Tl-201 dosing for CZT SPECT: More new information

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Thallium-201 was the original and the only myocardial perfusion imaging (MPI) tracer, first for planar (1973) and later for SPECT imaging (1980s), for almost 15 years. Introduction of Tc-99m-based tracers (sestamibi-1984, tetrofosmin-1989) knocked Tl-201 from the pedestal. The advantages of Tc-99m-based agents became obvious: higher energy (140 keV vs 69-80 keV), shorter half-life (6 hours vs 72 hours), flexibility of imaging protocols (due to lack of meaningful Tc-99m redistribution), and local production of the tracer (using molybdenum generator vs dose delivery of Tl-201). The higher energy Tc-99m gamma rays and a shorter half-life increased the acquired count density, and thus improved the quality of both perfusion and gated images compared to Tl-201.

The advent of coronary CT angiography (CTA) and the exponential increase of MPI volume unleashed the previously non-existent debate pointing to possible long-term harmful effects of low-dose radiation used for diagnostic imaging.[1] CTA technology evolved and answered rapidly with a substantial decrease in radiation exposure.[2]

Migration from Tl-201 to Tc-99m by the nuclear cardiology community was driven more by the ease of use of Tc-99m-based tracers, rather than by fear of substantially higher per study radiation exposure of Tl-201 (15 mSv vs 9-11 mSv). Most recently, the majority of criticism was aimed at dual-isotope protocols (Tl-201 rest/Tc-99m stress), which result in the highest radiation exposure per study (22-23 mSV) not offset by a relatively modest decrease of the length of the test.[3]

Using standard imaging technology (Anger camera) and standard Tl-201 doses (3-4 mCi), some advantageous Tl-201 characteristics remain:

(1) Tl-201 is by design ‘‘stress-first imaging.’’[4] Immediate review of stress images may reveal normal perfusion or an unexpectedly abnormal result such that the rest/redistribution portion of the test may then be avoided. This would significantly decrease the length of the test (from 4-6 hours to 1 hour) and additionally decrease radiation exposure to the laboratory personnel and to accompanying visitors.[5]
(2) As Tl-201 is excreted by the kidneys, high sub-diaphragmatic tracer accumulation is not an issue, compared to the gastrointestinal excretion of Tc-99m.
(3) Flow to uptake linearity is better preserved with Tl-201 compared to Tc-99m-labeled tracers. This is of particular importance with the use of coronary vasodilators. Coronary blood flow increases by non-physiologic amounts (200-300%) with vasodilators, compared to approximately 100% with moderate exercise.
(4) Tl-201 remains a preferred ‘‘viability tracer’’ due to its ability to visualize severely dysfunctional myocytes. Tl-201 crosses the cellular membrane, while Tc-99m tracers are transported into the mitochondria, an organelle more susceptible to ischemic damage.
(5) Because of early post-stress imaging, Tl-201 lung uptake can be quantified and used as a surrogate for pulmonary capillary wedge pressure.
(6) Past and likely future Tc-99m shortages will lead either to the abandonment of SPECT imaging in favor of PET or other non-invasive modalities, or to the resurrection of Tl-201 imaging.

So, one must ask how does the relatively recent introduction of high-efficiency SPECT technologies (CZT SPECT) affect our approach to Tl-201 imaging?

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Ishihara et al from Japan address in the current issue of the *Journal* the optimal dosing of Tl-201 for the D-SPECT high-efficiency CZT camera (Spectrum Dynamics, Caesarea, Israel).[6] Image quality, uniformity, resolution and contrast, and target to background ratio were studied using a myocardial phantom with 10 mm anterior and 20 mm inferior wall defects. The authors concluded that a total of at least 1.2 million counts were needed for adequate SPECT image quality.

Their clinical study included 292 consecutive patients with suspected or known CAD: 85 underwent exercise stress, 207 underwent adenosine infusion. The Tl-201 dose was 3-4 mCi, imaging time was 6 minutes, and rest imaging was performed 3-4 hours later. Optimal injected Tl-201 dose was found to depend on BMI (rather than on weight and gender) and type of stress (higher Tl-201 dose was needed for exercise stress compared to adenosine infusion). Based on their data, the authors establish BMI-based doses ranging from 2 to 4 mCi for 6-minute acquisition using the D-SPECT camera (Table 1).

Can we accept the results of this study and incorporate them into our current practice? Perhaps, except for several provisions:

(1) Two high-efficiency CZT SPECT cameras are currently available: the D-SPECT (Spectrum Dynamic, Israel) and Discovery (GE Medical, Haifa, Israel). Both use CZT semiconductors, but differ in collimation and reconstruction parameters. The data presented in the current study were derived from the D-SPECT camera and need to be confirmed for the Discovery camera as well.
(2) It has already been postulated that approximately 1 million counts are needed for high-quality CZT SPECT.[7] This recommendation was validated for Tc-99m tracers and weight-based dose recommendations were published.[8] The D-SPECT camera can already be set to complete image acquisition when a total number of myocardial counts have been obtained, while the Discovery camera cannot. By imaging to a specific amount of counts determined to be adequate for image interpretation, one can adjust the injected activity knowing that the imaging time will be adjusted accordingly based on count rate.
(3) The major objection for the use of Tl-201 in routine practice is the high radiation exposure. Current 2016 ASNC guidelines for Anger cameras recommend 2.5-3.5 mCi of Tl-201.[3] Six-minute acquisition, as recommended by the authors, requires 2-4 mCi of Tl-201. The emphasis of a progressive protocol should be not only shortening the imaging time, but also decreasing tracer (and radiation) dose. Achieving recommended Tl-201 doses for newer cameras by the 2016 ASNC guidelines (1.3-1.8 mCi) would therefore require at least doubling the imaging time (2-4 mCi for 6 minutes, 1-2 mCi for 12 minutes). This is still a somewhat shorter time compared to traditional Anger camera acquisition. Unfortunately, longer image acquisition times increase the chance of motion artifacts, and high-efficiency CZT cameras lack robust motion correction applications. It is possible that post-stress imaging time could be shorter (or injected dose could be lower), since the authors analyzed only redistribution images (3-4 hours post peak stress injection).

Previous work on Tl-201 imaging with high-sensitivity SPECT has found that lower injected activity can be used while maintaining diagnostic image quality if longer imaging times are accepted. In one study of a little over 100 patients, administered activity of 40-50 MBq (roughly 1/2 to 1/3 of the dose used in the current paper) achieved acceptable results even in obese patients with imaging times of 10 and 13 minutes.[9] Songy et al. compared images with similar standard doses of Tl-201 on a high-efficiency camera with 5-minute acquisition and a conventional SPECT camera with 10- to 15-minute acquisition.[10] Other previous work has raised concerns about the accuracy of gated images with lower dose of Tl-201 on high-efficiency cameras.[11] Finally, the correct dose of Tl-201 on high-efficiency SPECT cameras must also be put into perspective with the future possibility of calculating coronary flow reserve.[12]

Appropriate dose and imaging time need to be individualized with emphasis on lower doses in patients with longer expected survival. An elderly patient with back

Table 1. Recommended BMI and stress-type-based Tl-201 dosing for D-SPECT CZT camera

Adenosine		Exercise	
BMI (kg/m2)	**Tl-201 (mCi)**	**BMI (kg/m2)**	**Tl-201 (mCi)**
≤19.2	2	n/a	n/a
19.2–26	3	<17.4	3
26–32.6	4	17.4-24.2	4

pain could be imaged with great rapidity, but with only marginally decreased dose. A young patient with atypical pain could be successfully studied for less than 1 mSv by using a stress-first protocol, a very low dose, and standard imaging times.

(4) The imaging of patients with high BMI is challenging for all imaging modalities. The proposed dosing in this study covers underweight patients (BMI <19 kg/m^2) and those with BMI <30 kg/m^2. It is not clear if adequate imaging quality is feasible for obese and morbidly obese patients. The Discovery camera may not be optimally designed to accommodate large patients, while the D-SPECT camera has been successful in imaging patients with high BMI's.[13]

(5) No information was presented about the quality of gated images (early post-stress and at rest).

The current study is an attempt to create a simple, BMI-based Tl-201 imaging protocol for one of the models of high-efficiency SPECT cameras. By choosing 1.2 million counts (the reason for which is not completely clear as their assessment of image quality did not reach ‘‘good’’ on average until 1.5 million counts), the authors established Tl-201 doses for different BMI ranges for both exercise and vasodilator stress based on redistribution images (adjustment for post-stress images is not available). This work is all well and good, and likely helpful to your practice if you use Tl-201, enjoy imaging for 6 minutes (no more, no less), are ambivalent about gated image quality, and are not challenged with the imaging of overweight and obese patients. A desirable contribution to the Tl-201 literature in the CZT era would be the creation of tables of stressor- and gender-specific data which would demonstrate how injected activity and imaging time vary based on BMI, height, or weight. This would allow for patient-centered imaging protocols with a degree of reasonable prediction of the imaging time with any given injected activity.

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