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Research Article

From Coronary Arteriography to Stenosis Flow Reserve to FMTVDM. The Sequential Evolution of Artificial Intelligence in Cardiology and Oncology-Removing the Human Error Element

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Abstract

Background: Efforts to enhance results obtained from cardiology and oncology imaging has resulted in the development of true quantification of regional blood flow and metabolic differences. The purpose of this study was to enhance that quantification and remove the human error.

Methods: Proprietary quantitative equations provided the first machine-to-machine (M2M) exchange of data. Following first generational artificial intelligence from these proprietary equations, M2M exchange of data continued to provide machine learning (ML) and an artificial intelligence (AI) used to measure coronary artery disease (CAD) and cancer.

Results: M2M learning eliminated the erroneous human input, further modifying the proprietary equations, developing R^2 values of 1.0 for percent diameter stenosis (% DS) to stenosis flow reserve (SFR) and 0.99 for SFR to% DS.

Conclusion: M2M learning removed human introduced error to diagnosis and decision making for CAD and Cancer, evolving *FMTVDM AI.

Keywords: FMTVDM; Artificial Intelligence (AI); Machine Learning (ML); Machine-To-Machine (M2M); Cardiology; Oncology

Introduction

For decades coronary arteriography – cardiac catheterization – was considered the gold standard for determination of the presence or absence of coronary artery disease (CAD). Physicians, including radiologists and then cardiologists, learned to interpret the extent of coronary lumen narrowing – percent (%DS) diameter stenosis – from their teachers who provided their final subjective decision. Satisfactory completion of these training programs required agreement with the teacher and so teacher trained student.

This method of looking for CAD not only missed the true extent of CAD, which we now understand to be the buildup of inflammatory changes within the walls of the coronary arteries [1] and subsequent impairment of the ability of the coronary arteries to relax to increase the amount of blood they carried throughout the heart to meet increased cardiac demand [2], but the very process of training was flawed with human error [3]. While these reading errors proved to be – at least to some extent – correctable [4], they nonetheless missed the actual extent of disease and subsequently the ability to accurately determine the extent of true CAD [5-7].

It became apparent that a better method was seriously needed. The very act of human interpretive error results both in CAD being missed (sensitivity errors) when present and being interpreted as being present (specificity errors) when it isn't. In fact, these errors have resulted in treatment outcomes being significantly overestimated [3].

In spite of what retrospectively is an obvious flaw begging for an answer, most clinical medicine continued unabated and appeared to be unaware of the problem. Recognizing the importance of looking at the physiologic significance [2,3] of stenosis – or coronary - flow reserve (SFR or CFR), investigations into the various measureable components of CFR were interrogated and analyzed [8,9]. The results (Figure 1) were compared with work done by Wüsten who investigated changes in blood flow in mongrel dogs [10,11]. The notable problem - as already noted [8,9] by researchers in the mid-1930s to 1940s – being that the arterial flow characteristics of one species (e.g. canine) is not applicable to that found in another species (viz. homo sapiens); making the dog model completely useless for humans. Consequently, the work that proceeded from the dog model, which is currently being applied to the human model, has little if any value, introducing yet another source of error into the already confused literature.

Equipped with the first component for quantification of human coronary artery disease, a series of further investigations into simultaneous measurements of both anatomic and physiologic changes seen across the spectrum [12] of CAD began around the mid1990s, evolving over the next twenty-five plus years. The cul-

minating patent (*FMTVDM) [13] evolved through a series of validation phases beginning with correcting calibration errors which existed – and still exist - within the equipment being clinically used [14-19], to the initial development of proprietary equations translating the information from one machine measurement system to another [20-23], to the recognition of this machine learning (ML) utility patent by Sheikh in 2018 [24].

Misunderstanding the terms AI and ML

Current discussions in medicine – both in the medical literature and lay press – discuss algorithms focusing on trying to improve the sensitivity and specificity of the test results obtained by physicians. One key to understanding that what is being talked about is not TRUE AI, lies in recognizing the use of the terms sensitivity and specificity. The very use of these terms, demonstrate there is error being introduced. Thus it is not machine learning or artificial intelligence, but yet one more attempt by humans to couple yes-no test results with some quantification effort, together, with the hope that the outcome will improve.

One such classic example is the clustering of coronary artery calcium (CAC) scores, qualitative or at best semi-quantitative myocardial perfusion imaging (MPI), cholesterol levels, and the potential inclusion of multiple other tests, all lumped together in the hope that this will somehow lower the sensitivity and specificity error rate. Another example is the use of such algorithms developed for breast cancer [26]. As with the CAD algorithms, this is not AI or ML, but the continued accumulation of more and more tests to guesstimate the risk of breast cancer.

True artificial intelligence and machine learning does not require more and more tests with sensitivity and specificity errors introduced – rather it is the development of an accurate, consistent and reproducible measurement tool which defines where on a spectrum of health the patient exists [12]. We would in fact agree with Davenport and Glove, that "artificial intelligence (AI) systems that are capable of machine learning go beyond traditional medical transactions and record-keeping to analyze data, make decisions, and exercise judgment." [27].

The growth of AI – machine teaching machine (M2M)

One of the hallmarks of AI-ML is the increased accuracy, consistency and reproducibility of such a system, when activated. Recent investment and investigations have further integrated the FMTVDM system, allowing the exchange of data and information between the anatomic and physiologic measurements, and allowing the machines to improve the results, removing the original human error.

While the proprietary data and equations will not be shared – as they are intellectual patent property – the outcome data for Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET) and Quantitative Coronary Arteriography (QCA) graphed data comparisons between the anatomic (%DS) and physiologic (CFR) data are presented in the following graphics (Figures 1 and 2).

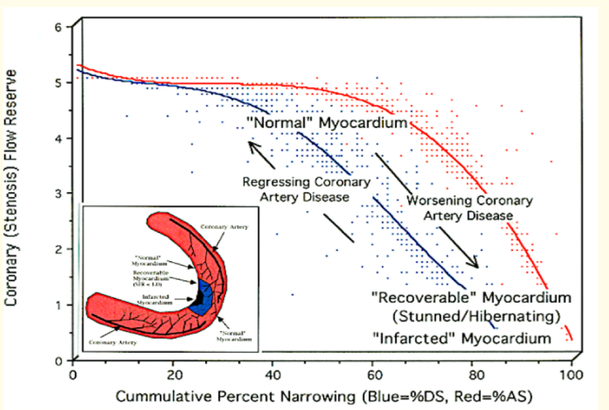

Figure 1: Quantification of changes in human coronary (stenosis) flow reserve and human coronary lumen narrowing defined as either percent diameter stenosis (%DS – blue data) or percent area stenosis (%AS – red data). The %AS bears a striking similarity with %DS results noted by Wüsten [10] in mongrel dogs.

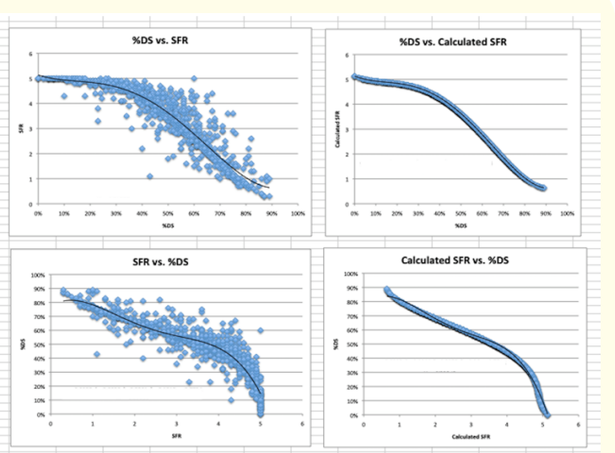

Figure 2: Information from the second generational exchange of information from SPECT and PET systems with QCA systems, provided the graphic comparisons seen in the left (top and bottom) graphs. With enhanced measurement information made possible from prior generations of proprietary equations, original errors incorporated into the equations by human intervention, were removed by exchange of %DS and SFR/CFR, resulting in today's AI-ML proprietary equations graphically depicted in the right (top and bottom) graphs.

Figure 1 shows some of the original data comparisons including information about both% DS and% AS in humans – versus mongrel dogs used elsewhere – and the CFR/SFR measurements. This first generation data was semi-quantified including operator dependent errors. Table 1 shows examples of some of the second generational measurements using quantification from both QCA and PET systems.

Proprietary equations from the first and second generation were further modified, following machine made measurements via M2M learning. Both SPECT and PET CFR data were supplied to the QCA system and the QCA system % DS data was supplied to the SPECT and PET systems – machine to machine (M2M) learning transpired – and the resulting measured outcomes ceased to show the human introduced error/variability as shown in figure 2.

This M2M learning eliminated the erroneous human input, further modifying the proprietary equations, developing R^2 values of 1.0 for percent diameter stenosis (% DS) to stenosis flow reserve (SFR) and 0.99 for SFR to % DS.

Frame #	System	artery	Region	study	Intervention %	Diameters %	Area stem	Density	SFR
210	1	LAD	1	PET	NONE	37%	0.55		4.7
63	1	LAD	1	PET	NONE	31%	0.55		4.7
3627	1	LAD	1	PET/PTCA	PTCA	29%	0.4		4.9
3791	1	LAD	1	PET/PTCA	PTCA	15%	0.4		4.9
	1	DIAG-1	1	PET/PTCA	PTCA	46%	0.71		4.1
	1	DIAG-1	1	PET/PTCA	PTCA	58%	0.82		2.5
63	1	LCX	2	PET	NONE	48%	0.7		4.3

Table 1: Second generation FMTVDM.

*FMTVDM = The Fleming Method for Tissue and Vascular Differentiation and Metabolism.

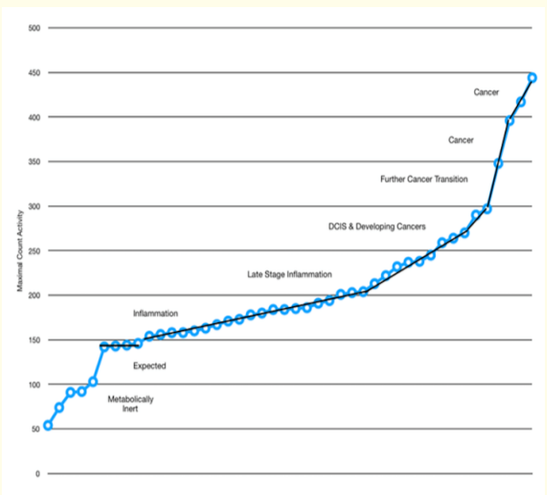

Figure 3: Changes in growth rates in various tissue types, quantifying regional blood flow (RBF) and metabolic differences using FMTVDM.

The changed proprietary equations resulting from M2M learning and the sharing of information – demonstrated data and decisions making by the machines by use of the equations to address human errors, producing a diagnostic result – judgment.

The same diagnostic quantified decision-making has been applied to tissue differentiation for breast cancer [12] as shown in figure 3. By quantitatively measuring [13] regional blood flow (RBF) and metabolic differences, following corrective calibration of machines using FMTVDM, FMTVDM has provided the AI-ML capabilities to address diagnostic errors, provide diagnostic result and decision making on where the patient is positioned on the health-spectrum [12].

Both the diagnostic measurement of CAD and Breast Health (e.g. breast cancer) is quantitatively made possible by removing the human error from the equation and providing machine derived measurements, thereby providing the location of the patient's health status on a measured continuum, against which it can be compared at another time to determine if treatment is working [28,29]. Diagnostic decision-making is no longer left up to the human element of error and images provided for CAD no longer provide two sets of images for the clinician to compare – rather a single image is provided for human benefit. Likewise, images of breast health are provided for the human element, while the actual determination is

Limitations

The currently developed M2M learning and sequential development of proprietary equations are the result of slightly more than 2000 exchanges. As the M2M exchange and learning progresses, we would expect further refinement of the AI and faster exchange of M2M.

Conclusion

M2M learning created changes in the proprietary equations used to quantify RBF and metabolic differences in tissue, used to define CAD and Cancer. The consequential AI eliminated the human error, providing enhanced diagnosis and treatment monitoring of CAD and Cancer – free of human error.

Disclosures

FMTVDM is a utility patent issued to first author. Authors MR Fleming, TK Chaudhuri and WC Dooley have no disclosures.

Acknowledgments

FMTVDM is a utility patent issued to first author. All figures reproduced with expressed consent of first author. MR Fleming, WC Dooley and TK Chaudhuri have no COIs.

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