# What is the value of motion and thickening in gated myocardial perfusion SPECT?

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Received Feb 4, 2018; accepted Feb 5, 2018
doi:10.1007/s12350-018-1239-2

**See related article, pp. 742–753**

Myocardial perfusion SPECT imaging (MPI) is a stress imaging modality, widely used in the detection and evaluation of coronary artery disease (CAD). This method is unique in providing simultaneous bi-modal functional imaging of relative myocardial perfusion and left ventricular (LV) function.[1] While perfusion images identify regions with relative hypoperfusion, gated SPECT allows assessment of global and regional LV function. The added prognostic information gained by global LV function to myocardial perfusion findings has been extensively shown.[2,3] However, accurate regional assessment of contractile function is also of great importance, since it could enhance the detection of CAD,[4] and provide additional prognostic information in predicting cardiac events.[5,6]

Similar to myocardial perfusion, regional motion and thickening can be assessed using semi-quantitative visual methods, based on segmental scoring. While motion score simply reflects the extent of inward shift of the ventricular wall, thickening is assessed as systolic brightening of the myocardium occurring due to the partial volume effect. This systolic apparent increase in count density occurs since myocardial thickness is commonly in the range up to 2 cm, less than twice the full width at half maximum of the point spread function of conventional gamma cameras with intrinsic spatial resolution of $\sim$1 cm.[7] Visual assessment of regional LV contractile function is expert dependent, and suffers from limited reproducibility with high inter- and intra-observer variability.[8] Therefore, several methods have been developed and validated, which automatically quantify motion and thickening, and provide useful and reproducible assessment of regional function.[9,10] Whether visually or automatically assessed, regional motion and thickening have been shown as important adjunctive parameters to perfusion in the diagnosis of CAD.

In the current issue of the *Journal of Nuclear Cardiology*, Yang et al. used resting gated SPECT MPI to demonstrate the relationship between myocardial thickening and LV remodeling among patients with history of myocardial infarction (MI). The 92 patients included in the analysis were divided into subacute MI (3-6 months before nuclear testing, $n = 54$) and old MI (>6 months before nuclear testing, $n = 38$) subgroups. In addition, all patients underwent FDG-PET imaging to identify myocardial viability as metabolic perfusion mismatch, and a scar score was calculated. LV remodeling was defined as end-diastolic volume index >62.53 ml/m$^2$, derived as mean value +2 standard deviations from gated SPECT of another 95 patients who had normal SPECT MPI and no evidence of CAD. Compared to patients with subacute MI, those with old MI had larger LV volume and worse cardiac function, larger perfusion deficit, and higher summed thickening score (STS). Interestingly, of all the demographic, clinical, perfusion, and metabolic imaging parameters evaluated, only the STS and the % of segments with reduced thickening among segments with normal perfusion were independently related to LV remodeling among the 92 patients in the analysis. Other imaging parameters including total perfusion deficit (TPD), viable myocardium, scar, and % reduced thickening segments among decreased perfusion segments were significant predictors of LV remodeling only in univariate analysis, but were not independent predictors in multivariate binary logistic regression. The importance of this study

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J Nucl Cardiol 2018;25:754–7.
1071-3581/$34.00

is in showing another application for myocardial thickening assessment. The authors demonstrated that not only the global thickening abnormality is related to LV enlargement, but abnormal thickening within normally perfused regions was independently associated with enlarged LV, as well. Whether abnormal thickening within remote areas with normal perfusion consists of a contributing factor to progressive post-MI LV enlargement and remodeling process, or just secondary to large LV volume is unclear. Remote thickening abnormality might indicate obstructive CAD in remote vessels, which might contribute to progressive LV enlargement and remodeling. Data on the value of thickening in predicting LV remodeling are conflicting. Ernade et al. assessed the value of low-dose dobutamine Tc-99m gated SPECT performed few days after PCI treated MI in predicting early (6 months) post-MI remodeling of the LV.[11] Using visual analysis of perfusion and of regional motion and thickening, these investigators demonstrated that infarct severity at rest had the best predictive values for LV remodeling with PPV 86% and NPV 88%, whereas combined analysis of wall thickening score and infarct severity did not improve prediction of LV enlargement over infarct severity alone. Others demonstrated the usefulness of wall thickening in addition to perfusion in the assessment of post-MI myocardial salvage, which might have implications in the prediction of LV remodeling.[12] Further assessment of the value of STS and abnormal remote thickening in predicting future LV enlargement and remodeling might illuminate this issue.

Previous studies have addressed the diagnostic importance of regional myocardial thickening. Attenuation artifacts often appear as a fixed or partially reversible perfusion deficit, and comprise the most common cause of a false-positive MPI. Motion and thickening data may assist in discriminating between attenuation artifacts and true regional hypoperfusion. Normal motion and thickening of segments with a fixed defect suggest attenuation artifact, whereas non-reversible perfusion deficit coupled with abnormal motion and thickening most likely comprise an old MI. Depuey and Rozanski show that incorporation of regional function data in the interpretation of perfusion imaging reduced false-positive rate from 14% to 3%.[13] Fleischman el al. demonstrated that among patients with no clinical history of MI, 90% of cases with fixed perfusion deficit but normal systolic function occurred in the inferior wall among men (87%) and anterior wall among women (3%), and concluded that these defects were most likely due to attenuation artifacts.[14] In the past 15 years, hybrid SPECT/CT technology has been developed and increasingly used for attenuation correction of SPECT data using CT transmission maps. However, while increasing specificity in the evaluation of the right coronary artery particularly among obese patients,[15] CT attenuation correction has been shown to reduce specificity in the left anterior descending coronary artery territory, was less effective in the correction of breast artifacts,[16] and frequently introduced apical artifacts.[17] Moreover, the sensitivity in the RCA territory has been shown to be reduced in CT attenuation corrected vs non-corrected MPI.[18] Therefore, regional motion/thickening evaluation is still relevant in identifying attenuation artifacts, even when CT attenuation correction is applied.

Assessment of regional contractile function may enhance the diagnostic value of MPI in the detection of severe obstructive CAD. MPI generates relative perfusion data, referenced to maximal tracer uptake within the LV, and often identifies the most severe perfusion abnormality. It has been well recognized that among patients with extensive CAD, relative myocardial perfusion might underestimate the extent and severity of the disease due to global hypoperfusion.[19] Although global post-stress LV stunning adds important diagnostic information to MPI,[20] regional motion/thickening data might be even more sensitive, detecting contractile abnormalities at the segmental level.[21] Several studies demonstrated that abnormal motion/thickening data increased the sensitivity of perfusion alone in detecting severe multi-vessel CAD.[22,23] Lima et al. determined quantitative thickening fraction based on the partial volume effect (ratio of end-diastolic counts over end-systolic counts), a method which did not require endocardial edge detection.[23] They demonstrated that combined perfusion/thickening data identified more abnormal segments per patient than perfusion alone among patients with three vessel CAD. Moreover, age and the number of abnormal vascular territories by perfusion/thickening analysis were the most powerful predictors of 3-vessel disease. Other investigators demonstrated low sensitivity but very high overall specificity (100%) of reversible regional wall motion abnormality in detecting >70% angiographic CAD, with high specificity in three vascular territories (94%-97%).[4] Moreover, reversible regional wall motion abnormality distinguished between 50%-79% and 80%-99% stenosis of the 3 coronary arteries with high positive predictive value (77%-88%). Investigators from Cedars-Sinai Medical Center developed a method of automatic quantification of rest-stress motion and thickening changes for assessing abnormal segmental function.[24] This method is based on registration of endocardial surfaces at end-diastolic and end-systolic frames, determination of motion and thickening at any point of the endocardial surface, and comparison to normal limits. Using this approach, combined ischemic

perfusion deficit and motion+ thickening rest-stress change was more sensitive than ischemic perfusion deficit alone in detecting 3-vessel CAD (52% vs 21%, respectively, $P < 0.0001$), but less specific (74%, vs 95%, respectively, $P < 0.0001$) (Figure 1A). Similarly, in identifying 2-vessel CAD, the hybrid approach of perfusion and regional function was more sensitive than perfusion alone but less specific (Figure 1B), whereas among patients with 1-vessel CAD the combined perfusion and function data had similar sensitivity and specificity to perfusion alone (Figure 1C). Importantly, all these studies demonstrated that motion-thickening data identified abnormal regional function within remote vascular territories with apparent normal perfusion among patients with multi-vessel CAD, and enhanced the diagnosis of extensive CAD.[4,21-24]

The use of Cadmium Zinc Telluride (CZT) technology in nuclear cardiology in the past decade allowed fast SPECT imaging combined with a considerable reduction in injected radioisotope dose and patient radiation exposure.[25-28] Compared to conventional SPECT cameras, CZT-SPECT systems are characterized by improved photon sensitivity and higher spatial resolution with a factor of 2, which translates into improved image quality.[25] However, the higher intrinsic spatial resolution of CZT cameras might attenuate the count-density myocardial thickness relationship, characteristic of the low-resolution conventional SPECT systems, and limit this effect to smaller wall thickness values. Thus, the accuracy of myocardial thickening assessment using a CZT camera might be compromised due to the higher spatial resolution. Indeed, several studies demonstrated a significant underestimation of wall thickening assessed by CZT SPECT compared to cardiac MR. Cochet et al. demonstrated higher agreement with MR for wall motion than wall thickening, with errors in wall thickening measurement increasing at greater thicknesses.[29] In a phantom study, Bailliez et al also demonstrated underestimation of regional wall thickening by CZT SPECT compared to cardiac MR, especially in patients with increased wall thickness.[30] Thus, using a CZT camera, assessment of regional wall motion might be preferred over thickening evaluation, particularly in patients with left ventricular hypertrophy.

The integration of regional contractile assessment with perfusion data in the interpretation of MPS enhances the accuracy and provides valuable diagnostic information. These data are useful in differentiation between attenuation artifact and real perfusion deficit and identify reduced regional motion and thickening within myocardial areas with normal perfusion, remote of perfusion deficit suggesting more extensive CAD than seen by perfusion alone, and may predict progressive LV enlargement and remodeling after MI.

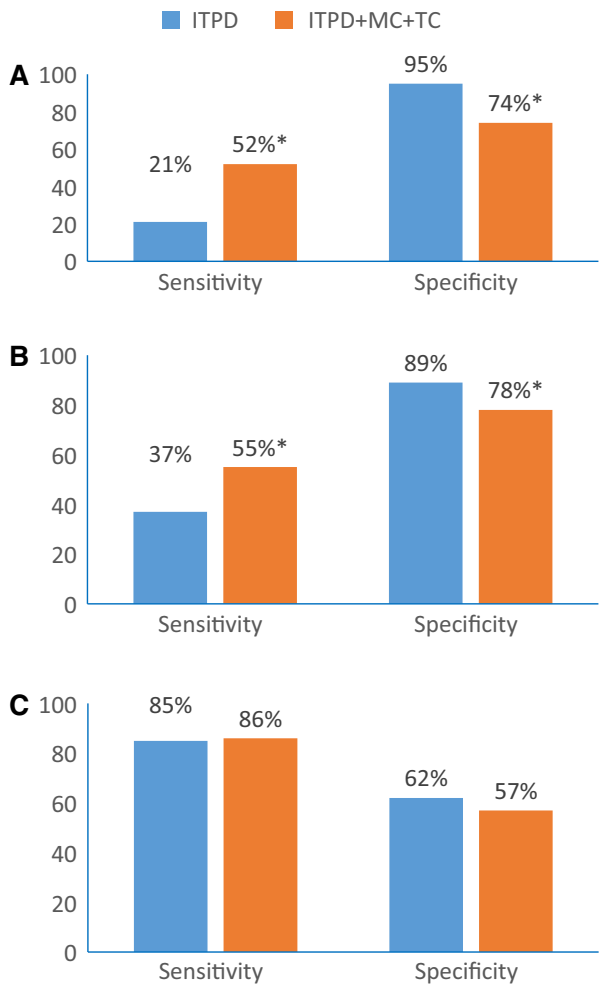


**Figure 1.** Sensitivity and specificity in the detection of 3 vessel (**A**), 2 vessel (**B**), and 1 vessel (**C**) coronary disease using ITPD or ITPD+MC+TC. *$P < 0.0001$ vs ITPD. *ITPD*, ischemic total perfusion deficit; *MC*, motion change; *TC*, thickening change. Modified and reprinted with permission from Karimi-Ashtiani et al. (Ref. 24); the unmodified version of the figure was originally published in the Journal of Nuclear Medicine by the Society of Nuclear Medicine and Molecular Imaging, Inc.

## Disclosure

*Tali Sharir has no conflict of interest.*

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