Low dose in nuclear cardiology: state of the art in the era of new cadmium–zinc–telluride cameras

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Introduction

Myocardial perfusion imaging (MPI) is widely used for diagnosing coronary artery disease (CAD).1 Its use has seen a tremendous growth during the last decade and has become the most commonly used non-invasive imaging tool for risk stratification in patients with suspected and known CAD.2 The number of stress single-photon emission computed tomography (SPECT) studies performed annually is likely to increase further due to increasing longevity of the population and changes in cardiovascular disease epidemiology.3 This reality is juxtaposed to an escalating emphasis on reduction in radiation exposure from medical imaging4,5 and cost containment. A systematically led revision of recent literature on the subject of strategies to minimize radiation exposure originating from SPECT, positron emission tomography (PET), computed tomography (CT), and coronary angiography was performed. It revealed a need for the determination of a selection of protocols both for individual patients and for standard laboratory operating procedures using an ‘as low as reasonably achievable’ approach. Weighing of the dosimetry of cardiac imaging protocols in use would be a first step towards the implementation of a test selection strategy to minimize overall risk to patients without detracting from high-quality diagnostic information. More recently, a position document of the European Society of Cardiology associations of cardiovascular imaging outlined the concept that cardiologist should make every effort to give the right imaging exam, with the right dose, to the right patient.6 Accordingly, from a clinical point of view, two important issues should be considered to approach diagnostic imaging: one is the great attention to the problem of radiation exposure and to related hazard, and the other is the awareness that imaging modality needs to show a great capability to influence patient management by improving clinical outcome. This consideration leads to choose an imaging modality, among the ones available, involving lower radiation dose according to the clinical benefit for a specific patient. In an effort to overcome these points, new low-dose protocols and new technologies were developed, enhancing the role of MPI in the clinical practice.

New technologies and related low-dose reduction

A dedicated solid-state cardiac cameras introducing a new design of both photon acquisition system and reconstruction algorithm have been developed,7,8 replacing the conventional sodium iodide (NaI)-based systems. The innovation is based on the use of the cadmium–zinc–telluride (CZT) detector, a semiconductor-based substantially smaller than a NaI-based detector, which directly converts gamma radiation to an electronic pulse and thereby eliminates the need for a scintillating crystal and photomultiplier tubes. Currently, there are two commercially available ultrafast camera systems. The detector configurations used in these CZT systems have in common the use of multiple CZT detectors in place of NaI crystals, but they differ substantially in terms of collimation and reconstruction algorithms, resulting in differences with regard to overall scanner performance.9 Because of its compact design, new and innovative detectors

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configuration can be used enabling multiple independent detectors to be positioned around the heart. The D-SPECT camera uses a system of rotational parallel-hole collimation involving nine rotating detector columns equipped with a wide-angle square-hole tungsten collimator, and the higher resolution is reached using a specific reconstruction algorithm. The Discovery NM530c camera is based on a stationary multi-pinhole collimation system, and high-count sensitivity is reached by the combined acquisition of the heart area through the 19 pinhole-detector blocks. For both systems, image quality is improved due to the higher sensitivity in detection of heart activity. Compared with the standard SPECT camera, these types of collimation provide a 3–5× increase in photon sensitivity, as well achieving a 1.7–2.5× increase in spatial resolution.

A phantom study comparing the sensitivity of scanners from different vendors found that D-SPECT and the Discovery NM 530c yielded substantially higher count sensitivity over standard SPECT (i.e. 850 and 460 vs. 130 counts·s⁻¹·MBq⁻¹). Similar results were documented when assessing myocardial counts normalized to injected activities in humans for the DSPECT, Discovery NM 530c, and standard SPECT (i.e. 11.4 ± 2.6, 5.6 ± 1.4, and 0.6 ± 0.1 counts·s⁻¹·MBq⁻¹, respectively) as well as when measuring central spatial resolution (i.e. 6.7 mm for Discovery NM 530c, 8.6 mm for D-SPECT, and 15.3 mm for standard SPECT). These data document a dramatic enhancement in image quality mainly because of a lower proportion of Compton photons within the acquisition energy window. In addition, this leads to marked improvements for dual isotope acquisition protocols such as those involving ⁴¹Tl and ⁹⁹mTc-labelled tracers. At this time, these main issues are used for enabling high-quality scans with a significant reduction in imaging time and dose. Moreover, CZT image quality was further improved by the development of a dedicated three-dimensional iterative reconstruction algorithm, based on maximum likelihood expectation maximization, which corrected for the loss in spatial resolution due to line response function of the collimator. A special mention must be given to the comparison with standard SPECT plus new collimation system, like IQ SPECT. The head-to-head analysis of the performance of IQ-SPECT, D-SPECT, and Discovery NM 530c in routine conditions from phantoms and from healthy subjects provided evidence that although other camera systems have been proven to yield promising advantages over conventional SPECT, the physical performance of CZT cameras bears the potential of further improvements.

All these innovations lead to direct benefits for the patients. First of all, with a reduced imaging time by a factor of 5 or greater, CZT imaging requires only 2 min of acquisition time, earning the name of ultrafast camera. CZT systems also apply either a wide cushioned table or a cushioned chair to support the patient during imaging improving comfort. Finally, and probably most importantly, the physical and intrinsic characteristics of CZT cameras allow reducing radiation dose, main target for clinical application. However, the claims of reduced imaging times, lower radiation exposure, and increased patient comfort are desirable but by themselves cannot be used to justify replacing conventional cameras with CZT cameras if accuracy in detecting CAD should be sacrificed.

Clinical state-of-the-art: published results

The introduction of novel CZT detectors represented a milestone in technical improvement of MPI. Preliminary reports and first clinical studies indicated clearly the possibility to obtain reduced acquisition time for stress and rest MPI. From these preliminary data, CZT camera represented a major breakthrough for daily use of MPI in clinical routine. Clinical validation studies indicated that novel CZT camera allowed a more than five-fold reduction in scans time and provided clinical information equivalent to conventional standard SPECT MPI. In the first publication comparing ultrafast vs. conventional camera for detection of obstructive CAD, using coronary angiography as the gold standard, CZT camera identified a higher number of vessels with obstructive CAD, despite an equivalent level of diagnostic confidence was observed on per-patient basis. From these data emerged that ultrafast camera allows a more accurate evaluation of both extent and severity of myocardial ischaemia in patients with CAD. Interestingly, the major benefit has been observed in the left circumflex and right coronary artery territories leading to a better delineation of multi-vessel CAD and outlining the great utility for the clinical use in patients with significant CAD, as confirmed by different studies. Despite the ultrafast camera was not considered superior to conventional cameras in lower-risk patients, where a much greater percentage of the population will present with a normal study, some important issues should be underlined. Many leaders and societies in nuclear cardiology have advocated strategy of stress-only MPI because of reduced radiation exposure and cost, improving laboratory efficiency. However, it has been demonstrated that for a real feasibility of stress-only MPI protocol, the return rate for rest imaging should be low. Thus, this protocol seems to be better applied to patients with a lower risk, where radiation exposure is the primary concern. A low-dose protocol with stress-only MPI seems to be reserved to the use of CZT systems that provide high image quality and/or utilizing depth-dependent resolution recovery and scatter correction reconstruction, preferably with attenuation correction. As a matter of fact, when planned with a low-dose stress-first protocol on a CZT camera, MPI provides high diagnostic performance and a dramatic reduction in patient radiation doses. Moreover, the opportunity to perform a stress-only examination when applying attenuation correction, due to enhanced specificity, may be a major advantage that needs further investigations. The integrated approach, combining assessment of perfusion and function by cardiac imaging with gated SPECT, has already proven to be useful in tissue characterization and prognostic stratification, providing important information for clinical decision-making in patients with suspected or known CAD. Different published data underline the impact of CZT cameras for the evaluation of LV function, providing important data on the possibility to use the new cameras for a combined assessment. The first clinical validation of MPI using CZT camera for the evaluation of LV global and regional function demonstrates excellent agreement between CZT technology and cardiac magnetic resonance (CMR). In particular, it has been demonstrated that the minimal systematic bias (−2.7%) has limited clinical relevance, and absolute wall thickening and wall motion.
measurements using CZT cameras can equally be used to detect myocardial scarring, as assessed by delayed enhanced CMR. However, in line with previous studies performing a comparison between CMR and conventional SPECT MPI, a significant underestimation of ventricular volumes even with 16-frame gating has been shown using CZT cameras and of regional wall thickening, especially in patients with increased wall thickness. Moreover, CZT-derived measures of left ventricular filling dynamics correlate with echocardiographic parameters of diastolic function improving the accuracy in detection of significant ischaemic heart disease. Published data have been provided on the prognostic value of rapid acquisition adenosine stress-rest MPI using CZT camera. In 1109 consecutive patients during a follow-up period of 21 months, the hard cardiac event rate associated with no significant perfusion abnormality was 0.4 vs. 6.8% with an abnormal scan by CZT camera. More recently, prognostic value of CZT camera has been compared with conventional Anger camera reporting similar results in predicting cardiac events. In some patients with multi-vessel CAD, ‘balanced ischaemia’ phenomenon determined that only 25% of patients with multi-vessel disease on angiography have abnormal perfusion or function by SPECT in the distribution of all three diseased coronary vessels. It has been demonstrated that dynamic SPECT using CZT camera may play a pivotal role in the evaluation of CFR leading to the characterization of high-risk coronary anatomy. Dynamic imaging opens the door to the quantification of blood flow and coronary flow reserve, which can be used to detect disease earlier and to avoid interpretation of three-vessel disease as normal. Recently, using a low-dose imaging protocol with a dedicated CZT cardiac camera, the relationship between measures of regional myocardial adrenergic innervations heterogeneity, cardiac perfusion, and mechanical function in patients with or without ischaemic heart disease has been investigated. A combined evaluation of cardiac adrenergic innervations and myocardial perfusion was performed with reduced acquisition time, high image quality, and a limited radiation burden. In particular, CZT-derived measures of adrenergic innervations heterogeneity compared with the classical planar indexes helped to better identify patients at higher cardiovascular risk, adding relevant regional information on cardiac adrenergic nerve activity. These important findings showed the possibilities of using CZT cameras to obtain prognostic information for clinical decision-making with a significant reduction in radiation burden.

Finally, the characteristics of the new cameras enable future application of the CZT for the evaluation of infection as well as of plaque imaging.

CZT drawbacks

Standard SPECT imaging has suffered from limitations in terms of specificity, due mostly to attenuation and/or motion artefacts. CZT cameras also present with artefacts, which are different from those of conventional cameras, and different between the two existing systems. Due to these main issues, proper interpretation of images acquired on this new equipment requires a long learning curve and experienced doctors. Reproducibility and robustness of interpretation still need to be more extensively evaluated.

Thus, operator variations in the processing of CZT myocardial perfusion images plus attenuation correction are significant and guidelines for processing hybrid images are necessary to improve the reproducibility. Finally, the introduction of CZT cameras, with their advantages over conventional SPECT cameras, has not solved the issue of image quality degradation from obesity. It appears that the current design of CZT cameras is more prone to artefacts in very obese patients. Therefore, patients with a BMI of 40 kg/m² and above should be scheduled on a conventional SPECT camera for MPI scanning.

Impact of dose reduction in clinical application and future role of nuclear cardiology

The increasing use of nuclear MPI has been paralleled by an increasingly active discussion on the potential deleterious risks related with ionizing radiation exposure. Arguably, the reason for such a vivid discussion is based on the fact that patients undergoing nuclear MPI have been exposed to a relatively high magnitude of radiation dose. A recent observational study performed by an expert team jointly with the International Atomic Energy Agency, including over 300 nuclear cardiology laboratories from 65 countries, demonstrated that the current median effective radiation dose per patient from a single nuclear MPI study in Europe results in 8 mSv. Thus, a single cardiac imaging examination may be equivalent to several hundred chest X-rays or many years of background radiation exposure. As it is likely that the need for nuclear cardiac imaging will continue to grow, the need for radiation dose reduction becomes evident.

However, while impressive improvements have been accomplished in this regard for other imaging modalities, such as for coronary CT angiography where a reduction in radiation dose ranging from initially over 20 mSv down to as low as 0.2 mSv has become feasible, developments of a similar magnitude for nuclear MPI have somewhat lagged behind. In nuclear MPI, image quality is a trade-off between injected dose and acquisition time with the former dictating the radiation dose exposure to the patient. In any given set-up, lowering the injected dose will inevitably result in reduced image quality unless acquisition times are increased. Conversely, shortening acquisition time mandates an increase in injected dose to maintain adequate image quality. Considerable efforts have gone into the development of new protocols and improved reconstruction algorithms to allow a reduction in dose and/or scan time. However, the still widely used conventional multi-head gamma cameras have shown limited potential with this regard because the moderate system sensitivity renders such cameras particularly prone to image quality degradation due to low count statistics. It is only with the recent advent of the novel-generation CZT technology that system sensitivity was substantially increased. In fact, the introduction of CZT gamma cameras constitutes a technological milestone in the evolution of nuclear cardiology as this technology—in combination with newest-generation reconstruction algorithms—offers three- to seven-fold higher system sensitivity compared with conventional gamma cameras. This advantage may be used to substantially shorten the time needed for image acquisition. Conversely, tracer activity may be reduced, resulting in a radiation dose exposure of ~2–3 mSv for a complete...
rest and stress study, placing nuclear MPI at the same level with PET and even below diagnostic invasive angiography.42

These advancements and the continually successful efforts with this regard are of importance because, although nuclear imaging may have its risk, it also offers undeniable benefits in terms of improved diagnosis and prognosis. A reduction in radiation dose exposure indubitably tips the benefit-to-harm ratio even further towards the favourable side of the scale with the potential to counterbalance increasing concerns about any negative effect from radiation associated with nuclear MPI that in some cases may have even led to unnecessary avoidance of essential procedures. The latter reflects the perception that among the vivid discussion on radiation risks, it is sometimes difficult to keep a sense of proportion with regard to the balance between risk and benefit for the patient. In fact, it has become apparent that it is very difficult to scientifically prove any harm that low doses of radiation may potentially inflict on our patients. Moreover, the current state of radiation biology knowledge includes as well the hypotheses that low doses of radiation may be irrelevant or even beneficial to health, which is not unlikely given that such low radiation doses approximate the annual background exposure from natural sources which life has been exposed to since its very beginning. It is against this background why a radiation dose of < 2–3 mSv should be considered as very low. These proportions should be kept in mind when comparing the potential risks among different cardiac imaging modalities that provide similar information, namely because its evidence shows that CMR imaging or echocardiography, although both certainly do not inflict any ionizing radiation on the patient, are not entirely free of risks, for example, due to the magnetic field potentially inducing DNA damage13 or possible cavitational effects of ultrasound.43 Thus, although the debates have in the past focused mainly only on a single risk such as radiation, careful attention should also be given to other procedural aspects such as invasiveness, the use of contrast agents and pharmaceutical stressors, or non-ionizing radiation that may—among others—be attributable to patient risk.

Even more important, however, the imaging modality should be related to the benefit of performing or not performing the test considering the drawbacks associated with the disease remaining undetected. Contrary to other imaging modalities, the long-term prognostic value—the desired level of evidence for imaging—has been demonstrated for nuclear MPI in many ten-thousands of patients, firmly establishing the importance and robustness of this modality for risk stratification in patients with known or suspected CAD with the ability to strongly affect medical therapy and provide guidance for interventions, and ultimately improving patient outcomes.14,45

A secondary non-negligible benefit of the above-mentioned dose-saving strategies arises from the fact that a reduction in radio-pharmaceutical dosage enables nuclear MPI to be more cost-effective—a trend that is most welcome against the background of the continuously growing use of nuclear MPI in an increasingly challenging fiscal environment with ever-rising healthcare costs. These combined aspects of a reduction in radiation dose exposure paralleled by lowering healthcare costs may very well prove to be important catalysts for the future development of nuclear MPI. With the evolution towards 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 as it continues to fulfil important clinical needs and remains effective in numerous clinical situations where other imaging modalities cannot be applied.

Conclusions

While MPI conveys numerous benefits in the evaluation of CAD, it exposes patients to ionizing radiation. Adherence to radiation safety best practices varied significantly between laboratories but the possibility to use the new cameras in nuclear cardiology can reduce dramatically the radiation dose without losing accuracy. Moreover, the physical characteristics of ultrafast technology could be able to open new doors for the evaluation of old parameters, changing the impact of nuclear cardiology in the diagnostic strategies.

Conflict of interest: None declared.

References


