

EDITORIAL COMMENT

Resurrection of Thallium-201 for Myocardial Perfusion Imaging*

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Thallium-201 has several virtues as a myocardial perfusion agent. It is one of the best of the soluble agents for measuring regional myocardial perfusion, because it has a blood clearance half-time of <30 s and a first pass extraction in the myocardium of >88% (1) (compared with the >1-min blood clearance half-time [2] and 50% to 60% first pass extraction of technetium-99m sestamibi) (3). These biological characteristics of thallium provide higher contrast between regions of normal perfusion and zones of ischemia, even on planar myocardial perfusion studies. Numerous publications confirmed the sensitivity, specificity, and diagnostic accuracy of myocardial perfusion imaging with thallium (4,5).

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Some biological characteristics of thallium, however, are not so favorable. The electron capture decay of thallium produces 88 X-ray photons at 70 to 80 keV and approximately 12 gamma photons at 135 and 167 keV for each 100 disintegrations. In addition to the low energy of the predominant photon, the physical half-life of 73 h and biological half-life of approximately 10 days (240 h) results in a relatively long effective half-life of approximately 56 h. In addition to myocardium, skeletal muscle, and liver—the tracer also localizes—in the testes and kidneys, producing an effective dose equivalent of 34.5 mSv/150 MBq (6). The result is a limitation of the administered dose to approximately 150

MBq, limiting image quality, and associated with a relatively high absorbed dose.

When technetium-99m-labeled sestamibi was approved by the Food and Drug Administration in December 1991 (7), there was rapid adoption of the tracer, even though it was inferior to thallium for the determination of regional myocardial perfusion. Human studies demonstrated reduced lesion size with stress sestamibi imaging compared with thallium, making regions of mild ischemia more difficult to identify on myocardial perfusion scans (8). This property of reduced contrast is also shared by tetrofosmin. In spite of longer blood clearance and lower myocardial extraction of both sestamibi and tetrofosmin, the technetium-99m-labeled perfusion agents have a shorter effective half-life and lower effective dose equivalent (12.3 mSv/1,480 MBq and 9.6 mSv/1,480 MBq, respectively) than thallium-201, allowing administration of much larger doses, resulting in “prettier” images. Hence, the technetium agents were used for >90% of the 8 million cardiac imaging studies in the U.S. (9) in 2006. Although some institutions adopted a dual tracer imaging protocol as a means of shortening the “1-day imaging protocol,” where thallium-201 was employed for the rest images and a technetium-99m-labeled agent for stress (10), this approach did not take advantage of the major virtue of thallium as a stress imaging agent. In the past, investigators, such as Steele et al. (11), attempted to perform dual tracer imaging with injection of thallium-201 at rest [148 MBq] and technetium-99m sestamibi at rest [222 MBq]. These investigators used a unique multi-aperture pinhole collimator mounted on a multidetector Anger camera to record single-photon emission computed tomography (SPECT) images, and relied on novel software to minimize scatter in their reconstructed data. Although the

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results were promising, their approach employed a 4-mCi dose of thallium-201.

Berman et al. (12), in their article in this issue of *ijACC*, use a new high-speed SPECT, coupled with a reduced dose of thallium-201 administered at stress, in a novel approach to regain the virtues of thallium-201 as a tracer for stress myocardial perfusion imaging, while minimizing the radiation burden. The authors report that doses of 2 mCi (74 MBq) of thallium-201 injected at stress and a 6-min image acquisition protocol produced images of good-to-excellent diagnostic quality in up to 97% of patients. The authors indicate that after recording the stress thallium images, a dose of 8.9 mCi (396 MBq) of technetium-99m-labeled sestamibi or tetrofosmin and a 4-min imaging protocol provided diagnostic quality images in approximately 96% of patients at rest.

The high-speed SPECT instrument offers the potential of simultaneous recording of dual tracer images. The solid state detector material, cadmium zinc telluride (CZT), has a spectral resolution of 6.5% at 140 keV (13). Simultaneous dual tracer imaging would minimize problems detecting small changes in regional perfusion and likely allow easier identification of attenuation artifacts.

Although the 6.35 mm (1/4 inch) or 9.52 mm (3/8 inch) sodium-iodide detectors used in modern Anger cameras have spectral resolution of approximately 10% at 140 keV and 15% at 80 keV, (far worse than CZT), it might be possible to use Dr. Berman's concept to record dual tracer images with these instruments. Back of the envelope considerations suggest that using a combination of asymmetrical windows and scatter correction algorithms with administration of 3 mCi (110 MBq) thallium-201 at stress and 10 mCi (370 MBq) of a technetium agent at rest might produce SPECT images of diagnostic quality. In fact, investigators have at-

tempted to do this (14) albeit with only modest success. However, the lower energy Tl-201 window data are substantially contaminated by the down-scatter from the higher (3 to 4 times greater) injected dose of the technetium-99m (Tc-99m) agent. Improved energy resolution does not assist much in this situation, because: 1) the origin of the scattered events is within the body; and 2) as the lower Tl-201 window measures a broad spectrum of X-rays with photon energies of 70 to 80 keV, the window is a reasonably wide one. Experience from previous work using Tc-99m and measuring Gd-153 transmission photons (window centered at 100 keV) showed that, in the thorax, the down-scattered photon count rate could be as high as 60% of that recorded in the 140 keV photopeak window (15). Similar amounts could be expected in the 70- to 80-keV window. Thus, trying to detect areas of decreased perfusion in the stress Tl-201 study will be particularly susceptible to the ability to accurately correct for the down-scattered Tc-99m photons.

Even if dual tracer simultaneous imaging is not feasible, the present proposal makes a major contribution with the documentation that sequential images of diagnostic quality images can be recorded in 6 min with an administered dose of 2 mCi of thallium-201 at stress and a subsequent 4-min image after injection of 8 to 9 mCi of a technetium perfusion agent at rest.

We look forward to future publications documenting the sensitivity and specificity of these novel imaging protocols in patients undergoing selective coronary angiography or CT coronary angiography.

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REFERENCES

1. Strauss HW, Pitt B. Thallium 201 as a myocardial perfusion imaging agent. *Sem Nucl Med* 1977;7:49-58.
2. Primeau M, Taillefer R, Essiambre R, Lambert R, Honos G. Technetium 99m SESTAMIBI myocardial perfusion imaging: comparison between treadmill, dipyridamole and trans-oesophageal atrial pacing "stress" tests in normal subjects. *Eur J Nucl Med* 1991;18:247-51.
3. Marshall RC, Leidholdt EM Jr., Zhang DY, Barnett CA. Technetium-99m hexakis 2-methoxy-2-isobutyl isonitrile and thallium-201 extraction, washout, and retention at varying coronary flow rates in rabbit heart. *Circulation* 1990; 82:998-1007.
4. Kaul S. A look at 15 years of planar thallium-201 imaging. *Am Heart J* 1989;118:581-601.
5. Van Train KF, Maddahi J, Berman DS, et al. Quantitative analysis of tomographic stress thallium-201 myocardial scintigrams: a multicenter trial. *J Nucl Med* 1990;31:1168-79.
6. Society of Nuclear Medicine Myocardial Perfusion Imaging Guidelines. Available at: <http://interactive.snm.org/docs/155.pdf>. Accessed January 22, 2009.
7. Ghosh PR. FDA approves two new technetium-labeled cardiac agents and a pharmacologic alternative to exercise in stress-thallium studies. *SNM Newsline J Nucl Med* 32;11N-19N.
8. Maublant JC, Marcaggi X, Lusson JR, et al. Comparison between thallium-201 and technetium-99m methoxy-isobutyl isonitrile defect size in single-photon emission computed tomography at rest, exercise and redistribution in coronary artery disease. *Am J Cardiol* 1992;69:183-7.

9. DRAXIS Names GE Healthcare as Exclusive Distributor of DRAXIM-AGE(R) Sestamibi in USA. Available at: http://salesandmarketingnetwork.com/news_release.php?pipe=0000ac177000191&ID=2022417&key=radiopharmaceutical. Accessed January 22, 2009.
10. Berman DS, Kiat H, Friedman JD, et al. Separate acquisition rest thallium-201/stress technetium-99m sestamibi dual-isotope myocardial perfusion single-photon emission computed tomography: a clinical validation study. *J Am Coll Cardiol* 1993;22:1455-64.
11. Steele PP, Kirch DL, Koss JE. Comparison of simultaneous dual-isotope multipinhole SPECT with rotational SPECT in a group of patients with coronary artery disease. *J Nucl Med* 2008;49:1080-9.
12. Berman DS, Kang X, Tamarappoo B, et al. Stress thallium-201/rest technetium-99m sequential dual isotope high-speed myocardial perfusion imaging. *J Am Coll Cardiol Img* 2009;2:273-82.
13. Mueller B, O'Connor MK, Blevins I, et al. Evaluation of a small cadmium zinc telluride detector for scintimammography. *J Nucl Med* 2003;44:602-9.
14. Weinmann P, Faraggi M, Moretti JL, Hannequin P. Clinical validation of simultaneous dual-isotope myocardial scintigraphy. *Eur J Nucl Med Mol Imaging* 2003;30:25-31.
15. Bailey DL, Hutton BF, Walker PJ. Improved SPECT using simultaneous emission and transmission tomography. *J Nucl Med* 1987;28:844-51.

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