FMTVDM-TFM©#: True quantification requires standardization of the tool being used to measure, with a known, unchanging standard to produce accurate, consistent and reproducible quantified measurements

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Journal of Nuclear Cardiology

ISSN 1071-3581

J. Nucl. Cardiol.
DOI 10.1007/s12350-018-1343-3


Volume 22 • Number 1
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Springer
12350 •22(1) 001-000 (2014)
ISSN 1071-3581

Official Publication of the American Society of Nuclear Cardiology

American Society of Nuclear Cardiology

Springer

LETTER TO THE EDITOR

FMTVDM-TFM©℗: True quantification requires standardization of the tool being used to measure, with a known, unchanging standard to produce accurate, consistent and reproducible quantified measurements

Everyone is beginning to understand the importance of quantification for use in Medicine, particularly Molecular Imaging. With the recent introduction of mandates by CMS, ASNC and the SNMMI for Quantification, it is not surprising that papers are being published on the topic. One recent publication by Zhao et al[1] demonstrates that there may be misunderstandings regarding modern molecular imaging.

THE MISUNDERSTANDING OF QUANTIFICATION

Quantification is not asking whether a tool can count, but rather whether the tool can count accurately. The Zhao paper presents several methods using phantoms and display "counts" of isotope scintillation activity, reporting on the ability of the cameras to count. Concluding that there is a camera calibration factor, which must be applied, there is an example regarding the counts obtained using a point source with a SPECT camera. When the SPECT camera was asked to count over time[2,3] using a 128×128 matrix setting, there was a 14.6% reduction in scintillation quantification over one hour, which, based upon the known standard of the decay of 99mTc, represented an error of 33.9%. Based upon the physical decay of 99mTc, the change in counts could only be 10.9%. So, the setting of 128×128 matrix did not count *accurately*.

When the same camera was set to a 64×64 matrix, the scintillation count difference over 1 hour showed the expected scintillation reduction of 10.9%, demonstrating that the scintillation tool for measuring/quantification was appropriately calibrated to a known standard. This difference between the 128×128 and the 64×64 matrix settings is caused by septal limitations, Fourier Transform, and modulation transfer function.

Qualitative imaging assumes a "*Yes/No*" phenomenon. *Yes*, the interpretation is that there is disease or *No*, the interpretation is that there isn't disease. The consequence of this approach yields sensitivity and specificity issues. *Quantitative* methods[3–10] for scintillation tools provide true *accuracy* with no need for mathematical models to manipulate the data.

THE MISUNDERSTANDING OF SESTAMIBI AND TETROFOSMIN REDISTRIBUTION

Since most of this has been discussed supra, we will turn our attention to the statement made under the "Delay Time for Imaging" statement[11] on page 19 of the new ASNC Guidelines.

> In contrast, the properties of 99mTc Sestamibi and 99mTc tetrofosmin, particularly the lack of clinically significant redistribution or washout, allow delayed imaging and, therefore, permit stress testing and tracer injection to take place at a location remote from the imaging laboratory. Image acquisition can simply be repeated when patient motion or extracardiac tracer uptake is considered responsible for the production of a perfusion defect. The standard delay between injection of 99mTc sestamibi or tetrofosmin and scan is 30 to 60 minutes for rest and 15 to 60 minutes for stress (the former for exercise stress).

While it is reassuring that the authors are no longer saying Sestamibi and Tetrofosmin do not redistribute (as the package Company inserts support), the language has softened over the last decade from there is "no redistribution" in humans to "definitive human studies to demonstrate possible redistribution have not been reported." Multiple studies[3–10,12–36] have however shown that these Tc99m Isotopes redistribute.

One of the very fundamental problems here is that the use of two injected doses of either Sestamibi or

J Nucl Cardiol
1071-3581/$34.00

Published online: 19 June 2018

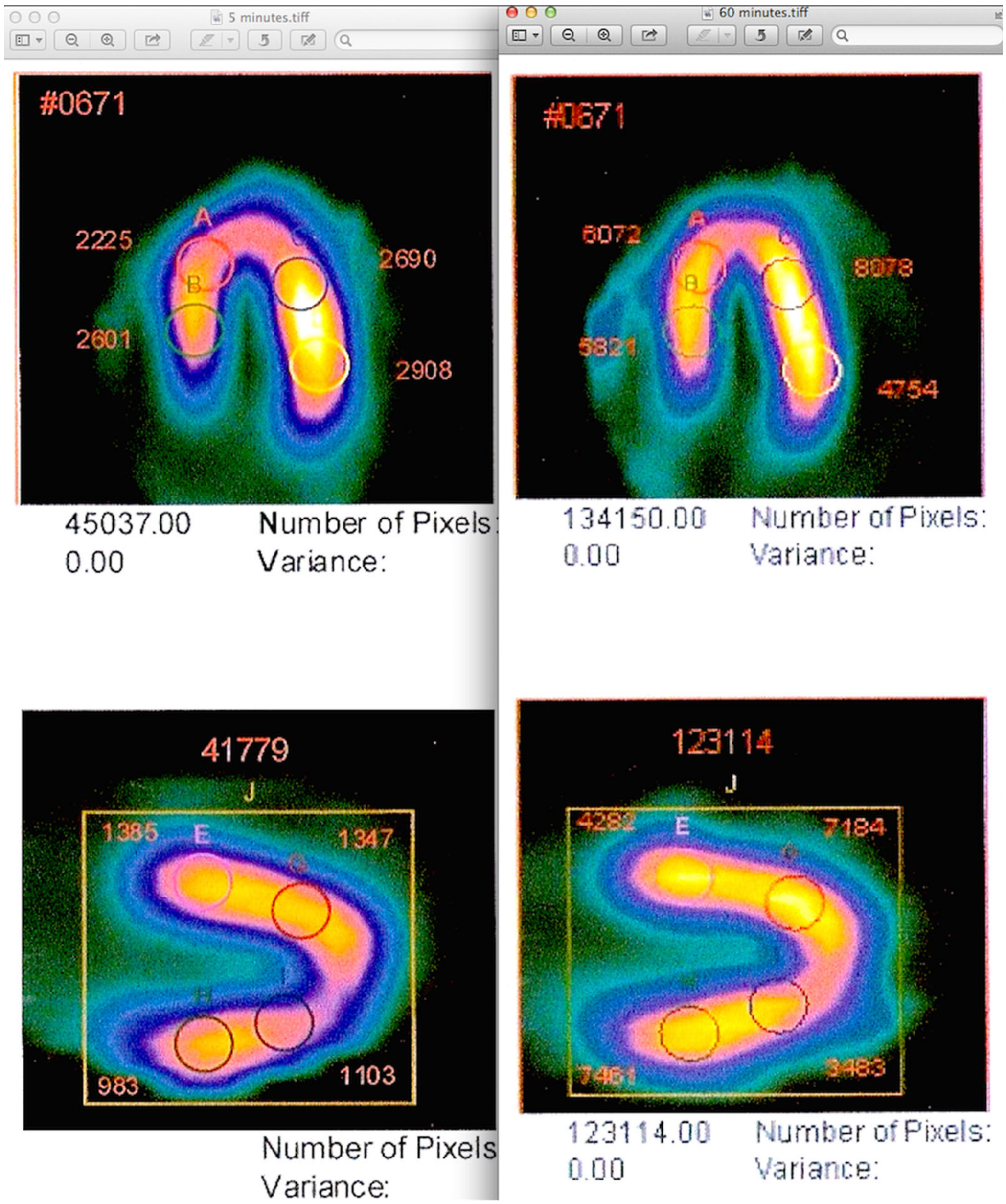

Figure 1. FMTVDM-FHRWW (Cardiac protocol)©®: Application of TRUE QUANTIFICATION following isotope redistribution. Legend: Image displays in horizontal (top) and vertical (bottom) long axis views show TRUE QUANTIFICATION using measurement of Sestamibi redistribution using FMTVDM©®. While each reconstructed image revealed "qualitatively" normal appearing MPI, the TRUE QUANTIFICATION measurement showed lower Sestamibi counts in each myocardial region at 5-minutes (left panels) compared with the 60-minute (right panels) acquisitions demonstrating "wash-in" seen with vulnerable inflammatory plaques and critically narrowed arteries. This TRUE (not virtual) QUANTIFICATION demonstrated triple vessel coronary artery disease in this individual requiring intervention.

Tetrofosmin cannot evaluate redistribution of either one of these injected doses. Current imaging protocols cannot differentiate the effect of one injected dose from the other. Redistribution is, by its very definition, the movement of a single injected dose of isotope over a period of time. Redistribution reveals differences in uptake, retention, and release of the isotope from the tissue being studied. Such redistribution reflects changes between normal tissue vascularity and viability to abnormal diseased tissue.

The flaw of using qualitative interpretation is demonstrated in Figure 1, where Sestamibi redistribution was quantitatively measured following nuclear camera calibration[4]. The visual images themselves in Figure 1 suggest that there is no redistribution, when in fact, the isotope redistributed.

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References

1. Zhao W, Esquinas PL, Hou X, et al. Determination of gamma camera calibration factors for quantification of therapeutic radioisotopes. EJNMMI Phys 2018;5:8.
2. Fleming RM, Fleming MR, McKusick A, Chaudhuri T, Dooley WC. The B.E.S.T. protocol for early breast cancer detection. In: 47th Annual Meeting Florida Nuclear Medicine Technologists (FNMT), Tampa, FL, USA, 6 May 2018.
3. Fleming RM, Fleming MR, Chaudhuri T, McKusick A, Dooley WC, Glover C. Both percent diameter stenosis (%DS) and coronary flow reserve can be derived directly from myocardial perfusion imaging using FMTVDM and measurement of isotope redistribution. J Nucl Med Radiat Ther 2018;9:1000353. https://doi.org/10.4172/2155-9619.1000353.
4. The Fleming method for tissue and vascular differentiation and metabolism (FMTVDM) using same state single or sequential quantification comparisons. Patent Number 9566037. Issued 02/14/2017.
5. Breast enhanced scintigraphy testing (BEST); BEST imaging. 1-655833872. Started 9-1-2011. Effective 9-16-2011, TX 7-451-243.
6. Fleming RM, Harrington GM, Baqir R, Jay S, Challapalli S, Avery K, Green J. The evolution of nuclear cardiology takes us back to the beginning to develop today's "new standard of care" for cardiac imaging: How quantifying regional radioactive counts at 5 and 60 minutes post-stress unmasks hidden ischemia. Methodist DeBakey Cardiovasc J 2009;5:42-8.
7. Fleming RM, Harrington GM, Baqir R, Jay S, Challapalli S, Avery K, Green J. Renewed application of an old method improves detection of coronary ischemia. A higher standard of care. Fed Pract 2010;27:22-31.
8. Fleming RM, Fleming MR, Chaudhuri T, McKusick A, Dooley WC, Glover C. Both percent diameter stenosis (%DS) and coronary flow reserve can be derived directly from myocardial perfusion imaging using FMTVDM and measurement of isotope redistribution. J Nucl Med Radiat Ther 2018;9:1000353. https://doi.org/10.4172/2155-9619.1000353.
9. Fleming RM, Harrington GM, Baqir R. Heart disease in men. Chapter 3. Using multiple images post-stress to enhance diagnostic accuracy of myocardial perfusion imaging: The clinical importance of determining washin and washout indicates a parabolic function between coronary perfusion (blood flow) and cellular ("uptake/release") function. Alice B. Todd and Margo H. Mosley editors, Nova Publishers 2009, pp. 75-100. (https://www.novapublishers.com/catalog/product_info.php?products_id=8409).
10. Fleming RM, Harrington GM. Chapter 13. Fleming Harrington redistribution wash-in washout (FHRWW): The platinum standard for nuclear cardiology. Establishing better standards of care in doppler echocardiography, computed tomography and nuclear cardiology. Richard M. Fleming editor, Intech Publishing 2011. ISBN: 978-953-307-366-8.
11. Dorbala S, Ananthasubramaniam K, Armstrong IS, et al. Single photon emission computed tomography (SPECT) myocardial perfusion imaging guidelines: Instrumentation, acquisition, processing, and interpretation. J Nucl Cardiol 2018. https://doi.org/10.1007/s12350-018-1283-y.
12. Franceschi M, Guimond J, Zimmerman RE, Picard MV, English RJ, et al. Myocardial clearance of Tc-99m hexakis-2-methoxy-2-methylpropyl isonitriles (MIBI) in patients with coronary artery disease. Clin Nucl Med 1990;15:307-12.
13. Dilsizian V, Arrighi JA, Diodati JG, Quyyumi AA, Alavi K, et al. Myocardial viability in patients with chronic coronary artery disease. Comparison of 99mTcsestamibi with thallium reinjection and [18F]fluorodeoxyglucose. Circulation 1994;89:578-87.
14. Sheikine Y, Berman DS, Di Carli ME. Technetium-99m-sestamibi redistribution after exercise stress test identified by a novel cardiac gamma camera: Two case reports. Clin Cardiol 2010;33:E39-45.
15. Li QS, Solot G, Frank TL, Wagner HN, Becker LC. Myocardial redistribution of Technetium-99m-Methoxyisobutyl Isonitrile (SESTAMIBI). J Nucl Med 1990;31:1069-76.
16. Sinusas AJ, Bergin JD, Edwards NC, et al. Redistribution of 99mTc-Sestamibi and 201Tl in the presence of a severe coronary artery stenosis. Circulation 1994;89:2332-41.
17. Richter WS, Cordes M, Calder D, Eichstaedt E, Felix R. Washout and redistribution between immediate and two-hour myocardial images using technetium-99m Sestamibi. EJNMMI 1995;22:49-55.
18. Fleming RM, Kirkeeide RL, Taegtmeyer H, Adyanthaya A, Cassidy DB, Goldstein RA. A comparison of Technetium 99-m teboroxime tomography to automated quantitative coronary arteriography and thallium-201 SPECT. J Am Coll Cardiol 1991;17:1297-302.
19. Fleming RM, Kirkeeide RL, Taegtmeyer H, Adyanthaya A, Cassidy DB, Goldstein RA. A comparison of Technetium 99-m teboroxime tomography to automated quantitative coronary arteriography and thallium-201 SPECT. J Am Coll Cardiol 1991;17:1297-302.
20. Fleming RM. Clinical presentation of 74 year old lady with significant LAD and RCA artery disease demonstrated with new dipyridamole teboroxime protocol and verified by quantitative coronary arteriography. (Atlas at Squibb pharmaceuticals).
21. Fleming RM. Chapter 31. Nuclear cardiology: Its role in the detection and management of coronary artery disease. In: Chang John C, editor. Textbook of angiology. New York: Springer; 1999. pp. 397-406.
22. Fleming RM, Harrington GM, Baqir R. Use of parabolic model in tomographic diagnosis of infarction and stenosis. In: The 1st Congress on Controvesies in Cardiovascular Diseases: Diagnosis, treatment and intervention (C-Care), Berlin, Germany, 4-5 July 2008.
23. Fleming RM, Harrington GM, Baqir R, Jay S, Avery K. Multiple post stress imaging more accurate than rest-stress imaging in detecting ischemia. In: 9th International Conference on Nuclear Cardiology. Barcelona, Spain. 10-13 May 2009.
24. Fleming RM, Harrington GM, Jay S, Challapalli S. Sestamibi redistrbution provides better detection of ischemia than rest-stress comparisons. In: BITs 1st International Congress of Cardiology: Combating heart disease, track 5: Diagnostics, therapeutics and clinical management. Shanghai, China. 5-7 Dec 2009.
25. Fleming RM, Harrington GM, Jay S. Quantitative measurement of sestamibi redistribution to detect hidden ischemia made possible by application of Blumgart's method. J Nucl Med 2011;52:1162.

26. Fleming RM, Harrington GM, Jay S. Reducing patient radiation exposure while improving diagnostic testing. In: Continuing Education Credits for the 58th SNM Annual Meeting, San Antonio, TX, USA. 8 June 2011.
27. Fleming RM, Harrington GM. TAM-A.7 Sestamibi redistribution measurement defines ischemic coronary artery lumen disease. In: 56th Annual Meeting of the Health Physics Society. (American Conference of Radiological Safety) West Palm Beach, FL, USA, 30 June 2011. http://hpschapters.org/2011AM/program/singlesession.php3?sessid=TAM-A.
28. Fleming RM, Harrington GM. FHRWW release of WiWo increases diagnostic detection of coronary artery disease and specifically the detection of vulnerable inflammatory plaques (cardiology's black holes). In: 1st Lombardy International Meeting of Cardiovascular Surgery. Milan Italy, 13-14 April 2012.
29. Fleming RM, Harrington GM, Kearney D, Tomsho M, Sheils J. Myoview and Sestamibi redistribution, stress once—image twice protocol improves detection of ischemia in addition to improving patient throughput and reducing patient radiation to 3.75 mSv. J Nucl Med 2012;53:1831.
30. Fleming RM. FHRWW: The end of the era of rest-stress nuclear cardiac imaging and why it misses critical heart disease. In: International Conference on Translational Medicine. San Antonio, TX, USA. 17-19 Sept 2012.
31. Fleming RM, Harrington GM, Kearney D, Tomsho M, Sheils J. Rapid image acquisition and assessment of coronary ischemia using FHRWW protocol. In: 4th Annual International Conference of Cardiology. Guangzhou, China, 2-4 Dec 2012.
32. Fleming RM. The redistribution properties of Tc-99m isotope agents, sestamibi and myoview. Invited Presentation. In: Toronto International Pharmacy Conference, Toronto, Canada. 27-29 Sept 2012.
33. Fleming RM, Harrington GM. RIA-FHRWW analysis of the redistribution properties of Tc-99m isotope agents, Sestamibi and Myoview, enhances the detection of ischemic heart disease. Invited presentation. In: 3rd International Conference on Clinical & Experimental Cardiology. Emerging interventions in clinical cardiology and cardiac surgery. Chicago, Ill. USA 15 April 2013. J Clin Exp Cardiol 2013;4:131.
34. Fleming RM, Fleming MR, McKusick A, Chaudhuri T, Dooley WC. The B.E.S.T. protocol for early breast cancer detection. In: 47th Annual Meeting Florida Nuclear Medicine Technologists (FNMT), Tampa, FL, USA 6 May 2018.
35. Won KS, SH Kim. Five-minutes post-stress gated myocardial perfusion SPECT using Tc-99m tetrofosmin. SNMMI 2012.
36. Medrano R, Lowry RW, Young JB, et al. Assessment of myocardial viability with 99mTc Sestamibi in patients undergoing cardiac transplantation. A scintigraphic/pathologic study. Circulation 1996;94:1010-7.

doi:10.1007/s12350-018-1343-3