Technetium 94m-labeled methoxyisobutyl isonitrile: Dosimetry and resting cardiac imaging with positron emission tomography

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Background. Development of a positron-emitting form of technetium has allowed the imaging of technetium radiopharmaceuticals with positron emission tomography (PET). We used 94mTc to compare the distribution of the myocardial perfusion agent sestamibi at rest with the conventional PET perfusion tracer 13N-labeled ammonia (13N-ammonia).

Methods and Results. Dosimetry calculations were performed with the known whole-body distribution of 99mTc-labeled sestamibi. Dynamic PET imaging of 13N-ammonia and 94mTc-labeled sestamibi (94mTc-sestamibi) for 32 minutes was performed in eight patients with previous myocardial infarction. Initial myocardial and extramyocardial distribution of 94mTc-sestamibi was compared with that of 13N-ammonia by qualitative and quantitative analysis. Quantitative comparison of the two tracers was performed with region-of-interest analysis and circumferential profiles. Qualitatively, the cardiac distribution of the tracers was similar in normal and infarcted myocardium. A decrease in the definition of the epicardial and endocardial borders of the heart was seen with 94mTc-sestamibi, presumably because of the lower dose of radionuclide injected. Quantitatively, there was no difference in infarct size, defined prospectively as tracer activity less than 20% of maximum activity for the section, between the two tracers. Circumferential profile analysis with 12-degree radial sections similarly demonstrated no difference in regional cardiac distribution of the tracers.

Conclusions. These results revealed no significant difference in myocardial uptake compared with 13N-ammonia suggesting that the myocardial uptake of sestamibi correlates with that of myocardial perfusion. (J Nucl Cardiol 1994;1:425-33.)

Key Words: positron emission tomography • nitrogen 13-labeled ammonia • technetium 94m-labeled sestamibi • myocardial infarction

The radionuclide 99mTc has gained widespread acceptance in clinical nuclear medicine because of its availability from a generator, relatively short half-life of 6.03 hours, and its decay by a 140 KeV gamma emission. Validation of pharmacokinetics of 99mTc radiopharmaceuticals has required the use of animal data or in vivo clinical studies. Clinical studies of the kinetics of 99mTc radiopharmaceuticals, however, have been limited to gamma camera imaging. The development of 94mTc chemistry, with the positron emitter 94mTc (53-minute half-life), allows the study of technetium radiopharmaceuticals with the higher spatial and temporal resolution and quantitative capabilities of positron emission tomography (PET).1

The utility of 94mTc PET was tested in the determination of infarct size by the myocardial perfusion agent 99mTc-labeled methoxyisobutyl isonitrile (99mTc-sestamibi). There has been some concern that 99mTc-sestamibi may overestimate the size of myocardial infarcts compared with 201Tl chloride gamma camera imaging or 13N-labeled ammonia (13N-ammonia) PET.2,3 These comparisons required two different nuclides (201Tl and 99mTc) or two different nu-
Imaging of 94mTc-labeled MIBI with PET September/October 1994, Part 1

Figure 1. 94mTc-sestamibi and 13N-ammonia PET images in 66-year-old women with previous posterolateral wall myocardial infarction. 94mTc-sestamibi images are in top row and 13N-ammonia images are in bottom row. Images are summed dynamic frames from last 16 minutes of acquisition and are oriented in transaxial views superior to inferior with patient’s right side on left side of image. Extensive posterolateral defect is seen on both images. Greater hepatic uptake of 94mTc-sestamibi than 13N-ammonia was also present.

cides (99mTc and 13N) with two different imaging techniques (gamma camera imaging and PET). To compare the pharmacokinetics of Tc-labeled sestamibi directly with those of 13N-ammonia, imaging was performed in patients with 94mTc-labeled sestamibi (94mTc-sestamibi) and 13N-ammonia with both nuclides imaged by PET.

The objectives of this study were to compare qualitatively and quantitatively the initial regional myocardial distribution of 94mTc-sestamibi with that of 13N-ammonia in normal and infarcted myocardium at rest.

METHODS

**Radionuclide Synthesis.** 13N-labeled ammonia was produced on the University of Wisconsin Medical Physics CTI RDS 11 MeV proton cyclotron (CTI-Siemens, Inc., Knoxville, Tenn.) by irradiating a high-pressure, flow-through aqueous target of 5 mmol/L ethanol. 13N-ammonia was separated by trapping on a cation-exchange column and eluted with 155 mmol/L NaOH and then titrated to pH 4 to 5 with HCl/citric acid buffer to physiologic saline solution. 94mTc was produced by irradiation of a 0.1 mm natural molybdenum foil target. 94mTc was separated by electrolytic dissolution in HCl and H2O2 solution and solvent extraction in methyl-ethyl ketone. After removal of methyl-ethyl ketone, 94mTc was diluted in normal saline solution and complexed to sestamibi in a fashion similar to that for 99mTc. 94mTc was added to the commercially available sestamibi kit (DuPont Merck Pharmaceutical Co., Billerica, Mass.) and heated at 100°C for 10 minutes. Quality control was performed by three chromatographic procedures: reverse-phase high-pressure chromatography with a mobile phase of 45% methanol, 35% 50 mmol/L ammonium sulfate, and 20% acetonitrile; thin-layer chromatography with ethanol as the solvent; and alumina Sep-Pak cartridge (unpublished data) (Waters Chromatography Division, Milford, Mass.). All doses had a radiochemical purity in excess of 95% by all three methods.

**Dosimetry.** Dosimetry was initially calculated as described previously,1 with published biodistribution data for 99mTc-sestamibi.6 At that time, because S values were not available for the other technetium isotopes, S values for 94mTc, 94Tc, 95Tc, 96Tc, and 95mTc were estimated by interpolation between published S factors of radioisotopes of similar radiation properties.7 Final dosimetry for this report was calculated with S values for the technetium isotopes8 from Michael Stabin of the Radiopharmaceutical Internal Dose Information Center, Oak Ridge Associated Universities, Oak Ridge, Tenn., and transfer rates for sestamibi from Richard Sparks (unpublished data), also of Oak Ridge Associated Universities. Human distribution data were obtained from published biodistribution data6 with confirmation of liver distribution from the PET studies of 94mTc-sestamibi. Cumulative organ activity was calculated with the modeling software STELLA (High Performance Systems, Hanover, N.H.), with activity of the