Advances in Cardiovascular Imaging

Achieving Very-Low-Dose Radiation Exposure in Cardiac Computed Tomography, Single-Photon Emission Computed Tomography, and Positron Emission Tomography

Damini Dey, PhD; Piotr J. Slomka, PhD; Daniel S. Berman, MD

During the past several years, the need to reduce radiation has become a central issue in cardiac imaging. During this time, radiation dose to the patient in cardiac computed tomography (CT), single-photon emission computed tomography (SPECT), and positron emission tomography (PET) has seen significant reductions without compromising image quality, primarily because of new developments in scanner hardware and reconstruction software. Sub-mSv radiation doses have been reported for cardiac CT.1–5 Stress and rest SPECT myocardial perfusion imaging (MPI) traditionally required ≈15 minutes to register the required number of photon events. New SPECT camera instrumentation and software have now enabled acquisition times as short as 2 minutes, to increase counting efficiency by up to a factor of 7.4 These new systems can also be used to reduce radiation exposure to patients during the MPI scan, allowing a corresponding marked reduction in the administered dose of radioactivity when used with the standard imaging time.7 It is important to keep radiation exposure as low as reasonably achievable. In this review, therefore, we briefly summarize recent technical advances in scanner hardware and reconstruction software, as well as the steps recommended to achieve very low radiation dose in cardiac imaging. We also review the current status of radiation in cardiac CT, SPECT, and PET as reported in multicenter studies and registries, as well as current clinical reports of radiation dose reduction, which illustrate the potential of the newest technology.

Advances in Cardiac CT

Direct imaging of the coronary arteries is challenging because of their small sizes and rapid motion. Cardiac CT requires high temporal resolution to freeze such motion and therefore has benefited from steadily increasing CT gantry rotation speed. Imaging of the coronary arteries also requires high spatial resolution and reconstruction of submillimeter slices. Multiple transaxial slices need to be acquired simultaneously for complete coverage of the heart in 1 breath-hold. To meet these requirements, technical advances in CT hardware have focused on improved temporal and spatial resolution and more detectors for increased coverage.8

Methods for Dose Reduction in CT

Table 1 summarizes the practical criteria and the cardiac CT scan parameters that can be modified to achieve low radiation dose. Patient-based criteria include consideration of the heart rate and rhythm, body mass index, extent of calcified plaque in the coronary arteries, and prior intervention (eg, stent placement). A further important patient-based criterion may be the clinical indication of the patient (eg, acute versus stable chest pain). As listed in Table 1, the scan parameters include scan acquisition modes, x-ray tube potential (tube voltage), x-ray tube current, pitch for helical scanning (defined as table feed per tube rotation in mm/z coverage per rotation in mm), and scan length.9

Scan Acquisition Modes in Cardiac CT

CT data are acquired with the use of either helical (spiral) or axial scan mode. Helical data are acquired with continuous rotation of the gantry and simultaneous table movement. Axial data are acquired by rotation of the gantry around the stationary patient table, followed by translation of the patient table, if needed, to cover the heart. CT imaging of the heart can be performed with or without intravenous injection of contrast agent. For contrast-enhanced coronary CT angiography (CTA), the typical contrast volume ranges from 50 to 120 mL, delivered at a rate of 4 to 7 mL/s.10 Coronary artery calcification can be detected and quantified by noncontrast cardiac CT with very low radiation exposure.10 Synchronization with the heart cycle is achieved by using the patient’s electrocardiogram (ECG). Image acquisition can be performed with prospective triggering, meaning that the CT system uses the patient’s ECG to trigger release of photons and data acquisition in a predefined segment of the cardiac cycle. Alternatively, retrospective gating can be used where the x-ray data are acquired continuously during several cardiac cycles, allowing retrospective reconstruction of images at any time point during systole or diastole. Cardiac scan modes can be characterized as retrospective ECG-gated helical, prospective ECG-triggered axial, or high-pitch prospective ECG-triggered helical modes.5

X-Ray Tube Current

The x-ray tube current, expressed in units of milliamperes (mA), is the number of electrons accelerated across an x-ray
Table 1. Practical Considerations to Achieve a Low-Dose Cardiac CT Study

<table>
<thead>
<tr>
<th>Criteria/CT Scan/Reconstruction Parameters</th>
<th>Parameters That Can Be Modified in Practice</th>
<th>Relationship to Radiation Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-based criteria: heart rate and rhythm, body mass index, extent of calcified plaque in the coronary arteries, prior intervention (eg, stents), clinical indication</td>
<td>Optimal heart rate reduction with beta-blockade (for coronary CTA)</td>
<td>Optimal heart rate can allow selection of scan parameters that lower dose, as allowed by patient-based criteria</td>
</tr>
<tr>
<td>Scan mode</td>
<td>Retrospective ECG-gated helical Prospective ECG-triggered axial* High-pitch prospective ECG-triggered helical (stable heart rate ≤60 bpm)*</td>
<td></td>
</tr>
<tr>
<td>Scan range</td>
<td>Minimal scan range should be selected, depending on the reason for the test</td>
<td>Decreasing scan range decreases dose linearly*</td>
</tr>
<tr>
<td>Tube current for the scan</td>
<td>Tube current, mA</td>
<td>Decreasing tube current×rotation time (mA×seconds) decreases dose linearly*</td>
</tr>
<tr>
<td>Peak voltage for the scan</td>
<td>Tube current×rotation time (mAmseconds)</td>
<td>Decreasing kV decreases dose*</td>
</tr>
<tr>
<td>Pitch for the scan</td>
<td>For helical scan modes, defined as table feed per tube rotation (mm)/2 coverage per rotation (mm)</td>
<td>Dose approximately proportional to square of kV Increasing pitch decreases dose*</td>
</tr>
<tr>
<td>Iterative reconstruction</td>
<td>For all scans</td>
<td>Improved image quality when x-ray photons are reduced</td>
</tr>
</tbody>
</table>

CT indicates computed tomography; and CTA, CT angiography.
*Reducing the total number of x-ray photons for the scan

ECC-Based Tube Current Modulation

Figure 1 shows a schematic example of prospective ECG-gated scan mode for cardiac CT. For retrospective ECG-gated acquisitions, dose modulation is used to minimize the radiation dose in parts of the cardiac cycle that are not required for assessment of the coronary arteries. This is typically done by continuously modulating the x-ray tube current with the ECG signal (ECG-based dose modulation) so that the x-ray tube current is reduced during systole when there is the greatest motion (Figure 1B and 1C). In addition, the time interval between the maximum x-ray tube current can be shortened to further reduce the radiation dose (Figure 1C). Figure 2 shows an example of low-dose retrospective ECG-gated helical acquisition with the full tube current applied only during a single mid-diastolic phase of the cardiac cycle (Figure 2), which still allows functional assessment of the heart. This is possible using the images in which the tube current was modulated because imaging for ventricular function does not require image quality as high as is needed for coronary artery assessment.12 Figures 3 to 4 illustrate an example case with prospective ECG-triggered axial acquisition. Figure 5 shows a schematic example of prospective ECG-triggered helical acquisitions for cardiac CT. A high-pitch prospective ECG-triggered helical mode in which the pitch can be ≥3.0 is currently available with a second-generation dual-source CT scanner (Figure 5B).

X-Ray Tube Voltage

The tube potential (or voltage) is the electric potential applied across an x-ray tube to accelerate electrons toward the target material, expressed in units of kilovolts (kV); this parameter determines the peak energy of the x-ray beam. Tube potentials ranging from 80 to 140 kV are available for diagnostic imaging on commercial CT scanners, with 100 and 120 kV being the tube potentials most commonly used. Radiation exposure with CT is approximately proportional to the square of the tube voltage. Several studies have shown the noninferiority of image quality of 100 versus 120 kV imaging of coronary arteries in nonobese adult patients (typically weight <85–90 kg or body mass index ≤30 kg/m²).13,14 Reducing tube voltage also results in increased attenuation of the vessel lumen and cardiac chambers when iodinated contrast media are used (Figure 4), resulting in greater image contrast.

Scan Range

The z-axis coverage of the scan (scan range or scan length) is linearly related to radiation dose. A simple step in radiation reduction for any CT scan is to limit the range to only cover only the part of the thorax as needed for the scan.9

It is to be noted that there is a fine balance between image quality and radiation dose reduction. When reducing radiation dose, effort must be made to ensure that sufficient image quality is maintained for confident diagnostic interpretation.15 Automated exposure control software that allows for selection of the optimal patient-specific scan parameters may be helpful in standardizing protocols by maintaining diagnostic image quality while reducing radiation dose to the patient.4,16 There are multiple steps and approximations in radiation dose estimation, including the commonly used conversion factor for the chest (k=0.014 mSv/[mGy·cm]), which has been shown to underestimate the radiation dose by a factor of ≈2.17,18

Iterative Reconstruction Software

Iterative reconstruction software for CT represents another possibility for dose reduction. Because of better noise modeling, it makes it possible to maintain image quality, even when...
the number of x-ray photons is reduced in the acquisition protocol. Although iterative reconstruction techniques have been clinically used for nearly a decade in nuclear MPI,\textsuperscript{18} they have only recently become available from all the major CT manufacturers with feasible reconstruction times for clinical CT. A growing number of recent studies have reported radiation dose reduction while maintaining image quality using iterative reconstruction technique in CT.\textsuperscript{1,4,20,21}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Retrospective ECG-gated helical computed tomographic acquisition, with continuous gantry rotation and simultaneous patient table translation. Radiation dose from the scan is (A) highest with ECG-based tube current modulation turned off, (B) lower with the full tube current applied for a diastolic portion (eg, 40\%-80\%) of the cardiac cycle, and (C) lowest with full tube current applied during only a single phase of the cardiac cycle. Adapted from Halliburton et al\textsuperscript{8} with permission of the publisher. Copyright \textcopyright{}2012. Elsevier. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.}
\end{figure}

**Current Status as Reported in Multicenter Studies and Registries**

The large, prospective multicenter Rule Out Myocardial Infarction Using Computer Assisted Tomography (ROMICAT) trial, which compared an evaluation incorporating coronary CTA with standard-of-care assessment in 1000 patients with symptoms suggestive of acute coronary syndrome between April 2010 and January 2012, reported a mean radiation dose of 11.3±5.3 mSv for coronary CTA and 14.1±4.8 mSv for cardiac SPECT.\textsuperscript{22} In 78 patients in this trial who underwent CTA with a newer 128-slice dual-source CT scanner, the mean radiation exposure was lower (6.2±3.8 mSv) than the other patients.\textsuperscript{23} From the multicenter Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment (CT-STAT) study comparing early coronary CTA with rest–stress MPI for the evaluation of acute low-risk chest pain in 699 patients from June 2007 to November 2008, the mean radiation dose was reported to be 11.5 mSv for CTA and 12.8 mSv for cardiac SPECT.\textsuperscript{23} In the multicenter Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography (DeFACTO) study evaluating 252 patients with stable coronary artery disease in 17 centers between 2010 and 2011, the median effective dose for coronary CTA was 6.4 mSv (interquartile range, 4.4–15.0 mSv).\textsuperscript{24} A multicenter international observational study of 1965 patients undergoing coronary CTA in 2007 in 50 sites reported an average median dose of 12 mSv, with significant differences between study sites and CT systems.\textsuperscript{25} In the multicenter, international Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter Registry (CONFIRM) registry evaluating a consecutive cohort of 24,775 patients without known coronary artery disease who underwent coronary CTA between 2005 and 2009 in expert centers, the reported radiation dose range was 3 to 18 mSv.\textsuperscript{26}

In the multicenter Coronary Artery Evaluation using 320-row Multidetector Computed Tomography Angiography and Myocardial Perfusion (CORE320) study evaluating the accuracy of combined coronary CTA and CT perfusion to identify hemodynamically significant coronary artery disease causing perfusion defect by SPECT (381 patients), the median effective radiation dose for the coronary CTA portion of the study was 3.16 mSv (interquartile range, 2.8–3.6 mSv) for CTA and 9.75 mSv (interquartile range, 9.1–13.0 mSv) for SPECT; in this study, all CT images were acquired with a newer 320-slice multidetector CT scanner with 320×0.5 mm coverage.\textsuperscript{27} The median effective radiation dose for noncontrast CT used for coronary artery calcium scoring was 0.85 mSv (interquartile range, 0.82–0.93 mSv).<ref>

**Prospective Multicenter Studies Evaluating Radiation Dose Reduction**

In a prospective, randomized, multicenter study evaluating 100 kVp tube voltage scan protocol in 400 nonobese patients, coronary CTA using 100 kVp was shown to maintain image quality with significantly reduced radiation exposure (31\% relative reduction), thus emphasizing that 100 kVp scan protocols should be considered for nonobese patients to reduce radiation exposure.\textsuperscript{13} A recent report from the multicenter, prospective imaging consortium participating in a quality improvement program, involving 11901 consecutive patients undergoing CTA at 15 imaging centers in Michigan from 2008 to 2011, has shown that consistent application of radiation dose–reduction techniques was associated with sustained reduction of radiation dose without affecting the proportion of diagnostic scans.\textsuperscript{28} This multicenter study also demonstrated that the use of newer scanner technology resulted in substantial dose reduction. In this study, reduction in tube potential from 120 to 100 kV was the strongest variable associated with achieving a target estimated dose of <10 mSv among all patients (odds ratio, 3.1 [95\% confidence interval, 2.6–3.7]), followed by nonretrospective gating (prospective ECG triggering with axial and high-pitch helical scan mode; odds ratio, 2.2 [95\% confidence interval, 1.97–2.54]), lower body mass index (odds ratio, 1.73 [95\% confidence interval, 1.49–2.0]), and the number of coronary CTA scans per month in each site (odds ratio, 1.38 [95\% confidence interval, 1.2–1.6]).
Most Recent Clinical Reports of Dose Reduction for Coronary CTA

Recent single- and dual-center studies have reported very-low-dose clinical studies with coronary CTA, which illustrate the potential of the newest technology. Table 2 summarizes several recent clinical studies with coronary CTA in which a mean or median effective dose $\leq 2.3$ mSv$^{1-5,20,29-31}$ has been achieved using the dose-saving methods as shown in Table 1.

Prospective ECG triggering, recommended for low and stable heart rates$^9$, was used in all of these studies. The mean patient heart rate during the scan was $<60$ bpm, underlining the importance of optimal heart rate control before the scan. Several of these studies combined multiple radiation dose–reduction strategies, and some used iterative reconstruction. Buechel et al$^{30}$ assessed the feasibility of prospective ECG triggering for achieving low-dose CTA in a large consecutive patient population (566 patients). They showed that low-dose CTA by this scan mode is feasible in a vast majority of everyday population and emphasized that a heart rate $<62$ bpm favors diagnostic image quality.$^{30}$ Wide detector arrays allow prospective ECG-triggered axial acquisition of the whole heart with no table movement. Depending on the heart rate, the scanner automatically acquires data during 1, 2, or 3 cardiac cycles. Recently, Chen et al$^4$ have reported a mean effective dose of 0.93 mSv with a single-beat wide-detector prospective ECG-triggered acquisition, with tube voltage (100 or 120 kV) and optimized tube current determined for each patient by automated exposure control. A few studies have reported sub-mSv radiation doses with high-pitch prospective ECG-triggered helical scan mode in patients with low and stable heart rates $<60$ bpm.$^{1-3}$ This mode is available on a dual-source CT scanner that allows high-pitch helical acquisition (pitch values typically $>3$) over 1 heartbeat, without gaps in the data. In a feasibility study of 21 underweight patients, Schuhbaeck et al$^1$ combined this scan mode with low tube voltage of 80 kV, low tube current–time product of 50 mAs, and iterative reconstruction to achieve a mean effective dose $<0.1$ mSv to rule out significant coronary artery disease. From their study, this level of lowest radiation dose reduction was feasible (with diagnostic image quality) in a selected patient population with body weight $<75$ kg with low and stable heart rates.$^1$

Clinical Reports of Dose Reduction for Coronary Calcium Scoring

Recent studies have also lowered radiation dose for coronary calcium scoring, with a mean effective dose $\leq 1.2$ mSv for coronary calcium scoring. Dey et al$^{32}$ investigated a low-dose prospective ECG-triggered axial acquisition protocol, with optimized tube current based on patient body size. In 66 patients, tube current–time product was reduced to 85 mAs for nonobese patients (body mass index $\leq 30$ kg/m$^2$) and to 120 mAs for obese patients; the reduced dose protocol was equivalent to the standard method at 40% lower radiation dose, with a mean effective dose of $1.0\pm0.2$ mSv.$^{32}$ The same team of investigators had shown earlier that reducing the tube voltage to 100 kV gives equivalent results to standard 120 kV at reduced radiation exposure.$^{33}$ It must be noted, however, for lower tube voltages that the corresponding calcium thresholds for calcium scoring need to be manually calibrated for the
scanner, whereas similar level of radiation dose reduction can be obtained without requiring such calibration by optimization of the tube current. In a recent study, Marwan et al investigated the use of high-pitch prospective ECG-triggered helical scan mode for coronary calcium scoring in 150 patients. This scan mode allowed coronary calcium scoring with effective doses with a mean dose of 0.3 mSv (and consistently <0.5 mSv) at 120 kV.

Advances in Cardiac SPECT

Hardware Advances

The key feature of the new dedicated SPECT cardiac imaging systems now available from several instrumentation vendors is significantly increased photon sensitivity. The higher sensitivity is primarily achieved by a radical redesign of the collimation methods. Traditional systems using low-energy high-resolution collimators are only able to detect <0.02% of the photon events. The new designs of collimation include the multiple pinhole collimators or ultra–high-sensitivity parallel detectors focusing on the heart. In systems being considered for development, the overall system sensitivity can be further improved by dedicated scanner geometry surrounding the patient. This optimized scanner geometry would allow simultaneous collections of counts from all directions without camera rotation. The combination of scintillation crystals with photomultiplier tubes, the standard for >50 years, has been replaced with solid-state photon detectors (cadmium zinc telluride) or alternatively with cesium iodide scintillation detector coupled with photodiodes.

Software Advances

The new SPECT scanners are coupled with improved image reconstruction algorithms implemented in software. New reconstruction algorithms include physical modeling of the collimators and detectors, as well as resolution recovery. Most systems now offer compensation for image resolution loss (especially needed for high-sensitivity collimation) via accelerated iterative reconstruction. Sophisticated software reconstruction methods can also improve image quality obtained by standard SPECT cameras, which can be exploited to reduce imaging time or radiation dose.
Estimated radiation doses for single-isotope (99mTc) stress–rest scans range from 10 to 15 mSv as reported by recent multicenter studies. A recent multiple site survey in 2011 by the American Society of Nuclear Cardiology found that dual-isotope stress–rest imaging, which is associated with a significantly higher radiation dose, dropped from 72% to 15.6% in 10 years since 2001. In this survey based on participating site responses, 51% of the sites reported using ≥1 approaches to reducing radiation exposure, by reducing injected radiopharmaceuticals while increasing imaging time (33%), the use of stress-only imaging (23%), newer camera systems (20.5%), and changing radiopharmaceuticals (19.2%). The survey results reported the underutilization of dose-reduction approaches and suggested significant opportunities for improving radiation safety for patients undergoing nuclear stress testing. Practical recommendations by American Society of Nuclear Cardiology to improve patient radiation safety in cardiac SPECT included increasing the use of low-dose stress-first imaging, further decreasing dual-isotope imaging, promoting wider integration of the appropriate use criteria into clinical practice, and fostering validation, use, and affordability of advanced technologies permitting reduced administered activity of radiotracers.

Clinical Reports of Dose Reduction
A few clinical studies have been conducted to evaluate reduced dose protocols with standard and new gamma cameras. In one of these studies, low-dose stress-only protocols allowed radiation dose as low as 4.2 mSv for a 12.5 mCi 99mTc scan. A low-dose rest–stress 99mTc protocol has been studied, resulting in 5.1 to 6.1 mSv exposure. Low-dose imaging was also demonstrated on a standard SPECT camera using an iterative reconstruction technique with standard acquisition times. In another study, the patient dose was reduced to 4.3 mSv for stress–rest protocols when background activity subtraction was applied.

Stress-Only Imaging
MPI radiation dose to the patient can be significantly reduced if the rest scan is not performed. Furthermore, stress-only protocols

BMI indicates body mass index.

### Table 2. Very-Low-Dose Coronary Computed Tomographic Angiography Clinical studies With Mean or Median Effective Dose <3.0 mSv

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Heart Rate, bpm</th>
<th>BMI, kg/m²</th>
<th>Dose-Reduction Methods</th>
<th>Mean Effective Dose, mSv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schuhbaeck et al²</td>
<td>21</td>
<td>50±6</td>
<td>23.9±3.2</td>
<td>Prospective ECG-triggered helical, tube voltage 80 kV, tube current 50 mAs, iterative reconstruction</td>
<td>0.06±0.01</td>
</tr>
<tr>
<td>Achenbach et al²</td>
<td>50</td>
<td>54±4</td>
<td>Body weight 77±11 kg</td>
<td>Prospective ECG-triggered helical, tube voltage 100 kV, tube current 320 mAs</td>
<td>0.87±0.07</td>
</tr>
<tr>
<td>Achenbach et al³</td>
<td>50</td>
<td>54±6</td>
<td>...</td>
<td>Prospective ECG-triggered helical, tube voltage 100 kV, tube current 320 mAs</td>
<td>0.76±0.08</td>
</tr>
<tr>
<td>LaBounty et al³</td>
<td>208 normal BMI patients, 103 with low-dose protocol</td>
<td>54.3±6.3</td>
<td>22.3±2.2</td>
<td>80 vs 100 kV</td>
<td>0.9 (0.8–1.7) mSv</td>
</tr>
<tr>
<td>Chen et al⁴</td>
<td>107</td>
<td>57.1±11.2</td>
<td>27.3 (24.6–32.3)</td>
<td>100 kV, single-heartbeat wide-detector prospective ECG-triggered axial scan, tube voltage, and tube current by automated exposure control</td>
<td>0.93 (0.58–1.74)</td>
</tr>
<tr>
<td>LaBounty et al⁵⁵</td>
<td>449, 202 with low-dose protocol</td>
<td>57±9</td>
<td>27±5</td>
<td>100 kV, lowered tube current 412 mA, prospective ECG-triggered axial</td>
<td>1.3 (0.8–1.9)</td>
</tr>
<tr>
<td>Buechel et al⁵⁵</td>
<td>566 consecutive patients</td>
<td>56.9±6.6</td>
<td>26±5 (range, 18–49)</td>
<td>Prospective ECG-triggered axial</td>
<td>1.8±0.6</td>
</tr>
<tr>
<td>Hausleiter et al⁵³</td>
<td>14</td>
<td>52.6±5.5</td>
<td>26.4±4.4</td>
<td>Prospective ECG-triggered helical, tube voltage 100 kV/120 kV, tube current 362–438 mAs</td>
<td>2.0±0.7</td>
</tr>
<tr>
<td>Leipsic et al⁵⁵</td>
<td>574, 243 with low-dose protocol</td>
<td>58±10</td>
<td>26±5</td>
<td>Prospective ECG-triggered axial, lowered tube current 450 mA with iterative reconstruction</td>
<td>2.3 (1.9–3.5)</td>
</tr>
</tbody>
</table>
could improve the overall efficiency of the imaging laboratory, lower the radiation exposure to the laboratory personnel, and enhance patient convenience because of less time needed for the overall test. There is ample evidence in the literature that when stress images are normal, there is no additional prognostic information added by performing the rest study. Similarly, when the stress scan is performed with attenuation correction (AC), it has been shown that the visual diagnostic performance is similar to that of a stress–rest scan. Without AC, the accuracy of stress-only imaging can be improved and the frequency of needing rest scans can be reduced with combined analysis of stress supine–prone or supine–upright data, which is aided by quantitative analysis. The supine–prone studies are performed with 1 injected stress dose. Stress-only protocols have been also proposed in conjunction with CTA imaging for sites that are equipped with CTA scanners. Husmann et al proposed a low-dose stress-only scan in combination with CTA. The total radiation dose for the MPI and CTA scan was 2.2±0.7 mSv, which is lower than a low-dose rest protocol suggest that stress-only studies is lower after stress injections than rest injections, these data from a low-dose rest protocol suggest that stress-only studies with 1 mSv radiation are possible with the CZT systems. Taylor et al have recently evaluated the diagnostic accuracy of 37

Figure 6. System sensitivity for a dedicated solid-state cardiac camera. The higher system sensitivity of high-speed system is demonstrated by significantly higher myocardial count rate (7–8×) compared with conventional single-photon emission computed tomography (SPECT) at stress and rest images. CPM indicates counts/min. Adapted from Sharir et al with permission of the publisher. Copyright © 2008, Elsevier. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

Low-Dose SPECT MPI With Newer Scanners

The initial applications of the new cardiac imaging instrumentation for SPECT MPI were directed toward drastic reduction of scan times, with only a few recent studies focusing on dose reduction. It should be noted from a technical point of view that the improvements in sensitivity provided by the new instrumentation can equally reduce time, acquisition, or radiation dose. As seen in Figure 6, improvement in the sensitivity of the new systems is of the order of 7× to 8×. Thus, the dose can theoretically be reduced by the same amount with standard imaging times. The minimum imaging time or dose needed for one of these scanners has recently been assessed by retrospective analysis of full-dose full-time data and reconstruction of only a fraction of the counts. This is made possible by the list-mode capabilities of new scanners for SPECT and PET, which allow retrospective simulation of a scan with an arbitrary activity or alternatively duration, from the original full-dose/full-time acquisition data. Nakazato et al determined the feasibility of very-low-dose MPI quantitatively, simulating gradually lowered count levels from list-mode data by reconstruction of various fractions of acquired counts (Figure 7). In 79 patients, 1 million counts in the myocardium produced MPI images that agreed well with standard 8 million count images for quantitative perfusion and function parameters. With a dedicated fast cardiac camera, these images can be obtained for 10 minutes with an effective radiation dose <1 mSv without significant loss of accuracy. Consequently, the results obtained in the studies with reduced imaging times (Figure 8) can be extrapolated to future studies with lower dose protocols if a similar count level in the left ventricular myocardium is maintained. In 101 patients, Einstein et al have recently reported a multicenter comparison of image quality, quantitative function, and perfusion parameters for low-dose (3.5 mCi) 99mTc injection at rest, imaged by solid-state CZT camera and with standard SPECT, and showed that ultra–low-dose rest imaging correlates highly with standard SPECT, with improved image quality while achieving a radiation dose reduction of 55% to 1 mSv. Because the proportion of the injected 99mTc dose that is retained in the myocardium is slightly higher with stress imaging than with rest imaging and because the extracardiac uptake is lower after stress injections than rest injections, these data from a low-dose rest protocol suggest that stress-only studies with 1 mSv radiation are possible with the CZT systems. Taylor et al have recently evaluated the diagnostic accuracy of 37

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Protocol</th>
<th>Injected Dose</th>
<th>Total Radiation Dose, mSv</th>
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<tbody>
<tr>
<td>Husmann et al</td>
<td>100</td>
<td>Stress-only/</td>
<td>Stress: 8.1 mCi</td>
<td>5.4±0.8</td>
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<td></td>
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<td>prospective gated CTA</td>
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<tr>
<td>Duvall et al</td>
<td>209</td>
<td>Stress-only</td>
<td>Stress: 12.5 mCi</td>
<td>4.2</td>
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<td>99mTc sestamibi</td>
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<tr>
<td>DePuey et al</td>
<td>160</td>
<td>99mTc sestamibi</td>
<td>Rest: 5.8±0.6 mCi</td>
<td>6.8</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Stress: 17.5±2.5 mCi</td>
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<tr>
<td>Nkoulou et al</td>
<td>50</td>
<td>1-day 99mTc</td>
<td>Stress/rest</td>
<td>4.3</td>
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<td></td>
<td></td>
<td>tetrofosmin,</td>
<td>8.6/17.3 mCi</td>
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<td></td>
<td></td>
<td>adenosine,</td>
<td>5 min/5 min</td>
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<td></td>
<td></td>
<td>stress–rest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duvall et al</td>
<td>131</td>
<td>99mTc sestamibi</td>
<td>Rest: 5 mCi</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5– to 8–min rest</td>
<td>Stress: 15 mCi</td>
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<tr>
<td></td>
<td></td>
<td>3– to 5–min stress</td>
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<tr>
<td>Gimelli et al</td>
<td>137</td>
<td>99mTc sestamibi</td>
<td>Stress: 5–6 mCi</td>
<td>5.10 (men)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tetrofosmin</td>
<td>Rest: 10–12 mCi</td>
<td>6.12 (women)*</td>
</tr>
<tr>
<td>Einstein et al</td>
<td>101</td>
<td>99mTc sestamibi</td>
<td>Rest: 3.5 mCi</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>at 3 sites</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Established by sex-specific phantom scans
patients who underwent coronary angiography and ultra–low-dose SPECT within 30 days with a stress-first protocol using <4 mCi 99mTc-sestaMIBI, imaged by a solid-state CZT camera. They showed that ultra–low-dose SPECT with patient dosimetry of 10% of typical rest–stress SPECT is diagnostically accurate for identification of significant coronary artery disease.63

**Low-Dose Attenuation Correction with Newer Scanners**

Attenuation correction (AC) has the potential to improve the diagnostic accuracy of cardiac SPECT imaging. It has been shown that AC can be used with stress-only imaging to reduce the frequency of requiring additional rest studies.58 AC is associated with a small additional radiation dose. The typical stress and rest doses from such AC scans obtained using SPECT/CT or PET/CT systems are low, in the order of 0.3 to 1.3 mSv.64 To reduce the AC radiation dose with SPECT/CT, 2 new designs have been developed by equipment vendors. An integrated system has been developed in which photons from x-ray source are detected by solid-state detectors with a fan beam collimator operating in high counting rate mode with an effective dose of 5 μSv.65 Another example of new AC technology uses a flat panel and achieves low-dose (0.12 mSv) CT AC imaging. The attenuation scan of the entire heart volume (14 cm axial field of view) is acquired in a single 60-second rotation with the patient breathing normally; the attenuation data are averaged over multiple respiratory cycles to match the position of the heart during the SPECT acquisition.66

**Advances in Cardiac PET**

**Technical Advances**

Modern PET/CT scanners from all the vendors operate in 3D coincidence detection mode. In PET, each annihilation event between emitted positron and electron produces two 511 keV photons traveling in opposite directions. Two detectors oriented at 180° to each other, within a certain time window (typically 5–20 nanoseconds), are used to detect these photons; this is known as annihilation coincidence detection. Three-dimensional acquisition and new software methods offer a potential for dose reduction in cardiac imaging, beyond already very low radiation levels associated with the short-lived PET myocardial perfusion tracers. Specifically for cardiac applications, current PET scanners have been optimized to cope with high count levels in first-pass 82Rb imaging for myocardial blood flow measurements67 and with additional 82Rb γ-prompt decays affecting 3D imaging.68 The system sensitivity of 3D PET scanners is 4x to 6x higher than scanners operating in 2D mode.69 Further technical advances include developments of photon time-of-flight methods70 and new high-definition iterative reconstruction techniques based on scanner-specific 3D modeling of system resolution with effective tomographic resolution as low as 2 mm.71 Preliminary reports have been published demonstrating the application of these improved PET reconstruction methods to cardiac imaging.72 Further image quality improvements have been proposed73 by combining new reconstruction with cardiac motion–frozen techniques to reduce blurring because of cardiac motion.74

It should be noted that as with SPECT, there is a small additional radiation dose associated with CT AC scans for PET imaging. Unlike SPECT, AC in PET is mandatory because of photon coincidence detection. In a recent study of 91 consecutive patients, Mylonas et al have shown that quantification of coronary artery calcium from standard nongated PET attenuation correction CT is feasible and accurate.75 Furthermore, it has also been shown that standard coronary calcium scoring scans can be used for attenuation correction.76 These studies suggest that in the future, the same low-dose CT scans could be used for both attenuation correction and allow assessment of coronary artery calcium.
Estimated patient radiation doses have recently been revised down to 2.0 to 3.7 mSv for standard \(^{82}\)Rb PET scans by precise patient-specific calculations, with 3.7 mSv corresponding to 80 mCi total injected dose for stress and rest with a standard 2D PET scanner. Because several of the other radiotracers for cardiac PET MPI are short-lived, the associated radiation doses are low. Typical radiation dose ranges from 2 to 3 mSv for stress–rest \(^{15}\)O-water (2.5 mSv for injected activity, 29.7 mCi for each stress and rest scan), and is \(\approx\)7 mSv for \(^{18}\)F-Fluorodeoxyglucose viability studies (for 10 mCi injected activity).^{47}

New PET systems registering the photon events in list mode allow reconstruction of both perfusion and blood flow data from 1 scan. As a result of increased sensitivity of 3D PET, it is possible to obtain high-quality \(^{82}\)Rb perfusion images at injected activities as low as 20 mCi.\(^{79}\) Estimated patient radiation doses have recently been revised down to 3.7 mSv for \(^{82}\)Rb PET scans obtained on a standard 2D scanner with 80 mCi total injected activity for stress and rest.\(^{77}\) Therefore, the effective radiation dose of stress–rest \(^{82}\)Rb scans obtained in 3D mode could be further reduced to \(\approx\)1.85 mSv (<1 mSv for stress scan). For the newly introduced fluorine-18 labeled radiotracer \(^{18}\)F-flurpiridaz, a mean effective combined rest–stress dose has been obtained to be 5 to 6 mSv in phase I and II trials.\(^{80,81}\) It is to be noted that pharmacological PET imaging offers true stress (rather than poststress) functional measurements and allows time-efficient (<30 minutes) stress–rest protocols.\(^{79}\) Analogous to stress-only SPECT MPI imaging, it is also possible to perform stress-only low-dose PET imaging. A recent study of 200 patients has shown that stress-only \(^{82}\)Rb PET MPI is a feasible approach to reduce resource utilization and radiation exposure associated with MPI; this strategy would be most applicable to patients with lower pretest likelihood.\(^{82}\) With F-18 flurpiridaz, exercise PET has been reported, with an injected activity of 6.48±1.23 mCi for exercise stress.\(^{83}\) It is likely that stress-only PET MPI studies will become common with this agent.

Cardiac imaging with CT, SPECT, and PET currently offers significant potential advantages because in addition to relative perfusion, it allows measurements of myocardial blood flow and perfusion flow reserve.\(^{76}\) New PET systems registering the photon events in list mode allow reconstruction of both perfusion and blood flow data from 1 scan. As a result of increased sensitivity of 3D PET, it is possible to obtain high-quality \(^{82}\)Rb perfusion images at injected activities as low as 20 mCi.\(^{79}\) Estimated patient radiation doses have recently been revised down to 3.7 mSv for \(^{82}\)Rb PET scans obtained on a standard 2D scanner with 80 mCi total injected activity for stress and rest.\(^{77}\) Therefore, the effective radiation dose of stress–rest \(^{82}\)Rb scans obtained in 3D mode could be further reduced to \(\approx\)1.85 mSv (<1 mSv for stress scan). For the newly introduced fluorine-18 labeled radiotracer \(^{18}\)F-flurpiridaz, a mean effective combined rest–stress dose has been reported to be 5 to 6 mSv in phase I and II trials.\(^{80,81}\) It is to be noted that pharmacological PET imaging offers true stress (rather than poststress) functional measurements and allows time-efficient (<30 minutes) stress–rest protocols.\(^{79}\) Analogous to stress-only SPECT MPI imaging, it is also possible to perform stress-only low-dose PET imaging. A recent study of 200 patients has shown that stress-only \(^{82}\)Rb PET MPI is a feasible approach to reduce resource utilization and radiation exposure associated with MPI; this strategy would be most applicable to patients with lower pretest likelihood.\(^{82}\) With F-18 flurpiridaz, exercise PET has been reported, with an injected activity of 6.48±1.23 mCi for exercise stress.\(^{83}\) It is likely that stress-only PET MPI studies will become common with this agent.

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References

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