FAST CT-BASED QUANTITATION OF MYOCARDIAL PERFUSION AND INTRA-VASCULAR BLOOD VOLUME - EVALUATION WITH A RADIOLOGIC FLOW PHANTOM

Erik L. Ritman

Department of Physiology and Medicine
Mayo Clinic, Rochester, Minnesota 55905, U.S.A.

This report is based on the ability to measure the characteristic curvilinear relationship between myocardial perfusion and the intramyocardial vascular blood volume. The fast Computed Tomography (CT) imaging method is based on the analysis of indicator dilution curves that result from the local change in gray scale of the CT images during the passage of x-ray contrast material through the coronary arteries and veins

INTRODUCTION

Blood flow through the heart's muscle wall (myocardium) is tightly coupled to the mechanical work performed by the heart. Under resting conditions the flow to the myocardium is of the order of 1 $mLg^{-1}min^{-1}$, but when the heart pumps at maximum capacity this can increase more than fivefold – its so-called reserve. The spatial location within the heart wall and the degree of reduced resting perfusion magnitude and/or of perfusion reserve is valuable clinical information for evaluating the impact of a partially blocked epicardial coronary artery (distributes blood flow to the myocardium) or due to impaired function of the small intramyocardial arteries. Although these manifestations of diseases, such as atherosclerosis, on the conduit function of the epicardial arteries is clinically routinely evaluated using selective coronary angiographic methods, the evaluation of the microvascular role in impaired myocardial perfusion is not readily accessible in a minimally invasive manner.

Fast, high repetition rate, CT imaging (despite it not resolving individual microvessels) can provide minimally invasive quantitation of myocardial microvascular function. The principle underlying this approach is based on the ability to measure the characteristic curvilinear relationship between myocardial perfusion (F) and intramyocardial vascular blood volume (Bv). The shape of this relationship is well represented by $Bv=AF + BF^{0.5}$, where A and B are coefficients which changes characteristically for various pathological changes in the myocardial microcirculation in that their values can discriminate a number of important disease states that affect coronary arterial wall structure and function[1,2]. The fast CT imaging method is based on analysis of the indicator dilution curves that result from the local change in gray scale of the CT images during the passage of x-ray contrast material through the coronary arteries and veins within the myocardium. This analysis involves use of the area under the indicator dilution curve and the timing characteristics of that curve. Although several approaches to analysis of these CT-based dilution curve characteristics have been developed[3-10], no wholly satisfactory conceptual model linking the indicator dilution curve characteristics and perfusion has been rigorously developed for the myocardium.

The myocardial blood supply geometry is such that the microvascular arteries and veins lie essentially parallel so that the entering arterial dilution curve and the delayed, returning, venous curves are superimposed. Consequently, the myocardial microvascular indicator dilution curve relationship to perfusion would be different from the commonly assumed model of flow entering at one end of a tissue

volume and leaving at the other end, with no superposition of the entry and departing blood flow. In addition, the entire issue of the cyclic on-off nature of coronary arterial flow is ignored, with the dilution curve samples being measured at the peak of the diastolic "on" phase of the cardiac cycle. Nonetheless, several practical analysis approaches have been shown, by comparison to generally accepted invasive methodologies (such as radio-labeled microspheres or flow meters), to be reasonably accurate for the purposes of many medical and clinical studies.

METHODS

We used a radiological test phantom to evaluate several mathematical models of the indicator dilution process. The phantom consists of a 16 cm long, 2.8 cm diameter cylindrical lumen inside a 7 cm x 7 cm plexiglass "brick". This lumen was tightly packed with small plexiglas spheres. Fluid enters the lumen at one end and exits at the other end. The entire phantom was placed inside a 20 cm diameter water-filled, thin walled, plexiglass cylinder. This phantom was scanned sequentially at 8 parallel transaxial slices at 58 ms intervals in a fast CT scanner. The first slice always passed through the inlet (i.e., no plexiglas spheres in the lumen) and the remaining seven passed through progressively downstream cross sections of the bead-packed lumen. This scan was repeated twenty times at 1 to 2 second intervals – the actual interval-duration being varied to ensure completion of the last scan only after the injected bolus of dye had completely passed through the lumen. Water flowed through the test phantom at a rate of 4, 6 or 8 mL/second. During the initial time of the scan, a bolus of an iodine solution of selected concentration, was injected into the inlet at a selected duration and volume of solution injected. The subsequent temporal sequence of gray-scale increase in each of the CT images provided the indicator dilution curves (i.e., C(t)) used for the analysis. In a separate experiment we scanned a balloon filled with different concentration iodine solution. The CT image gray-scale was measured for each concentration of iodine.

The variables computed from the dilution curves were Area under the curve (Area = $\int C(t)dt$), the first moment of the curve (MTT=$\int C(t)\cdot t\cdot dt/\int C(t)dt$) and the fluid fraction in the bead-packed test phantom lumen (Bv = Area under curve/Area under "inlet" curve).

RESULTS

The results of our analysis are summarized as follows:

1 CT image gray scale is proportional to iodine concentration
2) At any one CT slice the MTT is directly proportional to the duration of the iodine solution injection, but not to rate of injection. The MTT increased linearly with increasing distance of increasingly downstream cross sections.
3) The inverse of MTT is directly proportional to the flow through the test phantom.
4) The reciprocal of area under the dilution curve is proportional to flow through the test phantom lumen, other variables being constant.
5) The ratio Bv/ΔT (where ΔT is the difference between the MTT of the contiguous downstream and upstream CT images dilution curves) is linearly proportional to flow. This relationship is largely independent of variables such as amount and rate of indicator injection.

DISCUSSION & CONCLUSIONS

Despite these encouraging 'linear' relationships between the indicator dilution curve properties and flow, most would agree that there are several difficulties with CT-based indicator dilution curves. This phantom experiment was designed to address these difficulties in terms of evaluating the quantitative impact on our analysis of the curves. One difficulty is that very brief (ideally delta function) dilution curves at the inlet to a tissue sample is not practically achievable in vivo. Moreover, it is almost always true that the indicator is leaving a region of interest within the CT image before all of the bolus has entered that region. Consequently it is not possible to directly measure the total amount of contrast medium that passed through the region of interest. Another is the problem that the arterial input and venous return curves are superimposed in the myocardium.

Our evaluation of these issues, using the radiological test phantom, suggests that these theoretical concerns do not seriously affect practical analysis of in vivo CT-based indicator dilution curves.

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