Myocardial Kinetics of Potassium-38 in Humans and Comparison with Copper-62-PTSM

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The aim of this study was to define the kinetics of ^{38}K and its suitability to evaluate myocardial blood flow at rest and during pharmacological vasodilation in normal subjects. Potassium-38's kinetic characteristics were also compared to those of a ^{62}Cu-pyruvaldehyde bis(n^4-methyl-thio-semicarbazone) copper (II) (PTSM) flow tracer. **Methods:** Potassium-38 and ^{62}Cu-PTSM were injected at rest and after pharmacological vasodilation in six healthy volunteers. Dynamic PET acquisition was performed over 20 min and myocardial tracer retention calculated. Homogeneity of regional myocardial tracer distribution was also evaluated. **Results:** High image quality of the heart was observed at rest and after dipyridamole with both tracers. Potassium-38 demonstrated prolonged myocardial retention with minimal lung and liver accumulation. In contrast to ^{38}K, ^{62}Cu-PTSM demonstrated high liver uptake which may hinder observation of the inferior wall of the myocardium. Copper-62-PTSM dipyridamole-to-rest retention ratio was 1.49. **Conclusions:** Potassium-38 and ^{62}Cu-PTSM display suitable kinetics for the qualitative evaluation of blood flow and flow reserve in the human heart. Compared to ^{62}Cu-PTSM, potassium-38, which does not show high liver uptake, may more accurately estimate blood flow in the inferior wall of the heart. However, accurate quantification of myocardial blood flow using ^{38}K or ^{62}Cu-PTSM retention appears to be limited to decreasing retention fraction at hyperhemic states.

Key Words: potassium-38; copper-62-PTSM; myocardial blood flow; PET

J Nucl Med 1994; 35:1116–1122

Noninvasive evaluation of myocardial blood flow and flow reserve in coronary artery disease (CAD) is most frequently performed by scintigraphic techniques. SPECT with ^{201}Tl or ^{99m}Tc-sestamibi is the most widely applied technique in the clinical setting. However, qualitative assessment of myocardial blood flow with PET has also shown high accuracy for the detection of CAD which is superior to SPECT (*1,2*). Several blood flow tracers are available for the PET approach; ^{82}Rb and ^{13}N-ammonia have been most widely employed in conjunction with pharmacological vasodilation. Recently, ^{62}Cu-pyruvaldehyde bis(n^4-methy-thio-semicarbazone) copper (II) (PTSM), a new generator-produced blood flow tracer, has also been evaluated for the assessment of myocardial blood flow and flow reserve (*3,4*).

Despite a large amount of work, the ideal PET blood flow tracer has not yet been found. Such a tracer should be extracted by the myocardium in proportion to blood flow and should not accumulate in the blood, liver and lung to provide high image quality of the heart. In addition, the tracer uptake should be homogeneous throughout normal myocardium. Although this is true for ^{82}Rb, several studies have shown that there may be some heterogeneity of ^{13}N-ammonia and ^{62}Cu-PTSM distribution in the normal heart (*3,5,6*). Finally, tracer distribution should permit direct estimate of regional blood flow. With exception of ^{15}O-water, it is not the rule since the relation of tracer retention to absolute blood flow is not linear and plateaus at increasing flow rates (*7–12*). The cardiac blood flow at increased flow rates (i.e., after pharmacological vasodilation) is not necessarily reflected in the amount of tracer activity apparent in the scintigraphic images of the heart.

Cyclotron-produced ^{38}K may be a suitable tracer for the qualitative evaluation of myocardial blood flow in CAD (*13,14*). Preliminary studies performed in our laboratory have shown the high image quality of the heart obtained with ^{38}K (*15*). Furthermore, a recent animal study has also shown good correlation between microsphere, ^{15}O-water-determined blood flow and cardiac uptake of ^{38}K (*16*).

Therefore, the aims of this study were (1) to objectively determine the image quality of the heart obtained with ^{38}K; (2) to verify whether the distribution of the tracer was homogeneous throughout normal myocardium; and (3) to evaluate the relation of tracer retention to blood flow over a wide range of flow using the dipyridamole infusion. Since ^{62}Cu-PTSM is another potential blood flow tracer, this study simultaneously compared the tracer characteristics of ^{62}Cu-PTSM to those of ^{38}K.

METHODS

The study protocol was reviewed by the Medical Ethic Committee at the University Hospital of Liege.

Received Jul. 19, 1993; revision accepted Feb. 15, 1994.

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Subjects

Six healthy male volunteers (mean age 23.2 ± 1.7 yr) were enrolled in the study after informed written consent was obtained. None of them had evidence of cardiovascular disease by medical history, physical examination and electrocardiographic recording. All subjects were studied under fasting conditions (>12 hr) and abstained from beverages containing caffeine for 24 hr.

Tracer Preparation

Potassium-38. Multimillicurie batches of ^{38}K were prepared following the ^{35}Cl (α, n) ^{38}K reaction. A sodium-chloride powder target mounted on a water-cooled nickel backing was bombarded with 26 MeV helium-4 ions at a maximum beam current of 25 μA. The target was remotely disconnected from the bombardment port, transported to a hot cell and dissolved in sterile and pyrogen-free water. Potassium-38 has a radionuclideic purity higher than 99.99%. The full procedure of irradiation and processing has been described previously (*15*).

Copper-62-PTSM. Copper-62 was eluted from a $^{62}Zn/^{62}Cu$ generator system as first described by Robinson et al. (*17*). Zinc-62 was produced by the $^{63}Cu(p, 2n)$ reaction. After irradiation, the copper target was dissolved in concentrated nitric acid and converted to chloride by addition and evaporation of concentrated hydrochloric acid. The final residue was dissolved in 1.8 N HCl. The resin used for the separation of ^{62}Zn from the copper matrix was AG 1X8, 100–200 mesh in the chloride form and the same column was used for the separation and consists of the generator itself, which was specific to our system. After washing the column with 300 ml of 1.8 N HCl, the copper content in solution was determined by colorimetry with DDTC and was <1 μg/ml. Copper-62 was eluted with 7 ml of 1.8 N HCl and the eluted solution was neutralized with a mixture of NaOH/NaAc solution. Fifty micrograms of H_2PTSM were added and the complex Cu-PTSM was separated by chromatography on C-18 Sep-Pak™ as described by Green (*18*).

Positron Emission Tomography

Each subject was positioned in the ECAT 951/31R (Siemens, Hoffman Estates, IL) body scanner. Appropriate positioning of the heart within the field of view of the tomograph was confirmed by a 5-min transmission scan. A 30-min transmission scan was then acquired for subsequent correction for photon attenuation in the emission scans. Each subject underwent cardiac blood flow imaging with ^{38}K (13.5 ± 1.9 mCi) and ^{62}Cu-PTSM (13.4 ± 2.5 mCi) within 4.2 ± 2.5 days during resting condition and pharmacological vasodilation. Both tracers were injected intravenously as a slow bolus over 30 sec. Simultaneously, 20-min dynamic PET image acquisition was started with varying frame duration (10 × 6 sec, 4 × 15 sec, 2 × 30 sec, 2 × 60 sec, 2 × 150 sec and 2 × 300 sec). First, images were acquired under resting conditions. After the decay of tracer radioactivity to background level, dipyridamole (0.56 mg/kg) was infused over 4 min followed by a 2-min handgrip exercise. At 6 min after initiation of dipyridamole infusion, a second injection of tracer was administered and dynamic PET imaging protocol repeated as for the resting study.

Data Analysis

Determination of Tracer Kinetics and Image Quality. Data analysis was performed at the midventricular level and at the apical level with simultaneous definition of the liver. For this purpose, a midventricular image and an apical ventricular image were generated by the summation of two contiguous original transaxial images at these respective levels. On the last image frame, regions of interest (ROIs) were drawn over the entire myocardium, the blood pool, the right lung field and the liver. ROIs were automatically propagated to the entire scan sequence and time-activity curves generated for each organ. Heart, lung and liver time-activity curves were then expressed as a percent of the peak activity detected in the blood arbitrarily set at 100%.

Image quality was objectively determined by the activity ratios of myocardium-to-blood pool, myocardium-to-lung and myocardium-to-liver at 20 min after tracer injection.

Myocardial Tracer Retention. Myocardial tracer retention was calculated as previously proposed by Beanlands et al. (*3*):

$$R = C_t \Big/ \int C_b,$$

where R is the retention (sec^{-1}) of the tracer; C_t is the radioactivity of the tracer in the myocardium at 900 sec after injection; and C_b is the integral of the blood pool radioactivity. For ^{62}Cu-PTSM, the integration of the blood pool radioactivity was limited to the first 60 sec after injection since previous studies by Mathias et al. (*19*) have shown that about 60 sec after tracer injection, the blood radioactivity is only represented by metabolites. Potassium-38 is not metabolized and the integration of its blood pool radioactivity was performed for the 900 sec of scanning.

Polar Coordinate Map Display of Regional Tracer Uptake. The regional myocardial uptake of each tracer evaluated at rest and during pharmacological vasodilation was displayed on polar coordinate maps. For this purpose, a combined image was obtained from the original last three time frames. A SUN work station (SUN Microsystems Inc., Mountainview, CA) was used for reorientation of the combined transaxial images along the long-axis of the left ventricle in order to obtain 12 resliced images along the short-axis of the heart. On 9–10 short-axis images of each study, the endocardial and epicardial edges of the myocardium were manually defined with circles by the operator. The posterior intersection of the right and left ventricles was also defined and a radius automatically interpolated between the center of the circles and this point. A circumferential profile of activity was then defined for each plane with the radius as a starting point. The program automatically searched for the average maximum activity in each of 60 sectors included between the two circles of each plane. Subsequently, the heart was divided into five major regions (anterior, septal, inferior, lateral and apical) and the regional data expressed as a percent of the maximum activity ± standard deviation for each study.

Statistical Analysis

All data were expressed as mean ± 1 s.d. Blood pressure, heart rate at baseline and following dipyridamole infusion were compared by paired t-testing. Hemodynamic parameters for ^{38}K and ^{62}Cu-PTSM studies, percent of blood peak activity data in the different organs and regional tracer uptake in myocardial segments on polar coordinate maps were compared by analysis of variance (ANOVA) followed by Bonferroni's modified t-test when significant differences were indicated by ANOVA. Probability values ≤ 0.05 were considered significant.

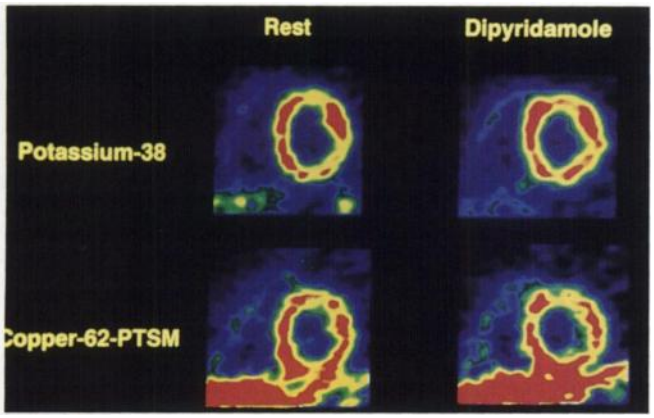

FIGURE 1. Example of ^{38}K and ^{62}Cu-PTSM studies in a normal volunteer in the short-axis view at rest (left) and after dipyridamole (right). Good image quality of the heart is obtained with both tracers. Note the high ^{62}Cu-PTSM liver activity adjacent to the inferior wall of the heart.

RESULTS

Hemodynamic Measurements and Symptoms

Six healthy volunteers were studied with ^{38}K and ^{62}Cu-PTSM at rest and after the infusion of dipyridamole. At rest, the systolic blood pressure averaged 113 ± 9 mmHg and heart rate 74 ± 9 bpm. After dipyridamole and handgrip exercise, the systolic blood pressure value increased to 127 ± 15 mmHg ($p < 0.001$) and heart rate to 112 ± 13 bpm ($p < 0.001$). Baseline and postdipyridamole hemodynamic variables were not statistically different during ^{38}K and ^{62}Cu-PTSM studies (p = NS). During the infusion of dipyridamole, no subject experienced a major adverse reaction such as chest pain, ST segment depression, conduction abnormalities or severe bronchoconstriction. Minor adverse events (i.e., headache, flushing, sweating, nausea, shortness of breath, abdominal discomfort) were reported by all subjects.

Image Quality and Activity Ratios

Figure 1 shows images of the heart of one subject obtained with ^{38}K and ^{62}Cu-PTSM at rest and during pharmacological vasodilation. Good image quality of the heart was observed with both tracers. Table 1 shows the mean myocardium-to-blood, myocardium-to-lung and myocardium-to-liver radioactivity ratios at rest and during pharmacological vasodilation measured at 20 min after tracer injection. In contrast to ^{38}K, ^{62}Cu-PTSM showed high liver uptake which may hinder the observation of the inferior wall of the heart. Potassium-38 activity was detected in the stomach of four subjects at rest and of two of them after dipyridamole infusion.

Tracer Kinetics

Typical myocardial time-activity curves for ^{38}K and ^{62}Cu-PTSM obtained at rest and after dipyridamole infusion are shown in Figure 2. For both tracers, blood pool activity peaked within 35 sec postinjection and then cleared rapidly. Potassium-38 and ^{62}Cu-PTSM displayed distinct myocardial kinetics. From 2 to 20 min after injection, the mean absolute ^{38}K myocardial activity increased by 31% ± 14% at rest and 18% ± 12% after dipyridamole. During the same interval, ^{62}Cu-PTSM myocardial activity decreased by 14% ± 5% at rest and 8% ± 4% after dipyridamole.

Figure 3 shows mean activities for blood, heart, lung and liver expressed as percent of peak blood pool activity. For the selected time points, ^{38}K and ^{62}Cu-PTSM myocardial activity was statistically greater after dipyridamole as compared to resting conditions ($p < 0.05$). For the last four selected time points, liver activity was statistically higher than heart activity for ^{62}Cu-PTSM ($p < 0.01$). Inversely, ^{38}K liver activity was statistically lower than heart activity ($p < 0.01$).

Myocardial Tracer Retention

Figure 4 shows individual data of myocardial retention for ^{38}K and ^{62}Cu-PTSM measured at rest and during pharmacological vasodilation. The infusion of dipyridamole determined a significant increase of myocardial retention of both tracers ($p < 0.05$). The dipyridamole-to-rest retention ratio increased to 1.62 ± 0.31 (range 1.13–1.98) for ^{38}K and 1.49 ± 0.36 (range 1.10–2.08) for ^{62}Cu-PTSM (p = NS, ^{38}K versus ^{62}Cu-PTSM).

Regional Tracer Distribution

Figure 5 shows the regional myocardial distribution of ^{38}K and ^{62}Cu-PTSM at rest and after dipyridamole. Potassium-38 regional distribution was homogeneous throughout the left ventricle. Copper-62-PTSM uptake was significantly greater in the inferior region of the heart as compared to anterior, septal, apical and lateral regions at rest and anterior, septal and apical regions during pharmacological vasodilation.

DISCUSSION

Previous studies performed in our laboratory have shown the good image quality of both canine and human hearts after the intravenous injection of ^{38}K (*15*). For the first time, the use of a multislice tomograph has permitted us to evaluate the kinetics of ^{38}K in the whole heart, liver and lung of normal subjects at rest and during pharmacological vasodilation. The results of the present study confirm the good image quality of the heart and demonstrate the suitable kinetics of ^{38}K for the qualitative evaluation of myocardial blood flow and flow reserve in man. The kinet-

TABLE 1
Activity Ratios

	Myocardium-to-Blood	Myocardium-to-Lung	Myocardium-to-Liver
Potassium-38			
Rest	3.5 ± 1.2	6.0 ± 2.0	1.9 ± 0.6
Dipyridamole	4.2 ± 1.0	9.6 ± 4.5	2.4 ± 0.3
Copper-62-PTSM			
Rest	2.9 ± 0.7	3.4 ± 0.8	0.6 ± 0.1
Dipyridamole	2.7 ± 1.1	4.9 ± 0.6	0.6 ± 0.2

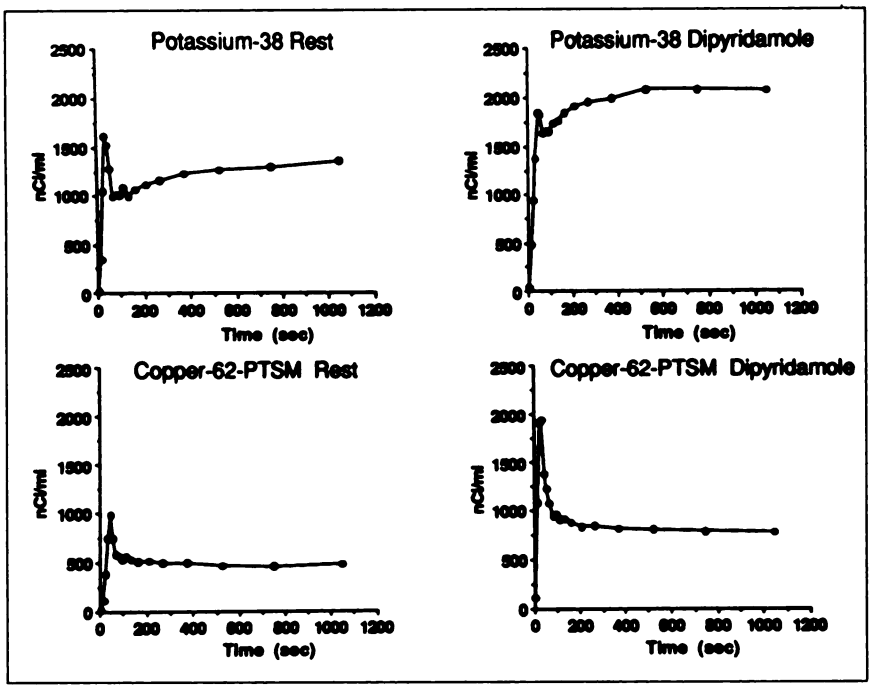

FIGURE 2. Typical myocardial time-activity curves for one healthy volunteer with ^{38}K and ^{62}Cu-PTSM at rest and after dipyridamole.

ics of ^{62}Cu-PTSM was first studied by Beanlands et al. (*3*). This study confirmed their results and moreover, allowed the accurate comparison of the kinetic characteristics of ^{38}K with those of ^{62}Cu-PTSM.

Potassium-38 Image Quality and Distribution

As shown in Figure 1, the image quality of the human heart is good. The rapid clearance of ^{38}K from the blood pool and the low tracer uptake in the lung and liver determines a high contrast of heart-to-background activity. Potassium-38 activity was observed in the stomach of several subjects, especially at rest. However, this stomach activity never hid the myocardium. The 7.6-min half-life of ^{38}K allows data acquisition during several minutes for adequate counting statistics without compromising repeated blood flow evaluations at one sitting. This is of particular interest in evaluating regional blood flow before and after interventions such as dipyridamole, drug therapy or PTCA. In our laboratory, ^{38}K may be delivered to the PET suite every 30–40 min and a rest-dipyridamole study may be completed in about 2 hr.

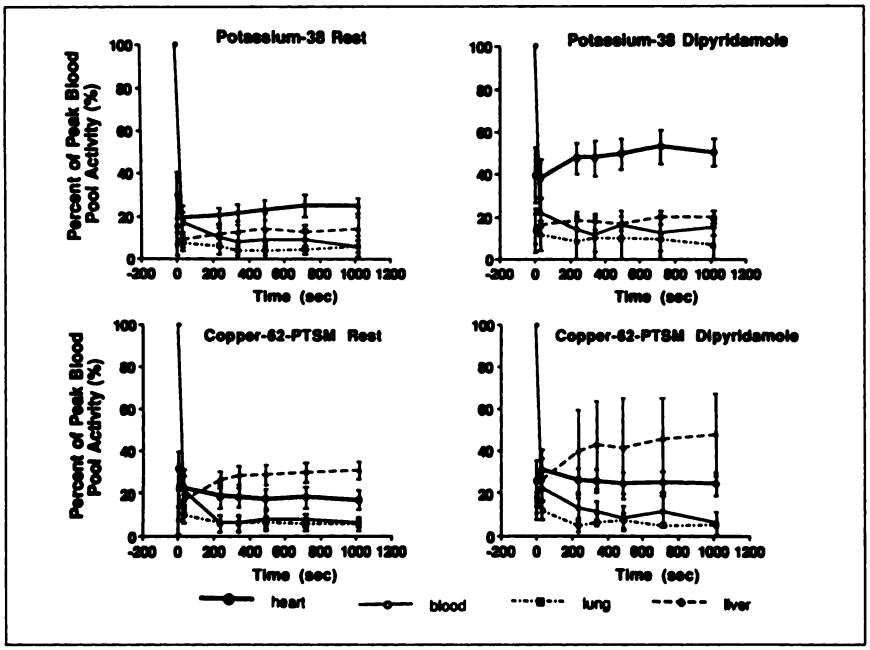

FIGURE 3. Means of the percent of peak blood-pool radioactivity in blood, myocardium, lung and liver. The time of peak blood pool radioactivity was assigned as time zero for each study.

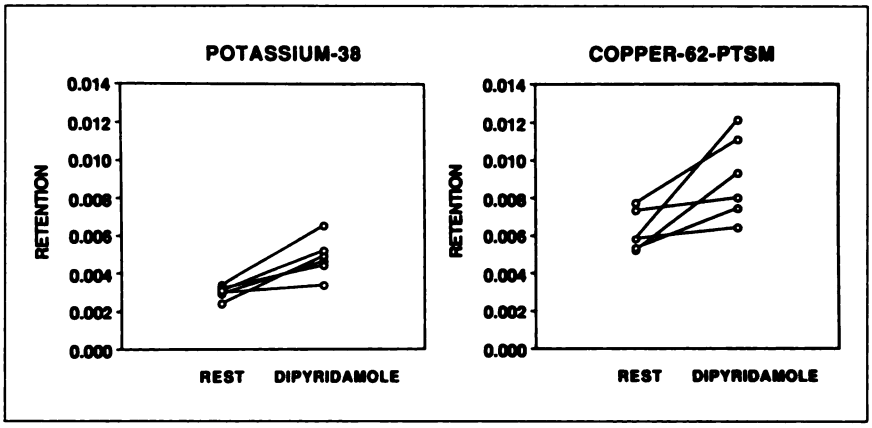

FIGURE 4. Myocardial retention (s^{-1}) of ^{38}K and ^{62}Cu-PTSM for the six healthy volunteers at rest and after dipyridamole ($p < 0.05$ rest versus dipyridamole).

Potassium-38 Kinetics

Potassium is the principal intracellular cation. Its transmembranous transport is mediated by Na^+/K^+ ATPase pumps. The use of potassium for the assessment of regional myocardial blood flow is based on the principle that the fraction of the tracer trapped in the myocardium at the time of the measurement (retention) should be proportional to blood flow. However, previous studies have shown that the extraction of cationic tracers is incomplete and tends to decrease as flow increases (*7–11,20–22*). This decrease of tracer extraction results in underestimation of "true" regional blood flow at higher flow rates. This point is of clinical relevance since the use of coronary vasodilators (dipyridamole or adenosine) results in a fourfold to fivefold increase of flow in normal vessel-related territories (*23–27*). At the time of cardiac imaging, the retention of a tracer in the myocardium reflects both the extraction and any subsequent backdiffusion of this tracer from the myocardium. Consequently, rapid backdiffusion of a tracer may also lead to underestimation of blood flow during delayed cardiac imaging.

Using the indicator-dilution method, L'Abbate et al. (*28*) showed that the maximal initial extraction of ^{42}K ranged from 77% to 90% (mean 85%) in the human heart under resting conditions. The net myocardial uptake of ^{42}K tended to reach a plateau which peaked within 20 min after tracer injection. Potassium-42 rapidly cleared from the blood pool with blood pool activity being only 22% at 2 min after the peak. In anesthetized dogs, Poe (*29*) also reported that the myocardial uptake of ^{42}K reached a plateau within 5–20 min. Potassium-42 myocardial activity then decreased during the next 90 min followed by a more gradual negative phase.

Our results on ^{38}K kinetics in the human heart support the data of these previous studies. Potassium-38 myocardial activity seemed to plateau between 10 and 15 min. However, the duration of data acquisition was limited by ^{38}K's short half-life and did not exceed 20 min in this study. Potassium-38 cleared rapidly from the blood pool with only 10% ± 5% activity at rest and 15% ± 6% activity with dipyridamole detected in the blood pool at 4 min after the peak. Potassium-38 showed homogeneous myocardial uptake and prolonged tissue retention during the 20-min imaging period after tracer injection.

The myocardial retention of ^{38}K was determined at rest and during dipyridamole-induced vasodilation. Previous studies using the intravenous administration of 0.56 mg/kg of dipyridamole over 4 min, as performed in this study, reported a fourfold increase of blood flow in normal myocardium (*23,25–27*). In this study, the ^{38}K dipyridamole-

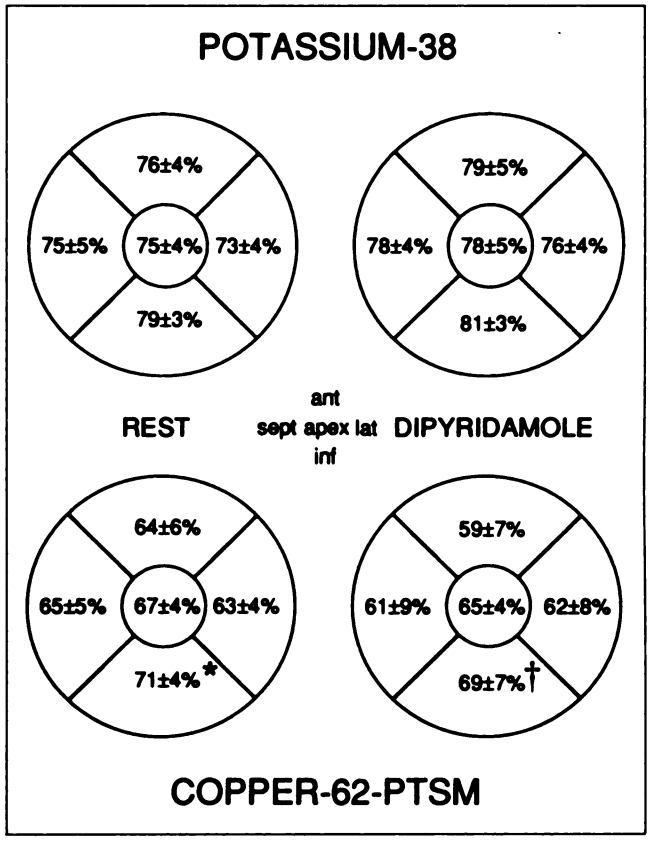

FIGURE 5. Polar map display of pooled data for the six normal volunteers. Mean regional myocardial ^{38}K and ^{62}Cu-PTSM tracer distribution is expressed as a percent of maximal activity for each study. Each heart is divided into five regions: anterior (ant), septal (sept), inferior (inf), lateral (lat) and apical (apex) regions. *$p < 0.01$ versus anterior, lateral, septum and apex; †$p < 0.01$ versus anterior, septum and apex.

to-rest retention ratio was only 1.62. Thus, this result reflects the nonlinear relation of tracer retention to blood flow at increasing flow rates which is responsible for the underestimation of absolute flow changes during pharmacological vasodilation.

Comparison to Copper-62-PTSM and Rubidium-82

The above results show a distinct difference in myocardial kinetics between ^{38}K and ^{62}Cu-PTSM. Our results for ^{62}Cu-PTSM are in accord with the report by Beanlands et al. (*3*). The study of each subject with both tracers has allowed us to accurately compare both tracer's characteristics as a myocardial blood flow tracer. The myocardial retention of both tracers underestimated absolute blood flow changes during dipyridamole-induced vasodilation. The dipyridamole-to-rest retention ratio was somewhat greater for ^{38}K than for ^{62}Cu-PTSM. However, the difference does not reach a statistical significance.

As compared to ^{38}K which was homogeneously distributed throughout the left ventricle, ^{62}Cu-PTSM showed a slightly increased uptake in the inferior region of the myocardium. As already mentioned by Beanlands et al., this enhanced activity in the inferior wall is probably related to liver cross-contamination and may result in underestimation of coronary disease detection in that region of the myocardium.

Eluted from a generator, potassium analog ^{82}Rb has been used extensively for qualitative myocardial imaging. Similarly to ^{38}K, ^{82}Rb myocardial uptake is nonlinearly proportional to flow (*12*). Rubidium-82 with its rapid decay (half-life = 76 sec) offers the advantage of rapid sequential imaging (rest-dipyridamole study completed within 55 min). However, a ^{38}K image of the heart is expected to be of better quality due to the problems with counting statistics imposed by the very short half-life of ^{82}Rb.

CONCLUSIONS

Potassium-38 displays suitable kinetics for the qualitative evaluation of blood flow and flow reserve in the human heart. High image quality of the heart is achieved by the rapid blood pool clearance and the prolonged tissue retention of ^{38}K. Compared to ^{62}Cu-PTSM, ^{38}K does not show high liver uptake which may represent a potential advantage for correct blood flow estimation in the inferior wall of the myocardium. However, accurate quantification of blood flow using ^{38}K and ^{62}Cu-PTSM retention appears to be limited by a decreasing retention fraction of both tracers at hyperhemic states.

ACKNOWLEDGMENTS

The authors thank Ms. J. Hodiaumont for technical assistance and the staff of the cyclotron for preparation of tracers. Dr. Pierre Melon is a research assistant supported by the National Funds for Scientific Research of Belgium.

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EDITORIAL

In Search of the Perfect PET Flow Tracer

Assessment of myocardial perfusion remains fundamental for the diagnosis of coronary artery disease and for objective evaluation of the efficacy of interventions designed to preserve myocardial blood flow. Because of its intrinsic quantitative capabilities, PET has proved to be accurate and sensitive for evaluation of myocardial perfusion. Nonetheless, there is no general consensus regarding the "best" radiotracer to use for such assessments. In this issue, Melon et al. (*1*) compare the imaging characteristics of two putative flow tracers, cyclotron-produced ^{38}K and generator-produced ^{62}Cu-pyruvaldehyde bis(N^4-methylthiosemicarbazone) (PTSM).

Production Aspects of ^{62}Cu-PTSM and ^{38}K

Blood flow tracers used in PET imaging include those prepared from cyclotron-produced radionuclides ($H_2{}^{15}O$, $^{13}NH_3$) and those prepared from generator-produced isotopes (^{82}Rb, ^{62}Cu-PTSM, future ^{68}Ga agents). In terms of convenience of radiopharmaceutical preparation, generator-produced radiopharmaceuticals for PET imaging have long been considered advantageous (*2,3*). One important advantage is the ability of a hospital to operate a PET center without having an "in-house" cyclotron. Particularly for cardiac imaging, FDG from a regional distribution center (for centers that use FDG for myocardial viability) along with a generator-produced flow agent would allow operation of a free-standing PET center.

Melon et al. (*1*) evaluated the myocardial kinetics of an alternative cyclotron-produced blood flow tracer, ^{38}K, and compared it with ^{62}Cu-PTSM, a well-studied, generator-produced radiopharmaceutical. Both radionuclides have similar half-lives and can be produced with good radiochemical purity. However, in terms of practicality, the issue of cyclotron-produced versus generator-produced radionuclides again arises.

In the study by Melon et al., ^{38}K was produced on what is referred to as a Level III cyclotron (26 MeV, 25 μA) using a sodium chloride target (^{35}Cl (α, n)). A Level III cyclotron is considered to be a "medium-energy, four particle" machine, while all medical cyclotrons currently being designed for use in PET centers are one (protons) or two (protons + deuterons) particle cyclotrons with maximum energies of 16 MeV protons and 8 MeV deuterons. Potassium-38 has been produced on a lower energy four-particle cyclotron (14.7 MeV) using a sodium chloride target (*4*), but the end of bombardment (EOB) yield at saturation (mCi/μA) was nearly a factor of four lower than at the higher energy. With a low-energy, two-particle cyclotron, ^{38}K can be produced by the ^{38}Ar(p, n) reaction (*5*), but ^{38}Ar has only 0.063% natural abundance, which makes this target cost-prohibitive. Also, recovery of ^{38}K from a gaseous target and allowing for re-use is a nontrivial task.

On first glance, the preparation of generator-produced ^{62}Cu might appear to be more convenient than that of cyclotron-produced ^{38}K, but the short half-life of the parent isotope, ^{62}Zn ($T_{1/2}$ = 9.3 hr), limits the practicality of the generator. Zinc-62 is produced on a medium-energy cyclotron (27.5 MeV) via the ^{63}Cu(p, 2n) reaction. Many medical cyclotrons are not capable of bombardment above 16 MeV; therefore ^{62}Zn is generally purchased from a centralized facility. The lifetime of the generator is 1–2 days. If there is a medium-energy cyclotron onsite, ^{62}Zn would have to be produced every 2 days for continuous supply of ^{62}Cu, otherwise ^{62}Zn would have to be purchased on a bi-weekly basis. Once the ^{62}Zn is loaded onto the generator, the ^{62}Zn/^{62}Cu generator can be eluted every 30 min.

As a radiopharmaceutical, ^{38}K is simple to prepare. There is no chemistry involved, only dissolution of the target and production of a sterile, injectable solution. In the case of many short-lived, cyclotron-produced isotopes, the system for bombardment, transfer of the target postbombardment to a hot cell and target processing has been automated for routine production of ^{38}K (*5*). The entire procedure for producing sterile, injectable solutions of ^{38}K takes 25–35 min. The preparation of ^{62}Cu-PTSM is relatively simple as well, since the ^{62}Cu-PTSM complex forms rapidly. An accepted ^{62}Cu-PTSM "kit" has not yet been developed. Many investigators use ^{62}Cu-PTSM without any purification (*6,7*), but others purify the complex away from free Cu^{2+} using C-18 Sep-Pak purification (*1,8,9*). With or without Sep-Pak purification, the time needed for preparation is under 10 min. For ^{62}Cu-PTSM, even if an acceptable kit formulation is developed, chemistry problems such as trace

Received Mar. 30, 1994; accepted Mar. 30, 1994.
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