

FMTVDM-TFM^{©P}: 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 al¹ 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 ^{99m}Tc , represented an error of 33.9%. Based upon the physical decay of ^{99m}Tc , 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” statement¹¹ on page 19 of the new ASNC Guidelines.

In contrast, the properties of ^{99m}Tc Sestamibi and ^{99m}Tc 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 ^{99m}Tc 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 Tc^{99m} Isotopes redistribute.

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

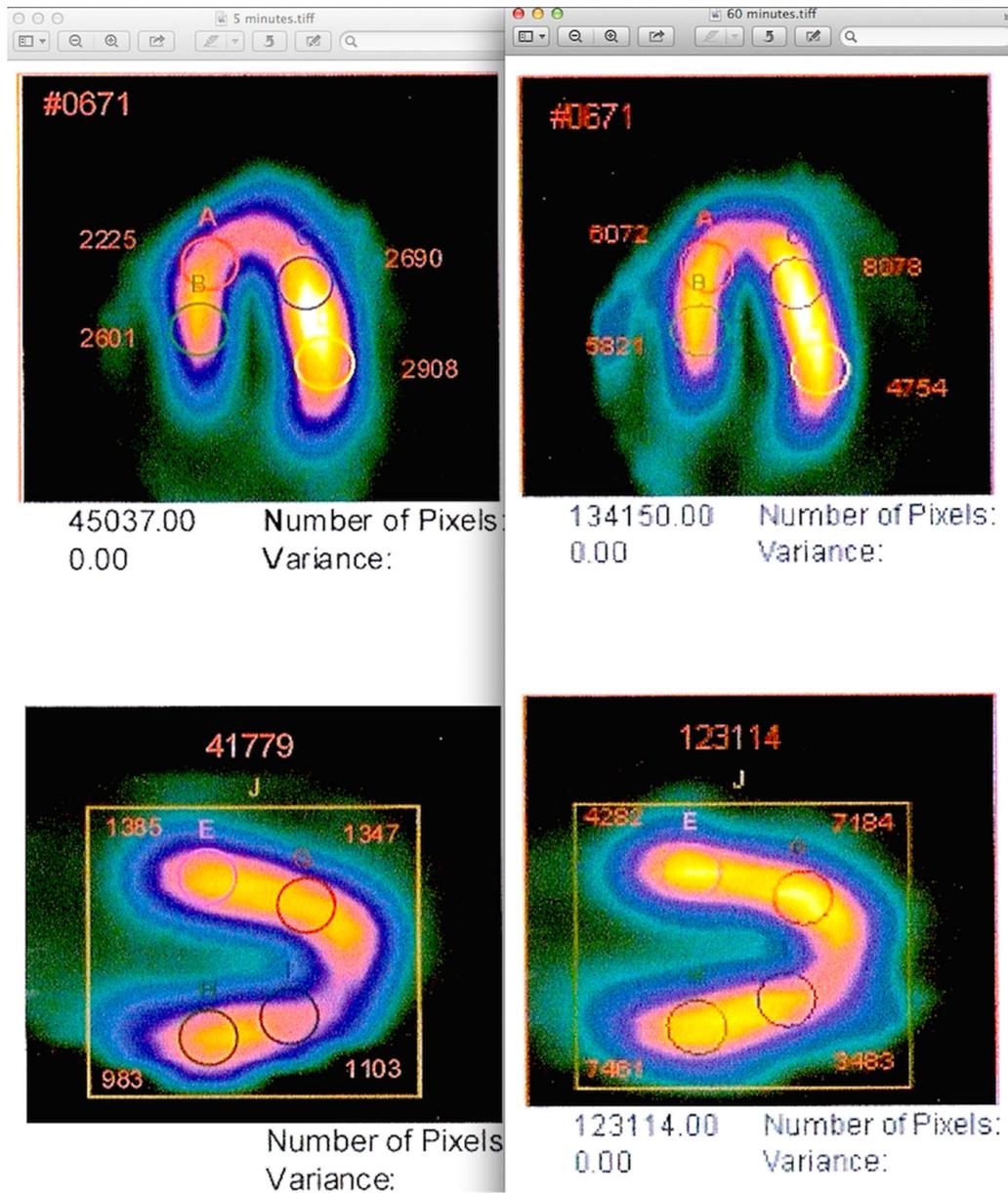


Figure 1. FMTVDM-FHRWW (Cardiac protocol)®: Application of TRUE QUANTIFICATION following isotope redistribution. Legend: Image displays in horizontal (top) and vertical (bottom) long axis views show TRUE QUANTIFICATION using measurement of Sestamibi redistribution using FMTVDM®. While each reconstructed 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 calibration⁴. The visual images themselves in Figure 1 suggest that there is no redistribution, when in fact, the isotope redistributed.

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