A big step towards clinical implementation of myocardial blood flow quantification with CZT SPECT

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One of the main benefits of positron emission tomography (PET) myocardial perfusion imaging (MPI) over other imaging techniques is its ability to perform accurate myocardial blood flow (MBF) quantification.[1] Quantification of MBF has been shown to increase diagnostic performance of PET MPI,[2–4] an increase attributed in part to improved detection of multivessel disease and identification of sub-optimal response to pharmacological stress.[1,4,5] In addition, integration of flow quantification with PET MPI leads to better risk stratification of patients with coronary artery disease, as demonstrated by a significant increase of major cardiovascular events and deaths in patients with reduced myocardial flow reserve (MFR), even in the absence of inducible ischemia or scar on perfusion imaging.[6,7] Moreover, the prognostic value of flow quantification has been established in various populations, such as patients with diabetes[8] and kidney failure,[9,10] as well as in several non-ischemic cardiomyopathies.[11]

Currently, only a few centers having the ability to perform MPI with PET and SPECT remain the mainstay of nuclear cardiology worldwide. As only short-lived isotopes are presently available for PET MPI, an on-site cyclotron or generator is required for tracer production. Furthermore, a dedicated PET camera system is desirable to perform PET MPI in order to optimize costs and department efficacy. This infrastructure is associated with substantial costs, hindering dissemination of the technology.[11] In that context, and given the wealth of evidence supporting the clinical value of flow quantification, it is of great interest to develop methods enabling MBF assessment with SPECT systems.

Wells et al. were the first to validate non-invasive quantification of MBF with a solid state SPECT camera system (CZT-SPECT) by demonstrating a very good agreement between SPECT MBF and microspheres MBF in a porcine model.[12] Several studies subsequently showed good agreement between SPECT measurements of MBF versus PET MBF, the non-invasive gold standard.[13–15] Clinical studies have also shown the potential clinical value of flow quantification with solid-state SPECT systems. For instance, Ben-Haim et al. showed that global and regional MFR index, defined as the ratio between the stress and rest K_1 values of a 2-compartment kinetic model, were reduced in regions supplied by obstructed coronary arteries and that there is an inverse relation between the degree of MFR index reduction and severity of coronary disease on angiography.[16] These findings were later confirmed in following studies, including the WATERDAY study, which demonstrated a correlation between regional SPECT MFR versus percent stenosis and FFR on invasive angiography.[17–19] In the WATERDAY study, 30 participants prospectively underwent FFR measurements as well as MBF quantification with both ^{15}O-water PET and CZT-SPECT.[15] For all 30 participants, FFR measurements were performed in each of the coronary arteries (LAD, LCX, and RCA) with diameter > 2 mm and for every stenosis $> 50\%$. The authors observed good correlation between PET and SPECT MFR measurements (2.64 vs 2.84,

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r = 0.75). With thresholds of 2.1 for SPECT-CZT MFR, 2.0 for PET MFR, and 0.8 for FRR, they obtained high concordance between FFR vs MFR for both PET (κ = 0.85) and CZT-SPECT (κ = 0.81).

In this issue of the Journal of Nuclear Cardiology, Otaki et al.[20] compared measurements of MBF and MFR obtained with CZT-SPECT imaging and analyzed using QPET (Cedars-Sinai Medical Center) to those of ^{15}O-water PET imaging. The authors used the SPECT and PET imaging data from the WATERDAY study[15] and re-quantified the PET data using dedicated software (Carimas, Turku, Finland). The original WATERDAY study used Corridor 4DM (INVIA, Ann Arbor, MI, USA) which is commercially available. The novelty of QPET is the incorporation of motion correction and optimal positioning of the region-of-interest for the arterial input function. The correlations between the SPECT and PET measurements with the QPET software were slightly improved compared to the original WATERDAY analyses for global measurements of MBF (r = 0.91 vs. 0.83) and MFR (r = 0.81 vs. 0.75), confirming the WATERDAY results using a different software package. However, regional MBF measurements differed with underestimation by SPECT in the RCA territory at stress and in the LCX and RCA territories at rest. Conversely, the WATERDAY results described higher rest and stress MBF in the LAD and LCX territories, but not the RCA. These differences in MBF measurements with the same raw datasets are most likely due to the differences in the software algorithms and suggest that the software packages cannot be used interchangeably. Notably, the raw data was not corrected for attenuation, which may result in lower uptake values in the inferior and lateral walls leading to lower MBF measurements in these areas. The diagnostic accuracy of CZT-SPECT MFR was excellent for the detection of reduced PET MFR. The thresholds for detection of reduced PET MFR were similar with the two CZT-SPECT analyses using the two different software packages. Finally, the use of QPET software led to improved and low inter-observer variability for both global MBF (r = 0.95) and MFR (r = 0.86).

This study of Otaki et al. strongly supports the capability of CZT-SPECT systems to quantify MBF using commercially available software and increases confidence in the technique. This represents a significant step towards clinical acceptance and implementation of measurement of MBF with CZT-SPECT. Prior to widespread clinical use of SPECT MBF quantification, several questions still need to be addressed. Multicenter validation studies are necessary as the majority of clinical studies have been single site and included small numbers of patients. A multicenter study assessing the feasibility of implementation is underway (NCT03427749) and studies evaluating diagnostic accuracy and incremental prognostic value of SPECT MBF are necessary.

Disclosures

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