^{43}KCl: A NEW RADIOPHARMACEUTICAL FOR IMAGING THE HEART

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Myocardial imaging after the administration of a radioactive tracer is a potential means of identifying and quantifying areas of myocardial ischemia or infarction. Several radioactive compounds (*1–8*) have been used for this purpose, but none has been completely satisfactory. We have evaluated a newly available radionuclide, ^{43}K, in the form of KCl. The images we have obtained in human volunteers and dogs with and without myocardial infarction are of a quality which leads us to believe that this radiopharmaceutical may be clinically useful.

MATERIALS AND METHODS

Three normal adult male volunteers were studied, two of them twice, together with five male patients who had sustained acute myocardial infarction 3-19 days before the scan. Relevant clinical data are summarized in Table 1. Seven healthy dogs were also studied, one before and after ligation of the anterior descending coronary artery.

Potassium-43 was produced in a nuclear reactor using the ^{43}Ca(n,p)^{43}K reaction. The ^{43}Ca-enriched (62%) stable calcium, as calcium oxide, was exposed to a fast flux of 1×10^{15} neutrons/cm^2/sec at the Oak Ridge National Laboratory reactor. After chromatographic purification using a Dowex AG 50W-X8 ion-exchange resin, the final product was radioassayed by multichannel gamma-ray analysis. The only detectable radiocontaminant was ^{42}K (activity level of less than 5% when injected). Solutions of ^{43}K (as KCl) were buffered to a pH of 6–7, sterilized, and injected intravenously.

Images were obtained using a rectilinear scanner or a gamma camera, or in some cases both. An anterior view was always obtained, with additional views whenever possible. The scanner was a commercial scanner having a 5 × 2-in. NaI(Tl) crystal and a 31-hole collimator with 3-in. focal depth and ½-in. resolution (full width half maximum) for a 364-keV photopeak. Its pulse-height analyzer was adjusted to detect energies between 234 and 414 keV for the ^{43}K studies. The camera was a Nuclear-Chicago Pho/Gamma III with 1,000 parallel-hole collimator. Its pulse-height analyzer was set to detect energies of 390 keV ±15%. Images were recorded on photographic film. In the early studies serial images were obtained at various times after injection; at present, a single image is obtained beginning 2–5 min after injection.

Confirmation of the anatomic site of ^{43}K concentration was obtained in two dogs and two of the normal men by comparing the ^{43}K scans with images of the intracardiac blood pool. These blood-pool studies were performed 5 min after the intravenous injection of ^{99m}Tc-labeled albumin before the subject received ^{43}KCl. The ^{99m}Tc spectrometer settings (140 keV ±12.5%) and a suitable low-energy,

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TABLE 1. CLINICAL DATA ON PATIENTS STUDIED

Patient	Age		CPK (mu/ml at 30°C)	SGOT units/ml)
A	53	Acute transmural lateral and posterior infarct	1,230.0	304
B	34	Acute inferior infarct	1.3	300
C	57	Anterior transmural infarct	670.0	354
D	69	Acute transmural anterior infarct	520.0	179
E	54	Transmural anterior infarct	NA	NA

CPK = serum creatine phosphokinase (normal 5–50)
SGOT = serum glutamo-oxaloacetic transaminase (normal less than 20)
NA = not available
Serum enzyme figures are maximum levels recorded in 2-week period preceding ^{43}K scan.

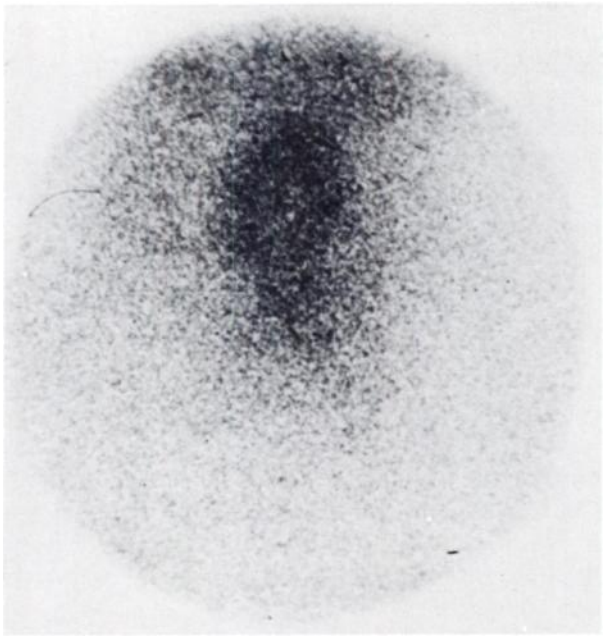

FIG. 1. Anterior myocardial gamma-camera image of normal dog.

217-hole collimator were used. The settings and collimator were then changed to optimize the detection of ^{43}K and completely exclude the ^{99m}Tc activity. The ^{43}K was injected, and further images were obtained. The position of the subject relative to the detector was kept constant during these procedures. In one of the men, ^{99m}Tc-albumin was given as a rapid intravenous bolus, and radionuclide angiography (*9*) was performed to obtain sequential images of the right and then the left heart chamber cavities. In each subject, the image of the distribution of ^{43}K was evaluated with reference to the intracardiac blood pool.

RESULTS

The heart muscle was visualized in all studies and was distinct from the lungs where the activity was much lower. There was significant concentration of the radiopharmaceutical in the liver, but the cardiac image was readily recognized and distinct from that of the liver. A typical Anger camera study obtained from a normal dog is shown in Fig. 1. In normal studies, the distribution of radioactivity appeared uniform except for a frequently seen central region of low activity ("cold area"). Comparison of ^{43}K images with the ^{99m}Tc-albumin blood-pool studies showed that this central "cold area" corresponded to the left ventricular cavity. The ^{43}K localization was predominantly in the left ventricular and septal muscle; with the imaging techniques used, the much thinner right ventricle and atria were not well defined. Results from a combined ^{43}K and ^{99m}Tc study in a normal man are seen in Fig. 2.

In all five patients with myocardial infarction, additional "cold areas" were visible, each corresponding to the position of the infarct determined electrocardiographically. Figures 3 to 5 refer to studies performed in three of these patients. The ECGs depicted were taken within 48 hr of the onset of chest pain. Figure 6 shows images obtained from the dog, 1, 2, and 60 days after ligation of the anterior descending coronary artery. A diffuse region of reduced activity, distinct from the central "cold area", is apparent in the study performed 2 days after ligation.

DISCUSSION

At the present time, myocardial scanning is not widely used because no satisfactory radiopharmaceutical has been available. Certain monovalent cations have been investigated (*1–4*) since they are rapidly accumulated in striated muscle and myocardium following intravenous injection. Isotopes of rubidium (^{86}Rb) and cesium (^{131}Cs) have been used but have not been completely satisfactory, mainly because their gamma ray and other emissions have not been suitable for detection by conventional imaging instruments in doses permissible in man. Cesium-129 and ^{127}Cs are at present under investigation (*5–7*). Because potassium is the primary intracellular cation, it was natural that it or its analogs should be tested. Potassium-42 has been investigated (*8*), but its high-energy photon (1.52 MeV) makes detection and imaging of the myocardium difficult.

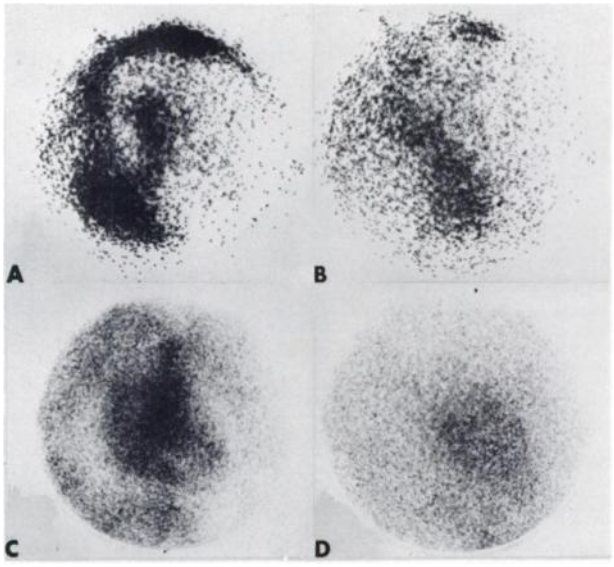

FIG. 2. Combined ^{99m}Tc-albumin radionuclide angiogram (A, B,C) and ^{43}K study (D) performed with gamma camera in normal man. A shows right heart phase; B, left heart phase; C, cumulative blood-pool image. Note that myocardial image (D) overlies and surrounds left ventricular cavity identified in B.

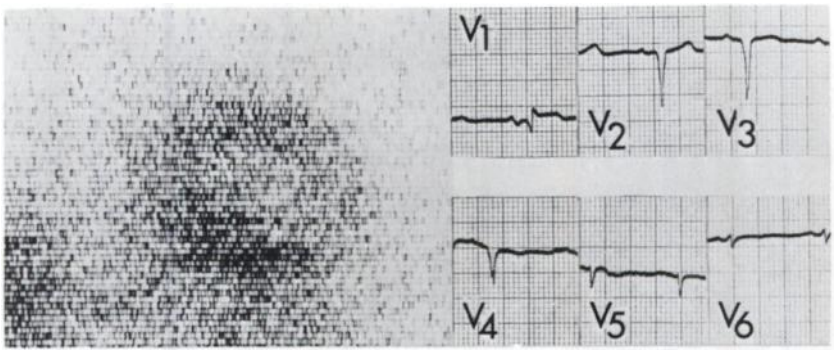

FIG. 3. Myocardial scan and ECG of Patient C: anterior infarction.

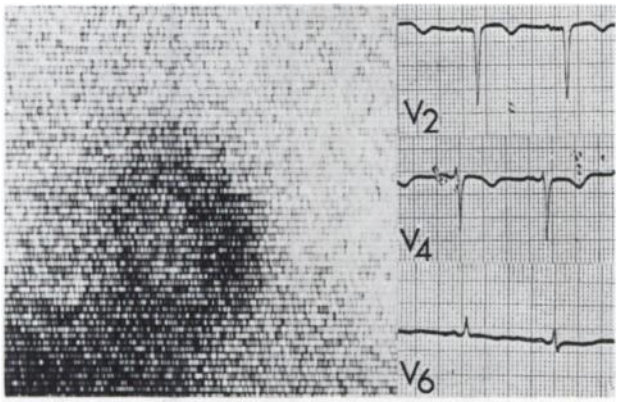

FIG. 4. Myocardial scan and ECG of Patient D with anteroseptal infarction.

Potassium-43 has a physical half-life of 22.4 hr and for each 100 distintegrations emits 98 photons of either 373 or 397-keV energies. Its beta emissions increase the radiation dose, and its photon energies above the useful imaging range are also undesirable properties, but these disadvantages do not present a serious problem in the doses used. We found that 0.5 mCi of ^{43}KCl was an adequate dose for obtaining a satisfactory image in a short time (about 20 min). The whole-body absorbed radiation dose from this amount of ^{43}K is approximately 0.35 rad for a 70-kg man, using the absorbed fraction method of calculation (*10*).

In all subjects studied, ^{43}K allowed visualization of normal heart muscle to a much greater extent than of infarcted myocardium. The normal central "cold area" did not obscure recognition of pathological regions of diminished uptake. Not only were anterior lesions well seen, but posterior and inferior infarcts of Patients A and B were also readily detected. In Patient E, the lateral view allowed both the anterior and inferior regions of damaged myocardium to be identified and the intact posterior wall was clearly seen. No patient with a proven infarct had a normal scan. In the dog with an infarct, the

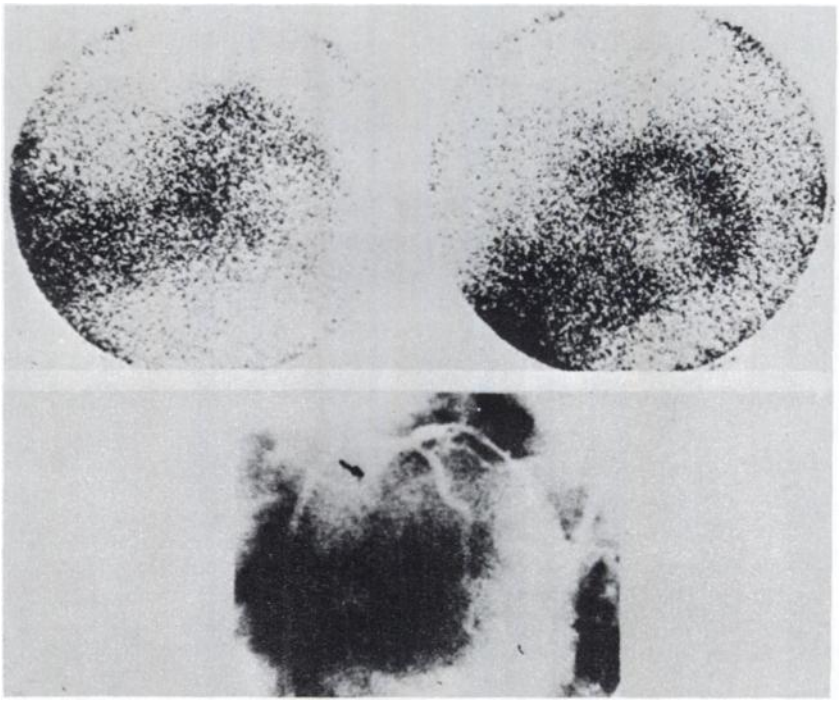

FIG. 5. Anterior and left anterior oblique gamma camera images of Patient E with extensive anterior and inferior myocardial infarction. In coronary arteriogram arrow shows block in left anterior descending coronary artery.

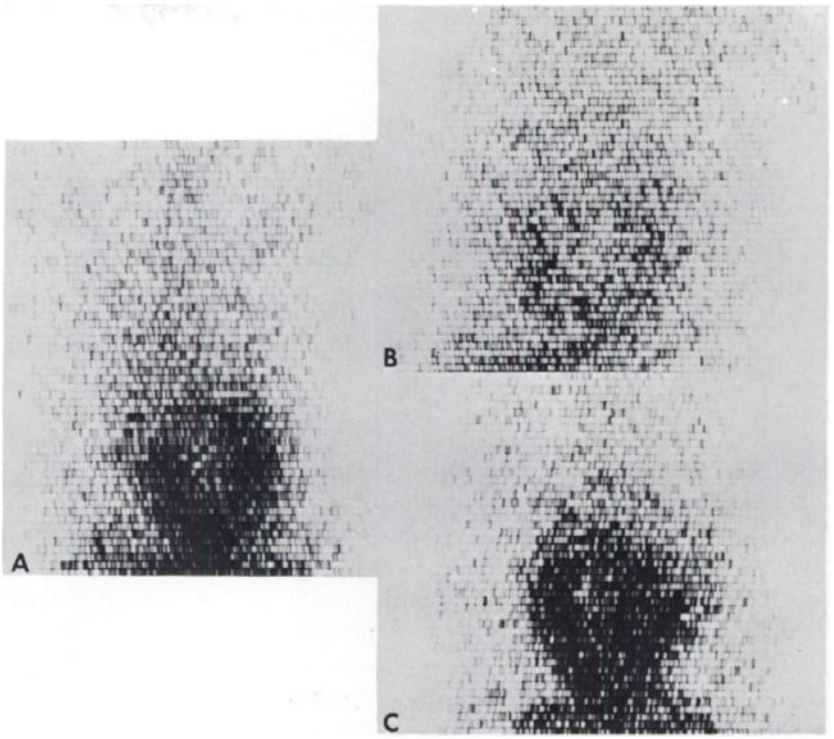

FIG. 6. Anterior scans of dog. A was taken 1 day, B 2 days, and C 60 days after left anterior descending coronary artery ligation.

scan image did not become overtly abnormal until the second day after ligation of the coronary artery. This observation suggests that the timing of a ^{43}K heart scan in patients suspected of myocardial infarction will prove to be important. Carr et al (*2*) have presented evidence that myocardial imaging with cesium also depends on the time elapsed since the infarct.

The value of documenting electrocardiagraphic and biochemical changes in patients suspected of myocardial infarction is well established, but there remain many patients in whom the evidence is equivocal. Even when the diagnosis is secure, conventional methods do not allow precise quantification of myocardial damage. Imaging of functioning heart muscle offers an added dimension in the diagnosis of infarction and may also aid in quantification of damage. Potassium-43 has the particular advantage that it allows a display of viable myocardium rather than the demonstration of coronary vessel anatomy provided by contrast angiography. The radionuclide can be manufactured in a nuclear reactor or a cyclotron. We have shown that ^{43}KCl can produce satisfactory scans; it should prove to be a clinically useful radiopharmaceutical.

SUMMARY

Potassium-43 chloride (^{43}KCl) was used to obtain scans or gamma camera images of the myocardium in normal men, patients with myocardial infarction, and dogs. In normal hearts, the left ventricular muscle was well visualized; a central "cold area" corresponded to the ventricular cavity. In patients with myocardial infarcts, an additional "cold area" could be seen.

REFERENCES

1. CARR EA, BEIERWALTES WH, WEGST AV, et al: Myocardial scanning with rubidium-86. *J Nucl Med* 3: 76–82, 1962

2. CARR EA, GLEASON G, SHAW J, et al: The direct diagnosis of myocardial infarction by photoscanning after administration of cesium-131. *Amer Heart J* 68: 627–636, 1964

3. CARR EA: In *Scintillation Scanning in Clinical Medicine*. Quinn JL ed, Philadelphia, WB Saunders, 1964, pp 93–103

4. MCGEEHAN JT, RODRIGUEZ-ANTUNEZ A, LEWIS RC: Cesium 121 photoscan. Aid in the diagnosis of myocardial infarction. *JAMA* 204: 585–589, 1968

5. YANO Y, VAN DYKE D, BUDINGER T, et al: Myocardial uptake studies with ^{129}Cs and the scintillation camera. *J Nucl Med* 11: 663–668, 1970

6. WATSON IA: Cyclotron production of the radionuclides ^{81}Rb, ^{82m}Rb, and ^{127}Cs. *J Nucl Med* 11: 373–374, 1970

7. SODD VJ, BLUE JW, SCHOLZ KL, et al: Cyclotron production of ^{129}Cs—a promising radiopharmaceutical. *J Nucl Med* 11: 362, 1970

8. LOVE WD, SMITH RO: Focusing collimators for use with the hard gamma emitters rubidium-86 and potassium-42. *J Nucl Med* 7: 781–786, 1966

9. HURLEY PJ, STRAUSS HW, WAGNER HN: Radionuclide angiocardiography in cyanotic congenital heart disease. *Johns Hopkins Med J* 127: 46–54, 1970

10. BROWNELL GL, ELLETT WH, REDDY AR: Absorbed fractions for photon dosimetry, MIRD Pamphlet No 1, *J Nucl Med* 9 Supplement No 3, 29–39, 1968