Myocardial Perfusion Imaging With $^{99m}$Tc-DMPE in Man*

Myron C. Gerson1,4, Edward A. Deutsch2, Hiroshi Nishiyama3, Karen F. Libson2, Robert J. Adolph1, Lawrence W. Grossman3, Vincent J. Sodd3, Donald L. Fortman1, Jean-Luc E. Vanderheyden2, Craig C. Williams4, and Eugene L. Saenger4

Division of Cardiology, Department of Internal Medicine1, Department of Chemistry2, Nuclear Medicine Laboratory, Dep, BRH, FDA3 and E.L. Saenger Radioisotope Laboratory, Department of Radiology4, University of Cincinnati, Cincinnati, Ohio

Abstract. Technetium-$^{99m}$ DMPE ($^{99m}$Tc-DMPE) is a newly synthesized myocardial perfusion imaging agent that shows intense myocardial accumulation in the dog. In the present study, dosimetry and potential clinical usefulness of this agent were assessed in four human subjects. Absorbed radiation doses were low, with the highest doses consisting of 200 mrad/mCi (54 μGy/MBq) to the gallbladder and 160 mrad/mCi (43 μGy/MBq) to the liver. No evidence of clinical toxicity was found. Technetium-$^{99m}$ DMPE did image the myocardium, but the ratio of target to nontarget activity was less favorable than that observed in the dog. Intense hepatic $^{99m}$Tc-DMPE activity interfered with clinical imaging of the cardiac apex in two of the four subjects. We conclude that the prototype radiopharmaceutical, $^{99m}$Tc-DMPE, is capable of myocardial perfusion imaging in man but the planar myocardial images produced are of inferior quality compared with $^{201}$Tl myocardial images. Further work is justified to develop related compounds to overcome the clinical limitations described.

Materials and Methods

Patients

Two 39-year-old asymptomatic volunteers and two patients with documented coronary artery disease were studied. Patient 1 is a 47-year-old man with clinical and electrocardiographic documentation of previous inferior and anterior myocardial infarction. Cardiac catheterization demonstrated greater than 50% stenosis of each of the three major coronary arteries with a left ventricular ejection fraction of 31%. Patient 2 is a 65-year-old man with historical, enzymatic, and electrocardiographic evidence of a recent anteroseptal myocardial infarction. Cardiac catheterization demonstrated diffuse severe three-vessel coronary artery disease and a left ventricular ejection fraction of 33%.

Radiopharmaceutical Preparation and Quality Control

Solutions of $^{99m}$Tc (DMPE)$_2$Cl$_5$", i.e. $^{99m}$Tc-DMPE, were prepared by heating in a sealed vial an aqueous ethanol solution of HCl, NaCl, $^{99m}$TeO$_4^-$, and excess DMPE ligand. This reaction mixture was then neutralized with NaOH and loaded onto a Sephadex SP C-25 cation exchange column (Pharmacia Inc., Piscataway, New Jersey); washing with water removed the excess DMPE ligand, and subsequent elution with 0.5 M NaCl removed the desired $^{99m}$Tc-DMPE radiopharmaceutical at a concentration of approximately 10 mCi/ml.

Every preparation of $^{99m}$Tc-DMPE was analyzed by high-performance liquid chromatography. In each case, the retention time of the predominant component was the same as that of the characterized (Deutsch et al. 1981) $^{99m}$Tc analog $^{99m}$Tc (DMPE)$_2$Cl$_5$ and the purity of this predominant $^{99m}$Tc-DMPE component was greater than 95%.

A portion of the $^{99m}$Tc-DMPE radiopharmaceutical was administered to an anesthetized dog immediately prior to the human study. In each case, typical (Deutsch et al. 1981) canine myocardial images were obtained.

Imaging Procedure

An informed consent statement explaining the purpose and potential risks of the study was approved by the University of Cincinnati Committee on Human Research and completed by each subject. Normal volunteers underwent exercise imaging with 2.0 mCi (74 MBq) $^{201}$Tl at least 5 days.
prior to the administration of $^{99m}$Tc-DMPE. Comparison resting images were obtained 4 h later. Thallium-201 images and the first two studies with $^{99m}$Tc-DMPE were performed using a gamma camera (Series 120, Technicare Corp., Solon, Ohio) equipped with a general purpose parallel-hole collimator. Subsequent $^{99m}$Tc-DMPE studies were performed using a high-resolution collimator. Myocardial images were displayed on Polaroid film and were also entered into a portable minicomputer. Images contained 400,000 counts per view.

An initial study was performed using 2 mCi (74 MBq) $^{99m}$Tc-DMPE in order to establish the radiopharmaceutical dosimetry and clinical safety of the compound. The first volunteer (E.D.) exercised on a treadmill for 13 min by the Bruce protocol to a heart rate of 167 beats per minute, a blood pressure of 172/70, and limiting fatigue. One minute prior to the conclusion of exercise, 2.3 mCi (85 MBq) $^{99m}$Tc-DMPE were administered IV. Imaging in the anterior projection was started within 2 min following the termination of exercise and continued with images acquired in the 40° left anterior oblique, 70° left anterior oblique, and left lateral projections. The second volunteer (K.L.) was imaged by administering 2.1 mCi (78 MBq) $^{99m}$Tc-DMPE IV at rest and no exercise study was performed. Serial images containing 400,000 counts were acquired in the left anterior oblique projection for 44 min following injection. Following calculation of resting and exercise $^{99m}$Tc-DMPE human dosimetry data, repeat imaging was performed in the first volunteer (E.D.) by administering 10 mCi (370 MBq) isotope at rest and acquiring a series of images in the left anterior oblique projection during the subsequent 1 h. The two patients were then imaged at rest following $^{99m}$Tc-DMPE doses of 10.4 mCi (380 MBq) and 8.9 mCi (330 MBq) respectively. Images were processed on a portable minicomputer (A2 Medical Data Systems, Ann Arbor, Michigan) using 30% background subtraction and a standard nine-point smoothing program.

**Dosimetry**

Absorbed radiation dose estimates were computed for the two normal volunteers. Data collection consisted of computer acquired scintillation camera images of the organs of interest, total body counts with a scanning whole body counter (Grossman et al. 1980) and assay of voided urine. Each patient was imaged and counted at 2, 4, 8, and 24 h post-administration.

Quantitation of total body and organ uptake was done by the method of conjugate counting (Sorenson 1971) whenever possible.

For some organs of interest, overlying activity from other organs prevented good visualization on both the anterior and posterior views. In this case, a representative mean depth was assumed and uptake was estimated from a single image.

Absorbed radiation doses were then calculated by the MIRD method (Loevinger and Berman 1976; Snyder et al. 1975) using the CAMIRD computer program (Feller 1974). Gallbladder doses were calculated manually using recently published S factors (Bernard and Chen 1980).

Patient safety data included continuous electrocardiographic monitoring and intermittent blood pressure monitoring for 30 min following $^{99m}$Tc-DMPE administration. A complete blood count, blood urea nitrogen, serum electrolytes, serum creatinine, serum glucose, alkaline phosphatase, gamma glutamyl transpeptidase, total and direct bilirubin, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), serum albumin, lactic dehydrogenase (LDH), and creatine kinase (CK) were collected prior to $^{99m}$Tc-DMPE administration and repeated 24 h, 48 h, and 3 weeks following drug administration.

**Animal Studies**

Comparison animal images were performed in an 18.6 kg mongrel dog and an 18.6 kg pig. The animals were anesthetized with sodium pentobarbital, and placed in the right decubitus position under a gamma camera with a high-resolution collimator in the 60° left anterior oblique view. Each animal received IV 5 mCi (190 MBq) $^{99m}$Tc-DMPE preparation used in the repeat imaging of the first volunteer (E.D.).

**Results**

Myocardial scintigraphy 16–19 min following administration of 2 mCi (74 MBq) $^{99m}$Tc-DMPE to a normal volunteer (K.L.) at rest is shown in Fig. 1a. Radioisotope accumulation was primarily observed within the cardiac blood pools during the initial 5 min after injection. High myocardial accumulation of tracer relative to lung and cardiac blood pool activity were observed beginning at 6 min following injection. Intense hepatic activity obscuring the cardiac apex is also present. A left anterior oblique image obtained

---

**Fig. 1.**

a. Left anterior oblique myocardial image acquired 16–19 min following IV administration of $^{99m}$Tc-DMPE to a normal volunteer at rest.

b. Resting left anterior oblique image acquired 4 h following $^{201}$Tl injection in the same volunteer.