EDITORIAL

Cadmium-zinc-telluride myocardial perfusion imaging: The dream of a single test gets nearer

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To infinity and beyond!
Buzz Lightyear, Toy Story, Walt Disney Pictures

Non-invasive functional cardiovascular imaging is a cornerstone in the management of patients with suspected or established coronary artery disease (CAD), given its capability to simultaneously provide diagnostic insight, risk-prediction, and guidance to decision-making.[1–3] Myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) embodies the key strengths of non-invasive functional cardiovascular tests, by combining the physiologic details provided by stress testing (exercise or pharmacologic) with accurate information on myocardial perfusion, viability, and contractility, thus justifying its historically prominent role in cardiovascular imaging.[1,4–6] The traditional acquisition technology for SPECT is the Anger camera, which has good diagnostic and excellent prognostic accuracy, as demonstrated by several studies with large sample size, despite its evident limitations in terms of spatial and energy resolution, as well as acquisition times.[7]

The recent introduction of the cadmium-zinc-telluride (CZT) cameras for SPECT has purportedly revolutionized MPI, thanks to their superior spatial and energy resolution.[8,9] Given their groundbreaking technical features and the differences between the two available but competing suites (D-SPECT, Spectrum Dynamics, Palo Alto, CA, USA; Discovery NM 530c or Discovery NM/CT 570c with Alcyone technology, GE Healthcare, Haifa, Israel), there are, however, ongoing developments and refinements in the application of this imaging technology to current cardiovascular practice.[10–12] Accordingly, the scholarly literature on CZT MPI is continuing to expand momentously, as demonstrated by the work by Jameria and colleagues published in this issue of the Journal.[13]

Specifically, Jameria et al report hereby a single-center retrospective observational study comparing acquisition of MPI with CZT vs Anger cameras, and focusing on several protocol subtleties such as stress-only vs stress-rest acquisition, and upright vs supine positioning, while using a D-SPECT suite and relying on coronary angiography as gold standard.[13] Notably, a total of 740 subjects underwent MPI with both D-SPECT and Anger cameras, even if only 112 (15.1%) patients had coronary angiographic details, with 48 (6.5%) of them eventually showing significant CAD at angiography. In this series, moderate defects were predominant, and all images were interpreted independently by two different nuclear physicians, with varying experience. The main finding of this work is that overall predictive values were similar with D-SPECT and Anger cameras, thus supporting a more widespread adoption of this CZT suite. Conversely, only the interpretation of D-SPECT images by the more experienced operator provided similar results for sensitivity, specificity, and

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normalcy rate in comparison to Anger images, whereas image interpretation by the less experienced physician had lower diagnostic accuracy with D-SPECT than with Anger cameras, especially in patients with reduced systolic function. Intriguingly, adding rest images to stress-only tests improved sensitivity of CZT MPI, by enabling the correct reclassification of attenuation artifacts (typically considered equivocal) into actual perfusion defects in as many as 11 patients eventually displaying significant CAD at angiography. In any case, the main take home message of the contribution by Jameria et al, notwithstanding the relatively small sample study and the heterogeneity in operator expertise, is that CZT MPI with D-SPECT is largely equivalent in terms of diagnostic accuracy to Anger cameras, even if a stress-only protocol is used. Experience is important though, as adding rest images in case of equivocal findings.

In light of the work of Jameria and colleagues, and the total body of evidence on this topic,[8–12] it is important to highlight the current and future prospects of CZT technology for MPI. First, it is paramount to recognize that the two available embodiments of this technology (Alcyone and D-SPECT) might not be identical in performance, despite aggregate analyses suggesting the contrary.[12,14,15] Second, irrespective of the chosen CZT technology, the spatial and energy resolution of these cameras is significantly superior to that of Anger cameras.[8] These technical advantages might translate into improvements in sensitivity and specificity, after an adequate learning curve, on top of providing some practical perks in testing procedures, such as stress-only protocol for radiation exposure reduction and dual-isotope imaging when a single acquisition is appropriate.[10,11] Exploitation of the superior sensitivity of CZT technology means that we can reduce acquisition time if radionuclide doses similar to those used with Anger cameras are chosen, but, much more importantly, that doses can be dramatically reduced if acquisition times are only moderately decreased. Indeed, longer acquisitions are likely going to be crucial to treasure the advantages of CZT cameras and achieving the goal of reducing (more than halving) radiation dose (even to 1.7 mSv as reported by Sharir et al).[16] Aiming for the same goal, the impact of operator experience is also crucial, as is dedicated training to best exploit images obtained with CZT cameras. Indeed, despite the possibility to use semiquantitative or quantitative scores (as with positron emission tomography [PET]), the role of the physician and his qualitative interpretation remains paramount (as in Jameria and colleagues, which highlights the operator dependency of this type of analysis).[13] Thus, a refined imaging of high visual quality continues to be a very important goal given that analysis relies significantly on such image interpretation.

The heightened sensitivity of CZT detectors may also open the room for an increase in stress-only exams for a likely ''shift'' from equivocal results to exams which are clearly negative, for two reasons. First, the availability of a more reliable end-diastolic imaging which completes exam interpretation. Second, we can acquire left ventricular ejection fraction (LVEF) early after stress and afterwards (even after 1 hour).[17] The presence of adequate perfusion also in the end-diastolic phase and of a normal LVEF reserve reduces equivocal exams increasing diagnostic true negatives and surely prognostic true negatives.

The negative predictive value is already high with Anger cameras, and thus the main advantage of using a CZT camera lies in the increase in the number of patients with negative tests, which translates into a more accurate appraisal of the warranty period.[18] Focusing on positive tests, the expected pros of CZT are a more correct classification of ischemic patients in terms of ischemia severity (e.g., in keeping with the Maximal Ischemia Score [MIS], distinguishing minimal, mild, moderate or severe ischemia), extension, and involvement of the corresponding coronary vessel, in particular, the left anterior descending (e.g., single-vessel-related ischemia [VRI] versus multiple VRI, with or without left anterior descending involvement).[4,5] Accordingly, we may more accurately proceed with risk stratification and choice of subsequent clinical management. Focusing on the evaluation of end-diastolic perfusion, another advantage of CZT is the possibility of significantly reducing false-positive results in patients with left bundle branch block (Figure 1), who typically display a perfusion abnormality which is more severe in the end-systolic phase than in the end-diastolic phase, at odds with ischemic patients (Figure 2). Other unique strengths of CZT cameras include the distinctively high-energy resolution which enables dual-isotope administration.[19] For instance, two key clinical advantages can be envisioned in the evaluation of patients with prior or recent myocardial infarction (stress or rest Tc and rest-delay Tl) and in patients with heart failure (rest Tl plus metaiodobenzylguanidine [MIBG]) to quantify prognosis and the risk of sudden death.

Thanks to the advantage of a significant reduction of radiation exposure, it is possible to acquire hybrid imaging with coronary computed tomography (CT).[20] For instance, the total radiation dose for a stress-only CZT MPI study with associated coronary CT amounts to 2.1 mSv.[21] Indeed, a specific suite (Discovery NM/CT 570c) already enables, with the same equipment, to complete both exams, functional and anatomic. The improved spatial resolution may lead to a more credible

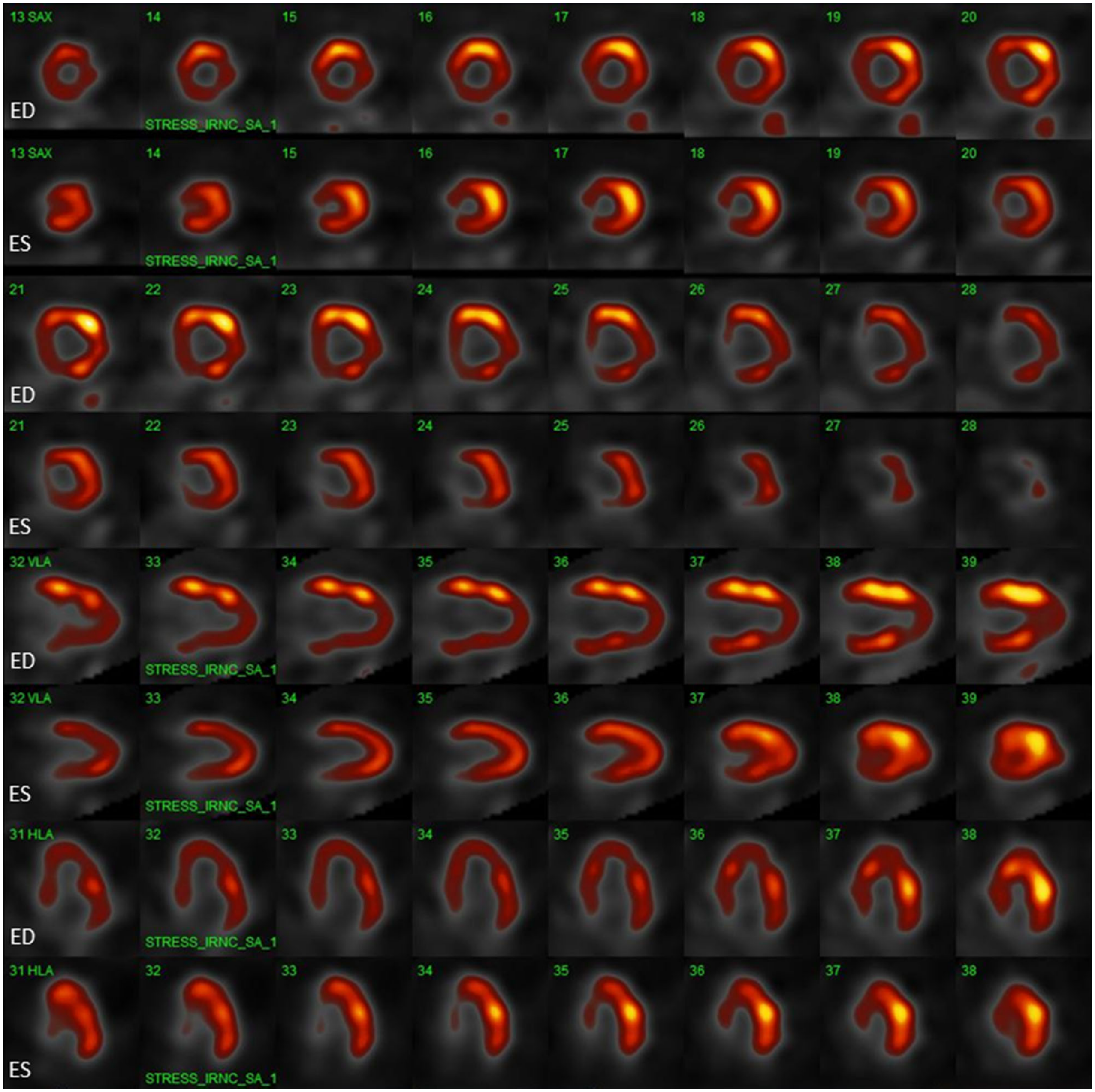

Figure 1. Case study of pharmacologic stress myocardial perfusion imaging with a cadmium-zinc-telluride camera (Discovery NM 530c, GE Healthcare, Haifa, Israel) in a patient with atypical chest pain and complete left bundle branch block. The septal defect is present only in the end-systolic phase (ES), and not in the end-diastolic phase (ED).

relation between myocardial region and corresponding coronary vessel. Two important clinical advantages can be envisioned. First, assuming a negative MPI result, it will be possible to distinguish among three competing scenarios: the absence of coronary disease, the presence of a non-significant coronary stenosis, or an angiographically significant stenosis. This will be pivotal to better define individual warranty period. The second advantage lies in the evaluation of intermediate coronary stenosis, which may show ample range of coronary reserve, from normal to significantly reduced.

Another key and quite novel feature of CZT technology is the possibility of appraising coronary flow reserve (CFR).[22] The sensitivity of MPI to recognize CAD is in general higher in patients with multivessel disease than in those with single-vessel disease, whereas balanced ischemia remains rare. The drawback of MPI may lie in the potential underestimation of ischemia

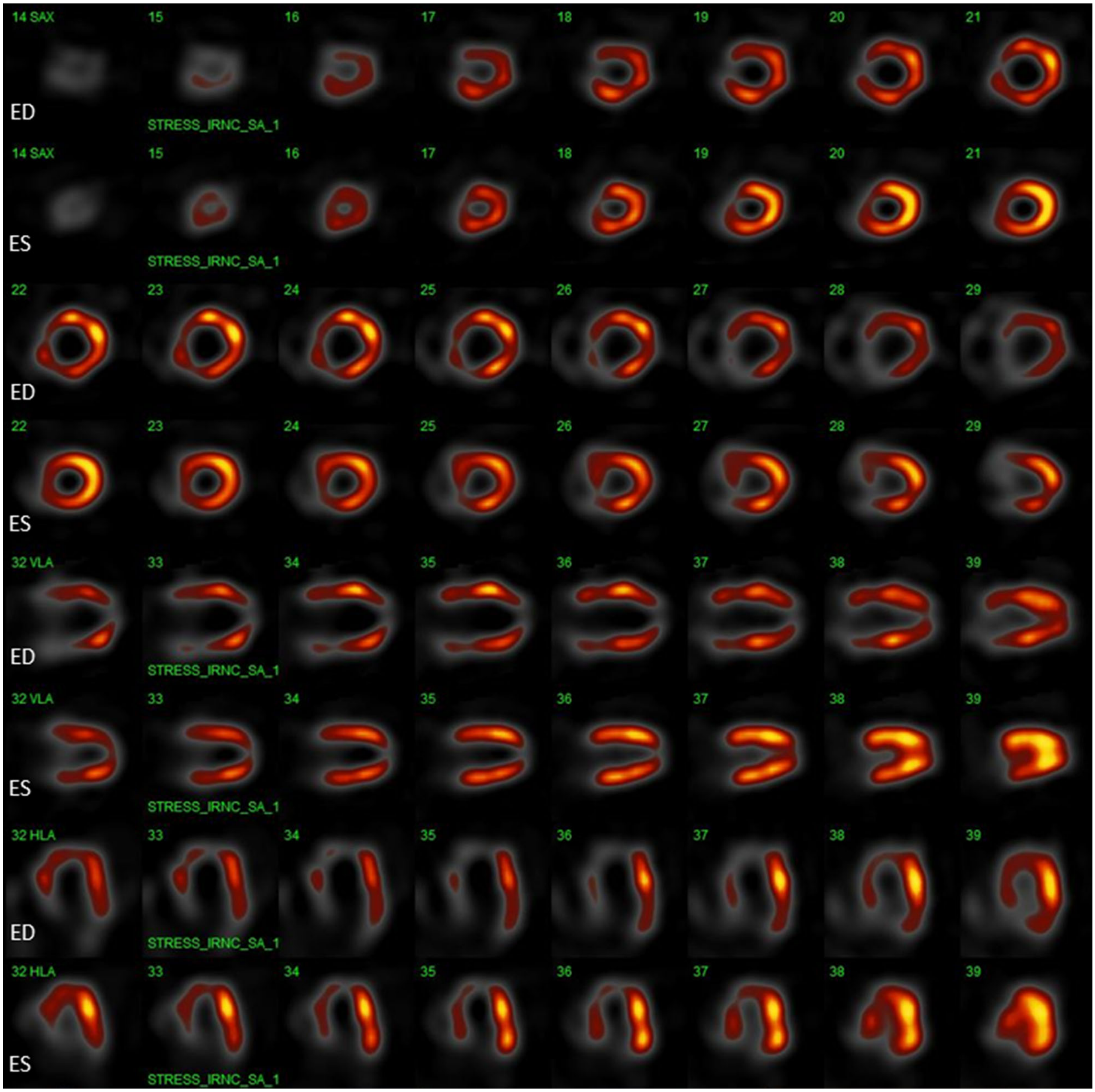

Figure 2. Case study of pharmacologic stress myocardial perfusion imaging with a cadmium-zinc-telluride camera (Discovery NM 530c, GE Healthcare, Haifa, Israel) in a patient with symptomatic angina. The septal and apical defect is present in the end-systolic phase (ES), but is more evident in the end-diastolic phase (ED).

severity and vessel disease extent, if the area of the highest myocardial activity is in itself depending on the diseased vessel, as this is the region used to compare the activities of the other regions, which may risk being labeled as ''less ischemic.'' When the region with the highest activity depends from a diseased vessel, both stress myocardial blood flow (MBF, measured in mL/min/g of myocardium) and CFR (the ratio between stress [hyperemic] MBF and rest [basal] MBF) will be reduced. Another intriguing indication to CFR is the evaluation of mild perfusion defects in the regions depending from the left anterior descending. Accordingly, CZT cameras may eventually topple the dominating role of coronary angiography, thus that the old paradigm that the functional detail may underestimate the anatomic detail will convert into the novel paradigm that the anatomic detail may overestimate the actual patient risk and cannot alone represent an indication to coronary revascularization.

In conclusion, CZT MPI represents a major breakthrough in the diagnostic, prognostic, and management work-up of patients with suspected or established CAD, and most interestingly, this development will open the way for the potential application of MPI in the primary prevention of cardiovascular disease in apparently healthy subjects. Further studies are, however, necessary to better understand and implement this promising development in non-invasive functional cardiovascular imaging.

Disclosure

None.

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