

## Failure to accurately identify the number of diseased coronary arteries: A weakness of SPECT MPI

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SPECT myocardial perfusion imaging (MPI) is widely used for the diagnosis of obstructive coronary artery disease (CAD), though the number of diseased coronary arteries is frequently underestimated.<sup>1,2</sup> The underestimation of the extent of CAD occurs for several reasons:

### **ASSESSMENT OF RELATIVE (RATHER THAN ABSOLUTE) MYOCARDIAL BLOOD FLOW**

With conventional SPECT MPI, myocardial tracer uptake in each myocardial region is assessed relative to the most normal myocardial region. In the setting of balanced myocardial ischemia due to multi-vessel CAD, the myocardial perfusion pattern may appear normal (homogeneous) due to the absence of a normally perfused myocardial reference region. The ability to assess absolute myocardial blood flow and myocardial blood flow reserve with PET represents a major advantage of PET MPI for detection of multi-vessel CAD compared to conventional SPECT. Efforts have recently been made to measure absolute myocardial blood flow with new generation cadmium-zinc-telluride (CZT) SPECT cameras,<sup>3</sup> though the utility of the SPECT methods for measurement of absolute myocardial blood flow require further clinical validation.

### **SPECT PERFUSION TRACERS UNDERESTIMATE ISCHEMIA**

The commercially available technetium-labeled myocardial perfusion tracers (<sup>99m</sup>Tc-sestamibi and <sup>99m</sup>Tc-tetrofosmin) have a relatively low myocardial extraction fraction resulting in an early plateau in myocardial tracer uptake at high myocardial blood flows. Therefore, the contrast in myocardial tracer activity between normally perfused and hypoperfused myocardial regions underestimates the true myocardial blood flow disparity. This limitation of the technetium-labeled tracers is especially problematic when attempting to detect the presence of mild to moderate coronary artery stenoses. Thallium-201 has more favorable myocardial uptake properties but its clinical use is limited by its high radiation dosimetry. The myocardial uptake kinetics of the PET perfusion tracers are superior to the technetium-labeled SPECT tracers resulting in higher sensitivity for detection of multi-vessel CAD with PET MPI compared to SPECT MPI.<sup>4</sup>

### **SOFT TISSUE ATTENUATION**

When soft tissue attenuation reduces apparent tracer activity in the most normally perfused myocardial region, the resulting perfusion pattern will appear homogeneous, and ischemia in myocardial regions remote from the soft tissue attenuation artifact will be underestimated when compared to the activity in the “normal” myocardial reference region (with artificially reduced tracer activity resulting from the attenuation artifact). Soft tissue attenuation artifacts can also reduce sensitivity for detecting CAD by shifting the “diagnostic threshold”. The interpreting physician might be led to ignore mild perfusion defects in order to preserve specificity. Severe gastrointestinal tracer interference (particularly problematic on pharmacologic stress SPECT MPI) also requires the interpreting physician

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to ignore mild to moderate perfusion defects, sacrificing sensitivity in order to preserve specificity. The robust attenuation correction of PET allows for more accurate detection of multi-vessel CAD and improves diagnostic confidence.<sup>4</sup> Improvements in detection of left main disease have been demonstrated with attenuation corrected SPECT<sup>5</sup> and improvements in detection of multi-vessel CAD have recently been demonstrated using a high-resolution SPECT camera incorporating line-source attenuation correction, noise reduction, and resolution recovery algorithms.<sup>6</sup> Use of a newer generation CZT SPECT camera has also been shown to result in improved accuracy for detecting multi-vessel CAD.<sup>7</sup>

### **DELAYED ACQUISITION OF GATED SPECT IMAGES POST-STRESS (RATHER THAN AT PEAK-STRESS)**

To allow gastrointestinal clearance of the technetium-labeled SPECT perfusion tracers, acquisition of gated SPECT images is delayed for 30 to 60 minutes post-stress. The delay in post-stress image acquisition reduces the likelihood of detecting an ischemic myocardial wall motion abnormality on the gated SPECT images, and therefore reduces the sensitivity for detecting balanced myocardial ischemia due to multi-vessel CAD. The ability to acquire gated images during peak-stress with rubidium PET represents another advantage of PET for detection of multi-vessel CAD.<sup>8</sup> Early (peak-stress) assessment of left ventricular systolic function was recently shown to be feasible with regadenoson stress using a high efficiency CZT SPECT camera,<sup>9</sup> though this technique is not widely used presently.

### **TERMINATION OF EXERCISE AT ONSET OF ISCHEMIA IN THE REGION WITH THE MOST SEVERE CORONARY ARTERY STENOSIS**

Exercise stress is terminated when the patient reaches an ischemic end-point (e.g. typical angina with associated ischemic ST depression). This occurs when the patient develops ischemia in the myocardial region subtended by the most severe coronary artery stenosis. Termination of exercise at onset of ischemia in the region with the most severe stenosis will reduce sensitivity for detection of myocardial ischemia in myocardial regions with less severe (but nonetheless obstructive) stenoses.

In this issue of the Journal, Yamauchi and colleagues evaluated the impact of segmentation with scatter and photo-peak window data for attenuation correction (SSPAC) on the diagnostic accuracy of SPECT myocardial perfusion imaging for identifying the number of stenosed coronary artery vessels. The

SSPAC method takes advantage of the low energy (scattered) activity to create a patient-specific attenuation map.<sup>10,11</sup> The current study was a retrospective comparison of the diagnostic accuracy of SPECT MPI performed with and without SSPAC using invasive coronary angiography as the reference standard. The authors reported significantly higher accuracy for identification of the number of stenosed coronary arteries with SSPAC. The higher accuracy for SSPAC compared to conventional SPECT was largely attributed to a higher sensitivity for detecting left anterior descending (LAD) and right coronary artery (RCA) disease, without a significant impact on specificity. The same group of investigators reported slightly different results in a previous study, with improved sensitivity for LAD disease and improved specificity for RCA disease with the use of SSPAC.<sup>12</sup>

There are several potential advantages of the SSPAC method.

1. SSPAC is a software approach. There is no need for additional hardware, and the SSPAC method adds only a few minutes to standard processing times.
2. Patient-specific attenuation correction is achieved without the need for external line-source radiation or computed tomography. No additional radiation exposure is required.
3. The perfusion data and attenuation correction data are acquired simultaneously. The SSPAC method should therefore be less susceptible to misregistration artifacts related to respiration or patient motion.
4. The SSPAC method is feasible in the majority of patients (98% feasibility in the present study).

However, there are several limitations to consider before widespread use of SSPAC can be recommended.

1. The clinical utility of SSPAC to predict the number of diseased vessels is limited by the small number of patients (35) with multi-vessel CAD in the present study. The results of the current study should be confirmed in a larger cohort of patients with single-vessel and multi-vessel CAD.
2. The present study was performed in a Japanese patient population with a mean body mass index (BMI) of 24 kg/m<sup>2</sup>. This limits the generalizability of the study results to patient populations with a higher prevalence of obesity. The feasibility and accuracy of the SSPAC method should be confirmed in a more diverse patient population including patients with moderate to severe obesity.
3. Quality control parameters are needed to verify that the SSPAC algorithm is performed successfully and that the application of SSPAC processing does not inadvertently create artifactual perfusion defects.

Clinical validation of the quality control parameters will be important to ensure that the SSPAC method can be safely applied to a larger and more diverse patient population.

The field of nuclear cardiology continues to search for ways to optimize SPECT MPI and improve detection of multi-vessel CAD. SSPAC represents another small step in the right direction.

## Disclosure

*Dennis A. Calnon disclosed the following relationship: Research Consultant, Navidea Biopharmaceuticals.*

## References

- Melikian N, De Bondt P, Tonino P, De Winter O, Wyffels E, Bartunek J, et al. Fractional flow reserve and myocardial perfusion imaging in patients with angiographic multivessel coronary artery disease. *J Am Coll Cardiol Intv* 2010;3:307-14.
- Berman DS, Kang X, Slomka PJ, Gerlach J, de Yang L, Hayes SW, et al. Underestimation of extent of ischemia by gated SPECT myocardial perfusion imaging in patients with left main coronary artery disease. *J Nucl Cardiol* 2007;14:521-8.
- Nkoulou R, Fuchs TA, Pazhenkottil AP, Kuest SM, Ghadri JR, Stehli J, et al. Absolute myocardial blood flow and flow reserve assessed by gated SPECT with Cadmium-Zinc-Telluride detectors using <sup>99m</sup>Tc-Tetrofosmin: head-to-head comparison with <sup>13</sup>N-Ammonia PET. *J Nucl Med* 2016;57:1887-92.
- Bateman TM, Heller GV, McGhie AI, Friedman JD, Case JA, Bryngelson JR, et al. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: Comparison with ECG-gated Tc-99m sestamibi SPECT. *J Nucl Cardiol* 2006;13:24-33.
- Duvernoy CS, Ficaro EP, Karabajakian MZ, Rose PA, Corbett JR. Improved detection of left main coronary artery disease with attenuation-corrected SPECT. *J Nucl Cardiol* 2000;7:639-48.
- Patil HR, Bateman TM, McGhie AI, Burgett EV, Courter SA, Case JA, et al. Diagnostic accuracy of high-resolution attenuation-corrected Anger-camera SPECT in the detection of coronary artery disease. *J Nucl Cardiol* 2014;21:127-34.
- Gimelli A, Liga R, Duce V, Kusch A, Clemente A, Marzullo P. Accuracy of myocardial perfusion imaging in detecting multi-vessel coronary artery disease: A cardiac CZT study. *J Nucl Cardiol* 2017;24:687-95.
- Dorbala S, Hachamovitch R, Curillova Z, Vangala D, Kwong RY, Di Carli MF. Incremental prognostic value of gated Rb-82 positron emission tomography myocardial perfusion imaging over clinical variables and rest LVEF. *JACC Cardiovasc Imaging* 2009;2:846-54.
- Brodov Y, Fish M, Rubeaux M, Otaki Y, Gransar H, Lemley M, et al. Quantitation of left ventricular ejection fraction reserve from early gated regadenoson stress Tc-99m high efficiency SPECT. *J Nucl Cardiol* 2016;23:1251-61.
- Maeda H, Natsume T, Yamaki N, Shirakawa S, Kikukawa K, Toyama H, et al. Attenuation correction for myocardial SPECT: Segmentation with scatter and photopeak window data for attenuation correction (SSPAC) method. *J Nucl Med* 2002;43:230.
- Okuda K, Nakajima K, Motomura N, Kubota M, Yamaki N, Maeda H, et al. Attenuation correction of myocardial SPECT by scatter-photopeak window method in normal subjects. *Ann Nucl Med* 2009;23:501-6.
- Yamauchi Y, Kanzaki Y, Otsuka K, Hayashi M, Okada M, Nogi S, et al. Novel attenuation correction of SPECT images using scatter photopeak window data for the detection of coronary artery disease. *J Nucl Cardiol* 2014;21:109-17.