SPECT-derived absolute myocardial perfusion measures: A step in the right direction

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Received Nov 18, 2019; accepted Nov 18, 2019

doi:10.1007/s12350-019-01972-w

See related article, pp. 1906–1918

The traditional imaging concept of regional blood flow analysis by comparing best perfused areas to those that are not as well perfused is imperfect due to its relative nature.¹ Quantification of absolute myocardial blood flow (MBF) at stress and rest, and the derivation of myocardial flow reserve (MFR) adds incremental diagnostic utility, powerful prognostic nature, and improved accuracy to relative perfusion imaging by positron emission tomography (PET).^{1–6} Consensus statement from the American Society of Nuclear Cardiology and the Society of Nuclear Medicine and Molecular Imaging Cardiovascular Council indicates that these PET-derived measures are at the cusp of translation into clinical practice.⁵ However, out of more than 6 million myocardial perfusion studies done annually in North America, greater than 99% are performed with SPECT cameras, given the favorable economics, lack of cyclotron availability and expertise for PET imaging.⁷ Given the wide spread availability of SPECT cameras and favorable economics, it is but natural that attempts have been made over the past several years to determine absolute MBF measures with SPECT imaging.⁸

Due to limited sensitivity and lower temporal resolution of traditional SPECT cameras compared with

PET, measurement of absolute MBF has been challenging. Despite these difficulties, attempts have been made to ascertain the feasibility of dynamic acquisitions with conventional SPECT cameras.^{8,9} With the advent of solid-state detector (e.g., cadmium zinc telluride) cameras, the sensitivity, spatial, temporal, and energy resolution of SPECT imaging have improved dramatically.^{10,11} These improvements in SPECT camera technology has made dynamic acquisition, a requisite for ascertainment of absolute MBF easier.^{7,8} Animal and human studies have demonstrated that solid-state detector SPECT cameras can measure MBF using either ²⁰¹Thallium or ^{99m}Technetium (^{99m}Tc)-based standard perfusion tracers which correlate with myocardial flow measured with microspheres and PET tracers.^{7,12}

The current study by Giubbini et al¹³ shows reasonable correlation between MBF and MFR measured by N13NH3-PET and ^{99m}Tc-tetrofosmin CZT SPECT and builds on the previous studies^{7,8,14,15} outlined in the Table 1 which have compared the accuracy of SPECT-derived MBF measures to PET measures. The study by Giubbini et al is the largest and also highlights the importance of motion and attenuation correction for accurate determination of MBF measures. Similar optimization of dynamic images was also performed in the study by Wells et al⁷ to obtain accurate MBF values.

While reviewing this study and others, we noticed several sources of variability including different PET and SPECT cameras, stress agents, stress and rest protocols, radiotracers, application of motion and attenuation correction, reconstruction techniques, and software packages. All studies noted correlation with PET measures but no systematic directional differences were noted in SPECT MBF or MFR as compared to PET measures.

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J Nucl Cardiol 2021;28:1919–22.

1071-3581/\$34.00

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Table 1. Sources of variability in MBF and MFR determination with SPECT and PET across studies

Study	Giubbini et al ¹³ (2019)	Waterday study ¹⁴ (2018)	Wells et al ⁷ (2017)	Nkoulou et al ¹⁴ (2016)	Ito et al ⁸ (2003)
N	54	30	31	32	29
Mean age (years)	69	65	64	64	57
Mean BMI	—	— (8% obese)	27.9	28	—
CAD (%)	26%*	100%	—	—	69%
<i>SPECT characteristics</i>					
SPECT	^{99m} Tc-	^{99m} Tc-	^{99m} Tc-tetrofosmin	^{99m} Tc-tetrofosmin	^{99m} Tc-sestamibi
Tracer	tetrofosmin	sestamibi			
SPECT camera	GE-CZT	D-SPECT	GE-CZT	GE-CZT	Non CZT dual head camera (ADAC Labs)
Attenuation correction with CT	Both AC and non-AC	No	Both AC and non-AC	Yes	No
Dose SPECT tracer	185 MBq after stress 370 MBq after rest	3 MBq/kg for rest and 9 MBq/kg stress	316 ± 71 MBq at rest and then 1122 ± 170 MBq at stress	330 MBq at stress and 3 times rest dose	370 MBq at rest and 370 MBq at stress
Stressor Protocol	Regadenoson Stress first same day	Regadenoson Rest first same day	Dipyridamole Rest first same day	Adenosine Stress first same day	Adenosine Rest first 2 day protocol
Software	Corridor-4DM-Reserve (v2015; INVIA, Ann Arbor, MI, USA)	Corridor 4DM (v2015, INVIA, Ann Arbor, MI, USA)	FlowQuant	PMOD software package (version 3.1; PMOD Technologies Ltd.)	Not reported
<i>PET characteristics</i>					
Comparison PET tracer	¹³ N-NH ₃	¹⁵ O-H ₂ O	⁸² Rb or ¹³ N-NH ₃	¹³ N-NH ₃	¹⁵ O-H ₂ O
PET camera	GE discovery 690	GE discovery VCT/RX	GE discovery 690	GE discovery ST/RX and Discovery VCT	Siemens-ECAT EXACT HR+
Dose of PET tracer	Bolus 370 MBq at stress Rest not reported	1.5–3 MBq/kg at rest followed by same dose for stress	10 MBq/kg (⁸² Rb) or 5 MBq/kg (ammonia) both at stress and rest	1053 (+/–110) MBq at stress followed by 1203 (+/–MBq) at rest	1000 MBq at rest then 1000 MBq at stress (2 min infusion at 500 MBq/min)
Software	4-DM-Corridor software package	Carimas 2.4 software (Turku, Finland)	FlowQuant software	PMOD software package (version 3.1; PMOD Technologies Ltd.)	Not reported

Absolute myocardial blood flow comparisons SPECT vs PET

Table 1 continued

Study	Giubbini et al ¹³ (2019)	Waterday study ¹⁴ (2018)	Wells et al ⁷ (2017)	Nkoulou et al ¹⁴ (2016)	Ito et al ⁸ (2003)
Comparison to PET mean global resting MBF	Similar with AC-CZT and different with non-AC CZT	CZT higher	Good correlation of global MBF measurements.	CZT similar	-
Comparison to PET mean global stress MBF	AC CZT lower Non-AC CZT higher	CZT higher	-	CZT lower	-
Comparison to PET mean global MFR	Lower with both AC and non-AC CZT	Similar MFR	-	CZT lower MFR	SPECT lower

MBF, myocardial blood flow; MFR, Myocardial flow reserve; BMI, body mass index; CAD, Coronary artery disease; SPECT, Single positron emission tomography; PET, positron emission tomography; CZT, cadmium zinc telluride; GE, general electric; D, spectrum dynamics; AC, attenuation correction; MBq, mega becquerel

This study along with others paves the way for MBF quantification using SPECT with several caveats and questions, which require further exploration:

1. Standardization of protocols, radiotracers, acquisition, reconstruction, kinetic modeling, and post-processing tools to reduce variability of MBF measurements.
2. Demonstration of intra- and inter-observer variabilities of these measurements or lack thereof in multicenter studies.
3. Assessment of variability introduced by the spatial resolution of SPECT, partial volume averaging, spillover, attenuation, motion and other artifacts while making these measurements.
4. Demonstration of the incremental value of SPECT-derived MBF and possible ways to incorporate this information in making clinical decisions.

In conclusion, there is clearly a growing interest to evaluate the role of SPECT-derived absolute myocardial perfusion for diagnosis and prognosis. This study along with others will encourage further investigation towards standardization of MBF measurement by SPECT and understanding its clinical utility. Till that time caution should be exercised including SPECT MBF quantification in routine clinical practice.

Disclosure

Authors have no conflict of interest to declare.

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