Newer generation cameras are preferred

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INTRODUCTION

While cardiovascular disease is already the leading cause of morbidity and mortality, its prevalence is likely to increase further with the ongoing aging of populations in developed countries. It is expected that this development will be paralleled by a further increase in the use of non-invasive diagnostic tests for known or suspected coronary artery disease (CAD). Currently, there is a large armamentarium of tests at the clinician's disposal, including treadmill stress tests, stress echocardiography, myocardial perfusion imaging (MPI)—through both single photon emission computed tomography (SPECT) and positron emission tomography (PET)—coronary CT angiography (CTA), and cardiac magnetic resonance imaging (CMR). While impressive improvements have been accomplished in this regard for other imaging modalities, particularly not only for CTA but also for CMR, developments of a similar magnitude for nuclear MPI have until recently somewhat lagged behind. Against the background of increasing competition among the various imaging modalities, technical evolution is crucial for nuclear MPI to meet today's demands. With this regard, milestone developments such as the introduction of cadmium-zinc-telluride (CZT) detectors may serve as an important catalyst for the future use of nuclear MPI. With the potential of offering superior image quality at a lower radiation dose and at a faster pace, the modality has definitely arrived in the 21st century and holds out positive perspectives while it continues to fulfill important clinical needs and remains effective in clinical settings.

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LIMITATIONS OF CONVENTIONAL SPECT CAMERAS WITH NAI-BASED DETECTORS

Since the introduction of the first SPECT camera, system designs have seen a variety of improvements mainly through optimizing performance of sodium iodide (NaI)-based detectors and implementation of multiple detectors. While such multi-head camera systems have admittedly reduced acquisition time to some extent, the time needed for obtaining a tomographic dataset of the heart today still lies in the range of 10 to 20 minutes, mainly because of the need of slow rotation of the detector heads around the patient and limited system sensitivity. Long acquisition times, however, not only lower patient throughput but also render image acquisition prone to patient motion. The latter is a well-recognized potential source of error in SPECT that results in undesirable effects ranging from loss of resolution and image blurring to artifactual defects or even non-interpretable datasets.[1] Further limitations arise directly from inherent shortcomings of the material that constitutes the detectors of conventional SPECT cameras: NaI crystals offer limited photon sensitivity which primarily affects overall system sensitivity and in turn not only leads to prolonged acquisition times but also prevents applying measures to reduce radiation dose, namely through lowering the injected activity of the radiotracer as this would lead to unacceptably long acquisition times. Moreover, NaI detectors offer a limited spatial and energy resolution. Both of the latter potentially have an adverse effect on diagnostic accuracy of the modality due to degradation of image quality. Furthermore, NaI detector-based systems depend on photomultiplier tubes (PMT) in order to transform the photoelectric effect into an electric signal usable for image generation. The need for PMTs determines the relatively large detector size of a conventional SPECT camera. As a result, conventional SPECT scanners are bulky and impose considerable requirements with regard to the infrastructure necessary to operate such a device which may be particularly challenging in an outpatient setting with limited space. Finally, conventional SPECT systems also have a specific limitation regarding

the maximum count rates that can be measured. At high count rates the detector's rate response is rendered non-linear leading to a roll-off phenomenon and even to paralysis at very high count rates due to detector dead-time that at some point exceeds the rate of incoming photons. In combination with limited temporal resolution of the kinetic frames due to slow gantry rotation, this drawback also hampers the utility of such systems for quantitative blood flow measurements.[2]

NEWER GENERATION CZT CAMERAS

Contrary to conventional SPECT cameras, newer generation cameras are based on semiconductor detector technology consisting of a CZT crystal. This artificially grown crystal has a very high effective atomic number and density yielding a substantially higher attenuation of photons than with conventional NaI-based detectors. More importantly, however, CZT detectors allow direct conversion of light into an electrical signal, thus avoiding the need for PMT, a feature that allows for reduction of the overall detectors' size while improving in-plane resolution. A detector element is comprised of the crystal and multiple underlying anodes, each reflecting a pixel. Assuming, for example, a detector consists of 16 × 16 pixels, each with an edge length of about 2.5 mm, this results in a form factor with an edge length of 40 mm which is strikingly smaller than a conventional NaI detector (Figure 1). Furthermore, the CZT crystals of the detectors are also thinner, and therefore, the anodes detecting the electrical charges are only millimeters away from the original photon-crystal interaction. This enables much more accurate spatial localization of the original incident than with conventional NaI detectors, leading to an intrinsic spatial resolution of current CZT cameras of approximately 4 mm which is substantially better than the typical 10 mm achieved with conventional SPECT cameras.[3] Aside from superior intrinsic properties, newer generation CZT cameras also offer important advantages with regard to extrinsic system properties as for example the collimator: In newer CZT cameras, the high intrinsic resolution of CZT detectors permits the use of parallel-hole or multi-pinhole collimators with relatively large holes focused on the heart, leading to improved count sensitivity. CZT detectors also offer better energy discrimination than NaI detectors, which allows more accurate discrimination of scattered from unscattered radiation, thereby further improving image resolution.[4] Moreover, in contrast to conventional NaI detectors, CZT detectors yield a linear count-rate response up to the system maximum which is limited only by its computational power. The most important advantages of newer generation cameras, however, arise from miniaturization of the CZT detectors with inherent advantages for the geometry of the scanner. The small size of the CZT detectors allows a system design consisting of a curved array of CZT detectors that are all focused specifically on the heart, thereby increasing detection of the true counts from the area of interest and enabling instantaneous tomographic acquisition of cardiac activity (Figure 2). Finally, it is the combination of such CZT detectors into a new heart-centered geometry with new collimator designs and modern iterative reconstruction algorithms in newer camera systems dedicated to cardiac imaging that has led to a five- to ten-fold increase in system sensitivity and two-fold increase in image resolution,[5] translating into better image quality than obtainable with state-of-the-art conventional SPECT cameras.[4]

PRACTICAL ADVANTAGES OF NEWER GENERATION CZT CAMERAS

The particular improvements in detector technology, camera design, and reconstruction software of newer generation cardiac SPECT cameras translate into

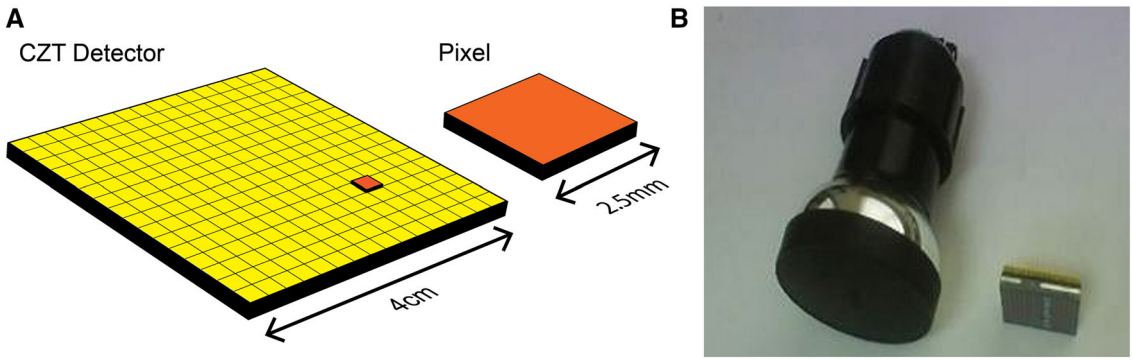

Figure 1. A A cadmium-zinc-telluride (CZT) detector consisting of 16 × 16 pixels, resulting in an edge length of 4 cm. **B** Consequently, the form factor of a CZT detector (*right*) is considerably smaller than that of a conventional NaI-based scintillation detector with photomultiplier tube (*left*).

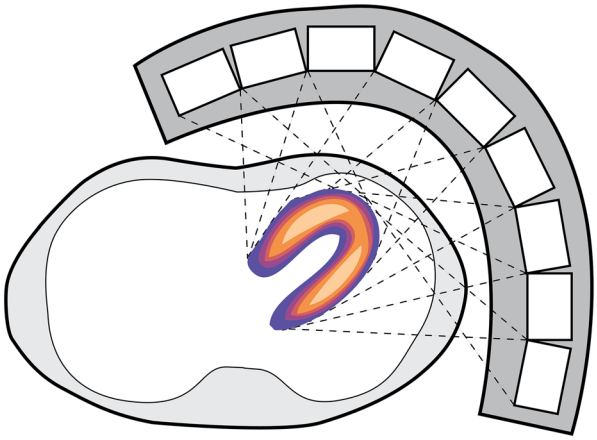

Figure 2. The small form factor of CZT detectors allows aligning an array of detectors on an arch around the patient and focused on the heart. Thus, rotation of the detectors is unnecessary and instantaneous tomographic acquisition of the heart becomes possible.

a number of practical advantages and open exciting new avenues for cardiac imaging: These devices are smaller and more compact dealing favorably with restricted space requirements in practices or hospitals. The higher count sensitivity enabled by the particular geometry and collimation allows cutting down significantly on image acquisition times and therefore improving patient comfort and throughput. Herzog et al. demonstrated that image acquisition times (using a one-day stress/rest protocol with standard injected dose) can be slashed down to 3 minutes for the low dose and 2 minutes for the high dose on a CZT SPECT camera yielding similar image quality, regional tracer uptake values, and clinical interpretation than conventional SPECT.[5] Subsequently, first validation studies of such ''ultrafast'' protocols (i.e., with acquisition times $\leq$5 minutes) on CZT cameras have reported good clinical agreement for perfusion and gated SPECT findings compared to conventional SPECT,[6,7] and good diagnostic accuracy compared to invasive coronary angiography with sensitivities and specificities well in the range of conventional SPECT.[8,9] The impressive reductions in image acquisition times may also allow for intermittent breath-hold imaging at maximal inspiration, and therefore reduce diaphragmatic attenuation or spill-over artifacts from sub-diaphragmatic activity.[10]

On the other hand, newer generation scanners offer the possibility to lower injected doses of radionuclides, reducing patient exposure to ionizing radiation and improving safety. Using sub-sampling of list-mode SPECT data obtained on a CZT camera to simulate lower injected doses, Nakazato et al. calculated that 1 Mio. counts from a left ventricular (LV) region of interest are sufficient for high image quality and

Table 1. Recent clinical studies with reduced dosing and new generation cameras

Authors	Sample size (*n*)	Protocol	Injected dose	Image acquisition time	Total radiation dose
Duvall et al.[17]	131	^{99m}Tc sestamibi (stress-only)	Stress: 12.5 mCi	Stress: 5 minutes	4.2 mSv
Nkoulou et al.[14]	50	^{99m}Tc tetrofosmin (one-day stress/rest)	Stress: 8.6 mCi Rest: 8.6 mCi[a]	Stress: 5 minutes Rest: 5 minutes	4.3 mSv
Duvall et al.[18]	131	^{99m}Tc sestamibi (one-day rest/stress)	Rest: 5 mCi Stress: 15 mCi	Rest: 5–8 minutes Stress: 3–5 minutes	5.8 mSv
Gimelli et al.[19]	137	^{99m}Tc tetrofosmin (one-day stress/rest)	Stress: 5–6 mCi Rest: 10–12 mCi	Stress: 7 minutes Rest: 6 minutes	5.10 mSv (men) 6.12 mSv (women)
Oddstig J et al.[20]	50	^{99m}Tc tetrofosmin (one-day stress/rest)	Stress: 5.5 mCi Rest: 14.8 mCi	Stress: 7.9 minutes Rest: 4.8 minutes	5.8 mSv
Einstein et al.[12]	101	^{99m}Tc sestamibi or tetrofosmin (''rest-only'')[b]	Rest: 3.5 mCi	Rest: 9.7–15.2 minutes	1.15 mSv

Table modified from Slomka et al.[21]
[a] One-day low-dose/low-dose protocol with image subtraction
[b] Comparison of low-dose versus standard dose single (rest) scan in the same patient

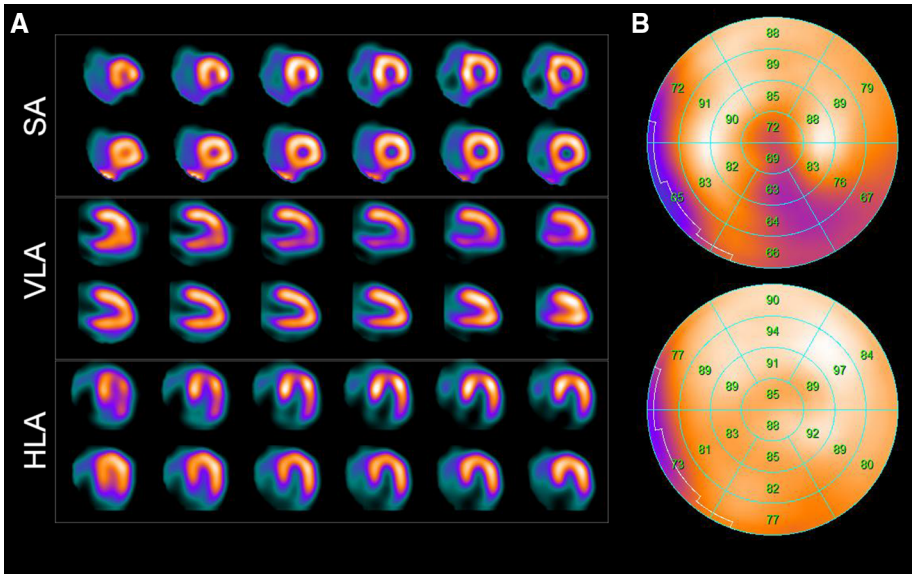

Figure 3. Low-dose myocardial perfusion SPECT imaging of a 75-year-old female patient presenting with atypical chest pain performed on a dedicated cardiac cadmium-zinc-telluride (CZT)-SPECT camera. Slices (**A**) of stress (*top rows*) and rest (*bottom rows*) in short axis (SA), vertical (VLA), and horizontal long axis (HLA) as well as the corresponding polar plots (**B**; stress on top, rest at the bottom) reveal a reversible perfusion defect in the inferolateral wall. Injected dose of ^{99m}Tc-tetrofosmin for this examination was 3.27 mCi for stress (8 min image acquisition) and 10.48 mCi for rest (6 min), resulting in a total effective radiation dose of 3.1 mSv.

interpretability of SPECT perfusion images.[11] This count level would correspond to a 2.5-mCi injected dose for a 14 minutes acquisition or 3.4 mCi injected dose for a 10-minutes acquisition. In the meantime, several single-center trials have documented feasibility, high image quality and good diagnostic accuracy of low-dose cardiac SPECT (summarized in Table 1). These trials taken together suggest feasibility of *half-dose* one-day protocols with image acquisition times in the range of 5 to 8 minutes (for the low dose) and 3 to 6 minutes (for the high dose) (Figure 3). In the multi-centric MILLISIEVERT trial, Einstein et al. demonstrated that a single low-dose scan (e.g., in the case of stress-only imaging) with 3.62 mCi injected dose and an acquisition time between 9.7 and 15.2 minutes provides higher image quality and similar clinical information at ultra-low radiation (1.2 vs 2.4 mSv) compared to a standard dose single scan.[12] Notably, low-dose imaging is also feasible in obese patients with a BMI >35 kg/m^2 at good image quality and with high diagnostic accuracy.[13]

As previously mentioned, newer CZT SPECT cameras offer significantly lower detector dead-time losses and therefore avoid detector oversaturation even at higher count rates. As a result, count-rate response is linear over the entire clinical dose range, which allows accurate subtraction of background activity from prior injections.[4] Nkoulou et al. validated a 1-day low-dose (stress)/low-dose (rest) protocol. Rest images were reconstructed using subtraction of background activity from the preceding stress scan.[14] Compared to a standard protocol, the low-dose/low-dose protocol revealed similar segmental tracer uptake and 98% clinical agreement without shine-through artifacts at an average dose of 4.3 mSv. With aforementioned half doses and appropriate scanning times, this would suggest the feasibility of an entire ultra-low-dose stress/rest subtraction imaging study at 2 to 2.5 mSv.

Newer solid-state CZT detectors offer higher energy resolution than conventional systems allowing for 30% reduction in the scatter component of measured counts and higher image quality.[4] Moreover, improved discrimination of emitted photons from different radiocompounds allows for dual-isotope protocols with little or no cross-talk between isotopes. Such protocols may allow exploiting the high first-pass extraction and low extracardiac activity of ^{201}thallium for stress imaging with the higher count rates and lower radiation doses of ^{99m}Tc-tracers for rest imaging.[15] With dose reductions as suggested by aforementioned studies, dual-isotope imaging could be feasible with radiation doses in the range of standard ^{99m}Tc-based protocols.

Finally, the introduction of newer cameras with its high photon sensitivity and the stationary assembly of detectors has refueled the interest in dynamic SPECT

imaging. Dynamic SPECT imaging tracks radiotracer activity in the left and right ventricular cavity and the LV myocardium upon injection over a given time period, to produce time-activity curves and calculate absolute myocardial blood flow and coronary flow reserve. First studies have shown feasibility of dynamic SPECT with ^{99m}Tc-sestamibi using new generation solid-state CZT cameras.[16] However, more widespread application awaits further clinical validation and comparison with more established techniques for blood flow quantification.

CONCLUSIONS

SPECT hardware has evolved significantly in the past few years. Newer generation cardiac cameras feature new solid-state semiconductor detector technology, dedicated collimators, heart-focused camera design, and optimized image reconstruction software, and offer improved count sensitivity, energy, and spatial resolution. Ultra-fast and ultra-low-dose imaging protocols with newer generation devices have been validated by several groups. Its widespread introduction represents an important step forward for cardiac radionuclide imaging enabling the technique to be faster, safer, more comfortable for the patient, and maintain its high image quality and established accuracy. With these improvements in performance and the perspective of newer innovative protocols in the near future (background subtraction imaging, breath-hold imaging, dynamic SPECT), myocardial perfusion SPECT will earn an important and competitive role among other imaging modalities of the 21st century.

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