Simultaneous dual-tracer ^{99m}Tc -tetrofosmin and ^{123}I -BMIPP acquisition with CZT for ischemic memory: The future approaches to image the past

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So far, cadmium-zinc-telluride (CZT) detectors technology did not disappoint the expectations and what we believed could be realized with the advent of CZT cameras for cardiac imaging is now a reality.^{1,2} The hardware implementation of this equipment with regard to traditional Anger camera consists in the utilization of CZT modules on a column of tungsten collimators rather than lead. CZT semiconductors operate at room temperature and can process > 10 million photons/second/mm² boasting the highest energy resolution among all the commercially available scintillators.³ In addition, lead elimination from the detector suite avoids the potential X-ray generation, which can degrade image quality. The application of this system allows higher energy and spatial resolution with narrower photo-peak energy windows as compared to conventional Anger cameras.⁴ As estimated, the advantageous characteristics of this novel technology provide dose reduction and acquisition time shortening with improved patient comfort and compliance and high diagnostic accuracy.^{2,5} These characteristics answer to the current dose-optimization challenge as also demonstrated by recent introduction of new iterative algorithms for conventional gamma cameras.⁶

Two industries applied CZT method by developing different geometry configuration (D-SPECT, Spectrum Dynamics, Palo Alto, CA, USA; Discovery NM 530c, and the hybrid version NM/CT 570c GE Healthcare, Haifa, Israel). Interestingly, the original cardiac dedicated approach imaging of D-SPECT system spread out to other applications such as thyroid and parathyroid imaging.⁷ Indeed, CZT concept showed such powerful strengths that manufactories made a great effort in developing general purpose SPECT scanners. Therefore, VERITIONTM model has been released by Spectrum Dynamics while Discovery NM/CT 670 CZT has been proposed by GE Healthcare. For this latter device, in the present issue of the Journal⁸ Yamada et al. explored the feasibility of simultaneous ^{99m}Tc -tetrofosmin and ^{123}I - β -methyl-iodo-phenyl pentadecanoic acid (^{123}I -BMIPP) dual-tracer imaging. The idea to perform dual-isotope imaging has deep roots.⁹ Indeed, simultaneous dual-tracer protocols offer the advantage of decreasing potential image misalignment and further reducing acquisition time, detecting in one examination two target patterns, such as perfusion by ^{99m}Tc -sestamibi and innervation by ^{123}I -metaiodobenzylguanidine (MIBG), or two faces of the same coin such as ^{201}Tl and ^{99m}Tc -sestamibi stress-rest imaging to evaluate myocardial viability and perfusion. Besides cardiac imaging, simultaneous dual isotope acquisition possibilities have been explored for different applications as for brain,¹⁰ and oncological imaging.¹¹ However, its realization has been extremely demanding, due to conventional gamma camera limitations, such as the consistent cross-contamination between different isotope energy windows. The cross-contamination issue has a much higher impact as the energy windows are closer.¹² In particular, ^{99m}Tc photo-peak of 140 keV is very near to the ^{123}I one,

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which is 159 keV. The introduction of CZT solid state cameras, permitting better photon energy discrimination, has reignited the interest in dual-isotope imaging setting-up.^{13,14} Even if the downscatter fraction from the higher peak into the lower still affects the count rate estimation,¹⁵ the availability of correction methods allows to extract images with better contrast for both ^{99m}Tc and ¹²³I.¹⁶ Some studies already investigated the feasibility of simultaneous dual-tracer imaging with CZT cameras.^{17,18} Yamada et al.⁸ study fits in this research field investigating ischemic memory evaluation by using the novel design Discovery NM/CT 670 CZT with simultaneous rest ^{99m}Tc-tetrofosmin and ¹²³I-BMIPP imaging. They compared the dual-tracer protocol with each single-tracer acquisition in thirty patients with previous myocardial infarction undergone primary coronary percutaneous intervention. They found that quantitative and semi quantitative values of global and regional left ventricle perfusion, function and fatty acid metabolism obtained by simultaneous dual-tracer protocol were comparable with those obtained by each single tracer modality, suggesting that the proposed protocol is feasible in clinical routine. The evaluation of perfusion-metabolism mismatch may detect jeopardized myocardium after an ischemic event. BMIPP is an analogue of 15-(p-iodophenyl) pentadecanoic acid. Rest imaging of ¹²³I-BMIPP is related to its metabolism in the mitochondria and its uptake during myocardial ischemia occurrence is dynamic. During the acute phase (1-6 h), the amount of the intracellular non-oxidized fatty acid pool rises with an increased ¹²³I-BMIPP uptake. Starting from the subacute phase (> 6 h), there is a reduction of ¹²³I-BMIPP uptake in the ischemia territory, and it recovers in the chronic phase (30 days).¹⁹ Therefore, the use of fatty acid radiotracers may capture recently occurred ischemia, without the need for a provocative test examination depicting ischemic memory. The comparison of ¹²³I-BMIPP findings with rest perfusion uptake offers three different patterns. The presence of a negative match result depicts physiological uptake distribution as expression of viable and perfused myocardium. The presence of a matched uptake defect identifies a region of injured myocardium that will not recover after revascularization. The mismatch between myocardial metabolism and perfusion can be attributed to regions of viable myocardium with abnormal fatty acid metabolism predicting potential full recovery with time. However, only a few number of studies investigate the prognostic impact of perfusion metabolism mismatch reporting that, discordant ¹²³I-BMIPP uptake is an excellent predictor of future cardiac events.

The improved energy and spatial resolution of implemented CZT detectors opens the way to such

imaging protocol proposal. Indeed, the evaluation of perfusion-metabolism mismatch may translate into a concept with a double meaning across the past to the future: imaging can be thought as a footprint to recall past ischemic events as well as a tool for providing information to predict outcome. In order to save out of the time an image, an event, a phenomenon, human being used more and more complex instruments, passing from watercolours paintings to the first films to digital cameras. In the same way, technological innovation has allowed medicine to photograph receptor and metabolic patterns, contributing not only to the diagnosis but also to the deeper knowledge of diseases. The recent hardware and radiopharmaceutical developments are offering new perspectives, for example the identification of ischemic memory by dual isotope imaging with CZT detectors, helping us to predict the future not only by shooting the present but also by investigating the past.

It remains to be evaluated the real clinical impact of information derived from this imaging protocol, identifying the category of patients that may most benefit from this diagnostic approach method. In fact, the Yamada's study⁸ is a single-center, observational report including a small number of patients without outcome measures. Moreover, from Figures 2 and 3 of Yamada's study, one patient with a severely dilated left ventricle showed a prominent discrepancy between the single- and dual-tracer results and another revealed discrepant results in the QPS for BMIPP, suggesting a failure in the quantitative perfusion SPECT processing to adjust the endocardial/epicardial contour. Finally, in the era of artificial intelligence,²⁰ there is to examine whether data obtained by such a diagnostic work-up may contribute in tailored therapeutic strategies modifying patient outcome and if there is space of future applicability of these information to machine learning.

Disclosure

None of the authors has financial conflicts of interest.

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