical centers in the near future.

The use of cumbersome three-dimensional models could be replaced by automated drawings or oscilloscopic representation of this type of display (*14*). The limited counting rates obtained in the present studies could be increased by the use of isotopes such as ^{43}K or ^{83}Rb which emit more usable gamma rays per rad delivered. The counting rates certainly could be increased by the use of additional NaI(Tl) crystals. Only 1.4% of the maximum 4π geometry is monitored by the crystal with the present apparatus. The effective geometry is reduced to 0.4% by collimation. Although it is customary to refer to scanning procedures as being "photon-limited," "NaI-limited" would be a more accurate term.

An important feature of the techniques being developed is that they are innocuous to the patient. Therefore, they have potential as a screening procedure for the detection of disease of the coronary arteries. As soon as a lesion has narrowed the lumen sufficiently to restrict regional blood flow during exercise, its presence should be detectable by this type of external isotope technique. Localization of such areas would be of interest to those engaged in study of arterial implantation into the myocardium. To determine this, the time course of radioactivity in each area can be followed until the myocardium has reached the same specific activity as that present in the plasma. At this instant, which is the moment that the counting rate reaches a peak value, the amount of radioactivity in the area is a measure of the amount of exchangeable potassium which it contains. Areas of fibrosis could be detected from their reduced potassium content.

ACKNOWLEDGMENT

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