Myocardial blood flow quantitation with the SPECT technique: Where do we stand?

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Since 2013, there are numerous research studies (more than 30) reporting myocardial blood flow (MBF) quantitation with the SPECT technique. Some of them highlighted the capability of SPECT technique for detection of coronary artery disease (CAD) using rapid rotating gantry (RRG) cameras integrated with full physical corrections (e.g. corrections for attenuation, scatter, collimator blur and statistical noise).^{1,2} The rest majority reported the ability of CZT SPECT cameras with collimators of stationary multiple pinholes or sweeping parallel holes, and with or without attenuation correction (AC).^{3–8} Technical validations were properly achieved by head-to-head comparison with PET MBF quantitation on the same cohort or the diagnostic assessment for CAD utilizing coronary angiography (CAG) or fractional flow reserve (FFR) as the reference standard.^{3–11} When the relevant physical interference in dynamic SPECT images was properly corrected, RRG and CZT cameras likely performed to the same level regardless of the CZT cameras possessing additional merits from higher count rate and less scatter by higher energy resolution.¹² It has been reported that resting MBF and stress MBF can be highly overestimated (20% to 40%) for CZT cameras without AC applied as compared to PET flow quantitation.^{11,13,14} For RRG cameras, the impact from no AC appended to other physical factors can be even more brutal (100% to

145%).¹⁵ Because myocardial flow reserve (MFR) or coronary flow reserve (CFR) can be relatively preserved within an acceptable range even missing AC, validation for SPECT MBF quantitation with invasive parameters (percentage of narrowed diameter in coronary artery and FFR) has been mainly focused on the single parameter, CFR (or MFR).^{3–8} The importance of stress MBF is still not yet explored for SPECT MBF quantitation due to the described limitation of SPECT systems and dedicated processing software.

In the study by Li et al.,¹⁶ CFR exhibited much better diagnostic value than stress MBF in defining significant hemodynamic coronary stenosis suggested by the area under the ROC curve (AUC) for the diagnosis of abnormal FFR (CFR: 0.864 vs stress MBF: 0.673). Although authors did not further investigate this particular finding in their study, comparing the difference in diagnostic performance of these two quantitative values, stress MBF and CFR, is of physiological importance. So far, there still exists debate as to the integration of best index from quantitative flow analysis. CFR has been shown to add incremental value for prognosis¹⁷; however, it seems that stress MBF can be superior to CFR for diagnosing hemodynamically significant CAD in previous quantitative cardiac PET studies.^{18–20} If stress MBF is sufficient for the diagnostic purpose, stress-only protocol with less radiation dose and shorter acquisition time should be more welcome. Because the calculation of CFR depends on both resting and stress MBF, diminished stress MBF does not necessarily cause a reduction in MFR if the resting MBF is in a very low level. While patients with a history of myocardial infarction having low resting MBF may still exhibit normal CFR (or MFR) values (Figure 1).²¹ As reported by the study, there was an inverse trend towards higher stress MBF in coronary arteries with stenoses than in vessels without stenoses while there was no significant difference in CFR between stenotic and non-stenotic

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Figure 1. A 70-year male patient with a history of old myocardial infarction. Both his rest MBF and stress MBF were relatively low (0.31, 0.91 mL/min/g) to yield a high MFR (2.90). Extent of the infarct was 51.67%.²¹

arteries. Lacking of AC should be recognized as the critical issue to affect the calculation of absolute MBF in their study. It is indeed a downside for the model of CZT SPECT camera utilized by Li et al. without the option to perform AC. Furthermore, only small sample size to evaluate the diagnostic accuracy of quantitative SPECT flow measurement using invasive FFR as the reference standard may exist statistical bias in their study. The work of Li et al. only included 33 intermediate lesions with FFR assessment. Nonetheless, good diagnostic performance in terms of sensitivity, specificity, and accuracy as 88.9%, 83.3%, and 87.9% for SPECT-derived CFR was still observed. From the Li's study, it is markable that SPECT-derived CFR may be useful to determine hemodynamical significance for intermediate lesions as the current practical utilization of invasive FFR still focuses to resolve this unanswered zone by CAG. However, the study was ineligible for further subgroup analysis on the discordance between CFR and FFR as authors commented. It is well known that there exists concordance and discordance between CFR and

FFR under various pathophysiological conditions, and discordance between CFR and FFR does not necessarily represent the mistake of CFR.²² For example, diffuse atherosclerosis or small vessel disease may not cause localized pressure gradient in FFR but present a reduction in CFR. FFR is now recommended as the golden standard for revascularization decision-making for CAD; nevertheless, combined pressure and flow measurement to guide treatment of coronary stenoses is worthwhile investigating. Since SPECT-derived CFR has showed good correlation and accuracy with invasive FFR by Li's work and other studies, large prospective studies in collaborative centers are still needed to warrant the potential role of quantitative SPECT flow measurement for both stress MBF and CFR as the gatekeeper for invasive FFR or even guiding clinical decision for revascularization for patients with CAD.

Disclosures

Drs. Fang and Hsu have nothing to disclose.

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