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Both Percent Diameter Stenosis (%DS) and Coronary Flow Reserve (CFR) can be Derived Directly from Myocardial Perfusion Imaging (MPI) using FMTVDM©℗ and Measurement of Isotope Redistribution

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Abstract

Background: Scientifically published studies have demonstrated that all isotopes, including Sestamibi redistribute. Measurement of this redistribution using FMTVDM©℗ provides an accurate method for determining wash-in and washout.

Methods: Using FMTVDM©℗ 1040 human coronary arteries were studied to determine their wash-in and washout redistribution measured on a pixel-by-pixel basis. From FMTVDM©℗ the percent diameter stenosis (%DS) for each artery was determined. This %DS was then used to calculate coronary flow reserve (Calculated SFR) using a proprietary quadratic equation (QCFR©, FCFR©) previously derived from quantitative coronary arteriography (QCA) measurements. These calculated CFR values were then compared with the actual measured CFR obtained directly from QCA.

Results: The results of the calculated CFR from FMTVDM©℗ with that obtained by direct QCA measurement showed a regression analysis of y= (0.8758•x)+0.4291, where y=the QCFR© and x=the QCA measured CFR. The R2 value (coefficient of determination) for this demonstrated a strong relationship at 0.87582.

Conclusions: The use of the FMTVDM©℗ for measurement of isotope redistribution, including Sestamibi, provides an accurate quantitative method for determining both redistribution wash-in and redistribution washout, from which %DS can be calculated on a pixel-by-pixel basis. This %DS can then be used with the proprietary equation (QCFR©, FCFR©) to calculate the CFR directly from the MPI result using FMTVDM©℗. The implementation of this power tool, will provide for additional determination of the physiological effect of CAD without requiring additional QCA equipment and expertise costs, making QCFR© possible in most if not all hospitals with nuclear medicine departments.

Keywords: Diameter stenosis; Coronary flow reserve; Myocardial perfusion imaging; Sestamibi Redistribution; FMTVDM©℗

Introduction

Despite popular misconception, scientific evidence has demonstrated that all isotopes, including Sestamibi redistribute [1-7]. This redistribution has been defined both as differences in isotope following a single injection of isotope or the comparison of more than one injection of isotope over time; as detailed in the Fleming Method for Tissue and Vascular Differentiation and Metabolism (FMTVDM©℗) [4-7] using same state single or sequential quantification comparisons. The measurement of this distribution must be carefully timed to the actual redistribution properties of the particular isotope. Specifically, the redistribution of Sestamibi is determined by comparing the 5-minute and 60-minute post injection images [3-7].

Measurement of coronary flow reserve from quantitative coronary arteriography (QCA) [8-14] has been used for decades to better understand the physiologic effect of coronary artery disease (CAD). Such measurements have required invasive techniques and are limited to coronary laboratories with the financial resources needed to support the additional equipment and clinician expertise. Prior publications have demonstrated that the relationship between QCA and percent diameter stenosis (%DS) in humans is a quadratic relationship [12,13] unlike the canine model [9]. The proprietary quadratic equation has intentionally been excluded from publication given its Intellectual Property. The specifics of the proprietary equation has been incorporated into FMTVDM©℗.

This study looks at the ability to utilize FMTVDM©℗ to determine %DS directly from MPI and the implementation of that %DS into the proprietary equation to non-invasively calculate the Quadratic Coronary Flow Reserve© (QCFR©, aka. FCFR©) from FMTVDM©℗ assessment of Sestamibi redistribution.

Materials and Methods

FMTVDM©℗: Following the protocol detailed in FMTVDM©℗ 1040 human coronary arteries were studied as shown in Figure 1. This protocol can be used either for redistribution measurement following

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rest-rest imaging to determine tissue viability or stress-stress imaging for determination of ischemia and subsequent calculation of %DS as was done in this study.

Calculation of %DS from Isotope Redistribution: The derived isotope redistribution was then calculated using pixel-by-pixel isotope measurement to determine redistribution wash-in (initial delay in isotope uptake) and redistribution washout (failure to retain isotope) as shown in Figure 2. The calculated redistribution produces a parabolic relationship (wash-in, normal, washout) between isotope redistribution and lumen %DS [4-8]. This parabolic relationship Figure 3 is described by Equation 1.

$$[\%DS = (0.011)\ (Redistribution2) \quad (1)$$

Calculation of Quadratic Coronary Flow Reserve (QCFR©, aka. FCFR©) from Isotope Redistribution determined %DS: The proprietary equation derived from actual QCA human coronary artery analysis

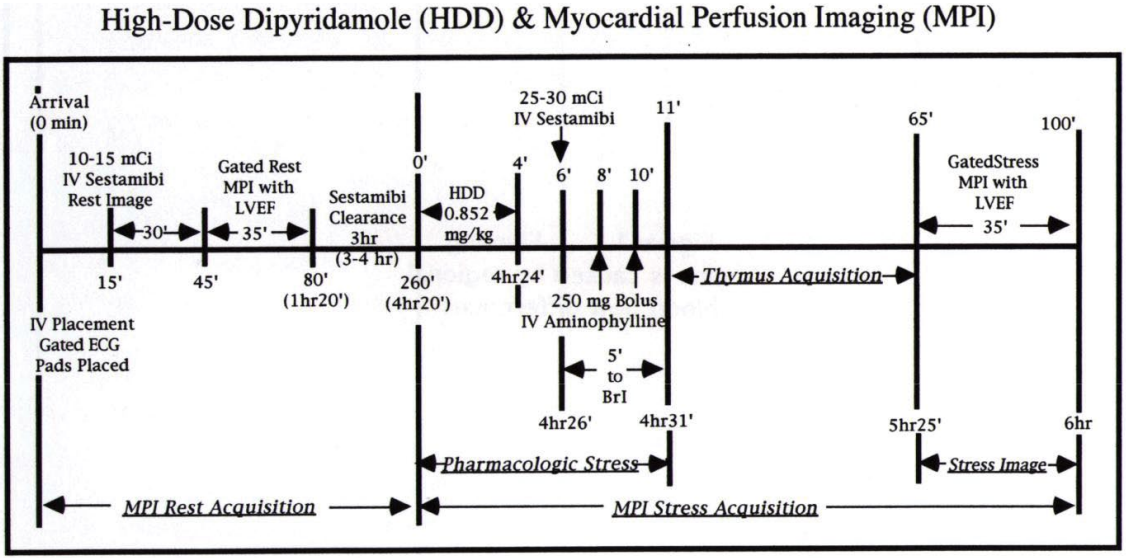
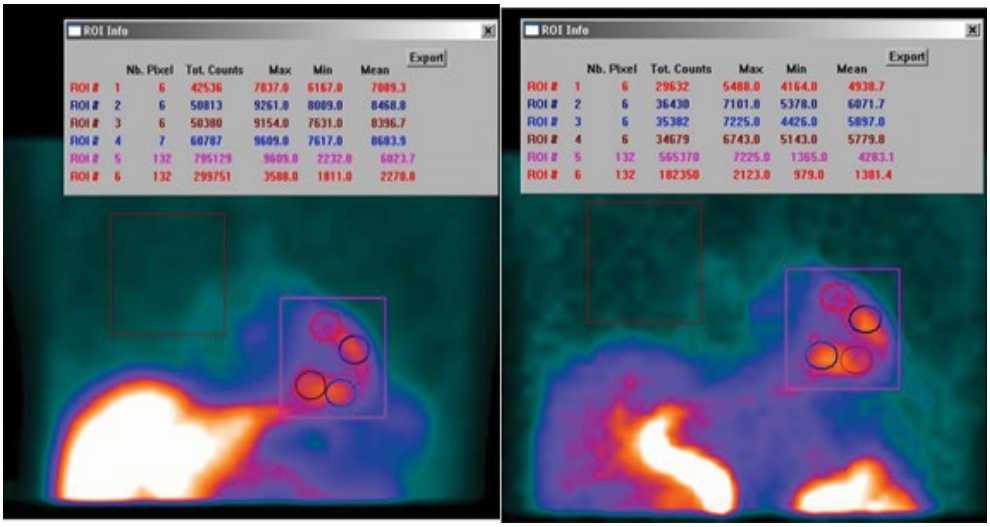


Figure 1: FMTVDM©℗ protocol for evaluation of Sestamibi Redistribution.
Determination of tissue viability is made from pixel-to-pixel redistribution measurements using 5-minute and 60-minute post isotope injection during MPI Rest Acquisition. Determination of ischemia and %DS calculation is made from pixel-to-pixel isotope measurement with calculation of redistribution wash-in and redistribution washout. Further markers of inflammatory processes associated with CAD can be determined using thymus acquisition as previously reported [15,16].



Example of Sestamibi Redistribution washout. The 5-minute image is the left image and the 60-minute image is the right image. E.g. the basal anterior wall of the myocardium shows a Sestamibi count of 7089.3 at 5-minutes, with only 4938.7 at 60-minutes. The expected isotope decay over 55-minutes would represent only a 10% reduction in Sestamibi activity. This additional loss in Sestamibi isotope count demonstrates Sestamibi washout.

Figure 2A: Pixel-by-pixel isotope measurement used to derive Redistribution wash-in and Redistribution washout.

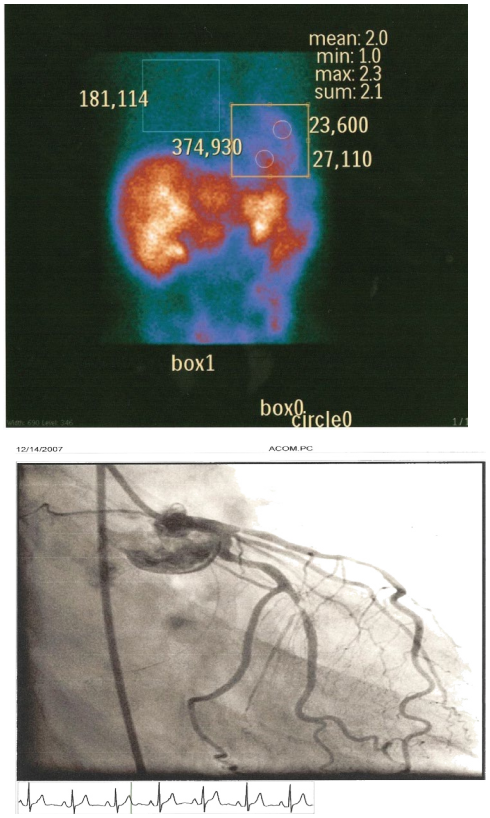


Figure 2B: Example of Sestamibi Redistribution wash-in with critically narrowed LAD, D1 and OM1 as seen on coronary angiography and QCA analysis. The 5-minute image is the upper left image; the 60-minute image is the upper right image followed by the patients coronary arteriogram in the bottom image. The 5-minute image shows anterior wall Sestamibi isotope count of 23,600. At 60-minutes, this has increased to 30,470, demonstrating Sestamibi redistribution wash-in. This Sestamibi redistribution wash-in matches the arterial disease seen on coronary arteriographic and QCA analysis.

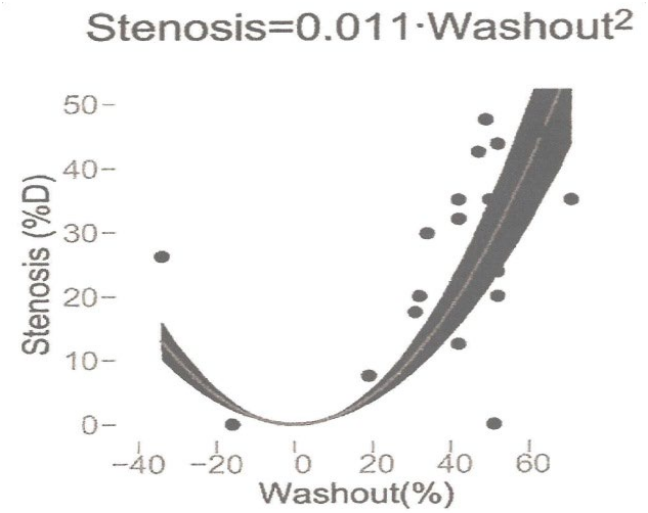


Figure 3: Parabolic relationship of pixel-by-pixel measurement of Sestamibi redistribution wash-in and redistribution washout as seen using the FMTVDM©℗

The negative washout (%) values represent "wash-in" and are associated with a delayed uptake of isotope 5-minutes post injection with a greater isotope uptake at 60-minutes. The positive washout (%) values represent isotope washout associated with initial uptake of isotope at 5-minutes followed by a failure to retain 90% of the isotope at 60-minutes.

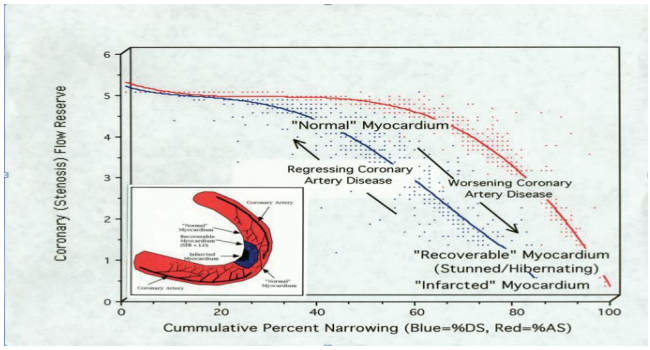


Figure 4: Regression analysis of %DS against CFR graphically displayed for human coronary arteries following QCA analysis.

takes into account multiple measurements including stenosis flow reserve (SFR, aka. CFR), percent diameter stenosis (%DS), percent area stenosis (%AS), the length of the lesions in millimeters (mm), the absolute diameter of the narrowed lumen in mm, the entry angle into the lesions in degrees, the exit angle from the lesion in degrees and the percent of maximum density measurement. The graphic representation of the results are shown in Figure 4 and demonstrate a quadratic function between CFR and %DS. Equation 2 shows the quadratic relationship between %DS and CFR, absent the specific values of the proprietary numbers.

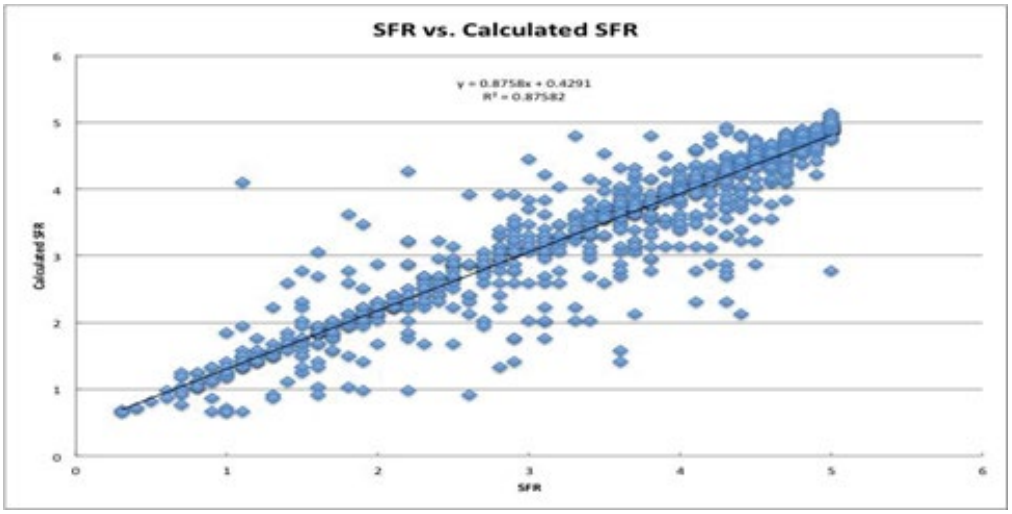


Figure 5: Regression analysis of FMTVDM©℗ derived Calculated SFR (QCFR©, FCFR©) against QCA determined CFR.

$$QCFR = (A)-(B \bullet \%DS)+(C \bullet \%DS2)-(D \bullet \%DS3)+(E \bullet \%DS4) \quad (2)$$

Comparison of FMTVDM©℗ determined isotope redistribution to determine %DS and the subsequent calculated Quadratic Coronary Flow Reserve (QCFR©, aka. FCFR©) with the measured QCA derived CFR: Using the FMTVDM©℗ and the proprietary equation (QCFR©, aka. FCFR©), 1040 human coronary arteries were studied and the results of the measured QCA CFR was compared with the FMTVDM©℗ proprietary equation derived QCFR© (aka. FCFR©). Residual plots were analyzed for data bias.

Analysis: The comparison of QCFR© (aka FCFR©) derived from the FMTVDM©℗ with QCA measured CFR was performed using regression analysis and best fit linear regression modeling.

Results

The results of the calculated quadratic CFR (QCFR©) derived from the proprietary equation used with the FMTVDM©℗ determination of Sestamibi redistribution wash-in and Sestamibi redistribution washout, compared with that obtained by direct QCA measurement showed a regression analysis of y=(0.8758•x)+0.4291, where y=the QCFR and x=the QCA measured CFR. The R2 value (coefficient of determination) for this relationship is 0.87582, indicating that QCFR© has a strong clinically relationship with that obtained by direct cardiac cath lab QCA measurement. Examination of the residual plots revealed no data bias.

Figure 5 shows the actual data values for the regression analysis of FMTVDM©℗ derived Calculated SFR (aka QCFR©) against QCA determined CFR.

Discussion

Sestamibi like all isotopes undergoes redistribution. This redistribution and its clinical implication can be better understood by looking at whether there is an initial delay in isotope uptake at 5-minutes post injection (wash-in), whether there is initial uptake of the isotope, which cannot later be retained as avidly (washout) or whether the blood flow and uptake/release of the isotope is normal, which is reflected by what "appears" to be a failure of the isotope to redistribute, but which is in fact, actually a demonstrated balance of isotope redistribution uptake and release in "normal" non-diseased tissue, minus isotope decay and elimination from the body through normal excretory processes.

To better understand the redistribution property of any isotope requires a thorough understanding of the unique uptake and release of the isotope in question. Sestamibi much like Teboroxime has been shown to have its initial uptake at 5-minutes[1-8] thus requiring much earlier imaging to detect redistribution wash-in [17]. Clearly, redistribution washout can be seen much later [1,2,4-7]. FMTVDM©℗ was initially developed following this discovery [4-7].

Following 5-minute and 60-minute acquisitions of Sestamibi isotope redistribution on a pixel-by-pixel basis allows for a determination of the individual pixel wash-in and washout followed by the calculation of %DS based upon the measured redistribution of Sestamibi using FMTVDM©℗. This %DS can then be used via the proprietary equation to calculate the expected QCFR©. This calculated QCFR© is strongly correlated with the results obtained by cardiac catheterization measured CFR. The greatest variability is seen with more moderate disease and the implementation of FMTV DM©℗ in more centers is expected to reduce this variance through the input of additional information and acquired experience. FMTVDM©℗ pursuant to the patent derives these results from any isotope using any camera system; inter alia planar, SPECT and PET.

Conclusions

The clinical implementation of FMTVDM©℗ and the incorporation of the proprietary equation through camera software provides a clinically important MPI tool for use throughout the world, increasing the accuracy and detection of CAD through both the detection and treatment of redistribution wash-in and redistribution washout of nuclear isotopes commonly used to non-invasively assess CAD. The implementation of this powerful tool, will provide for additional determination of the physiological effect of CAD without requiring additional QCA equipment and expertise costs, making QCFR© possible in most if not all hospitals with nuclear medicine departments.

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