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Simulation Evaluation of Quantitative Myocardial Perfusion Assessment from Cardiac CT

Michael Bindschadler^a, Dimple Modgil^b, Kelley R Branch^a, Patrick J La Riviere^b, and Adam M Alessio^a

Michael Bindschadler: mikebind@u.washington.edu

^aUniversity of Washington, Seattle, WA

^bUniversity of Chicago, Chicago, IL

Abstract

Contrast enhancement on cardiac CT provides valuable information about myocardial perfusion and methods have been proposed to assess perfusion with static and dynamic acquisitions. There is a lack of knowledge and consensus on the appropriate approach to ensure 1) sufficient diagnostic accuracy for clinical decisions and 2) low radiation doses for patient safety. This work developed a thorough dynamic CT simulation and several accepted blood flow estimation techniques to evaluate the performance of perfusion assessment across a range of acquisition and estimation scenarios. Cardiac CT acquisitions were simulated for a range of flow states (Flow = 0.5, 1, 2, 3 ml/g/min, cardiac output = 3,5,8 L/min). CT acquisitions were simulated with a validated CT simulator incorporating polyenergetic data acquisition and realistic x-ray flux levels for dynamic acquisitions with a range of scenarios including 1, 2, 3 sec sampling for 30 sec with 25, 70, 140 mAs. Images were generated using conventional image reconstruction with additional image-based beam hardening correction to account for iodine content. Time attenuation curves were extracted for multiple regions around the myocardium and used to estimate flow. In total, 2,700 independent realizations of dynamic sequences were generated and multiple MBF estimation methods were applied to each of these. Evaluation of quantitative kinetic modeling yielded blood flow estimates with an root mean square error (RMSE) of ~ 0.6 ml/g/min averaged across multiple scenarios. Semi-quantitative modeling and qualitative static imaging resulted in significantly more error (RMSE = ~ 1.2 and ~ 1.2 ml/min/g respectively). For quantitative methods, dose reduction through reduced temporal sampling or reduced tube current had comparable impact on the MBF estimate fidelity. On average, half dose acquisitions increased the RMSE of estimates by only 18% suggesting that substantial dose reductions can be employed in the context of quantitative myocardial blood flow estimation. In conclusion, quantitative model-based dynamic cardiac CT perfusion assessment is capable of accurately estimating MBF across a range of cardiac outputs and tissue perfusion states, outperforms comparable static perfusion estimates, and is relatively robust to noise and temporal subsampling.

Keywords

Cardiac CT; CT Perfusion; Kinetic Modeling; Dynamic CT; Myocardial Blood Flow

1. Introduction

Myocardial perfusion is commonly assessed with cardiac SPECT imaging. These studies provide qualitative measures of flow requiring normal regions to serve as a reference and suffer from poor spatial resolution. Contrast enhanced CT has been proposed and used in a few clinical trials to assess perfusion. Most applications use static imaging based on the assumption that reduced contrast enhancement is associated, although not proportional, with reduced flow^{1,2}. Quantitative assessment can be performed with dynamic imaging, in which kinetic models are fit to the curves associated with contrast enhancement over time³. There is no consensus on the optimal approach for perfusion assessment with CT both in terms of flow estimation technique⁴ and acquisition technique. It is widely appreciated that dynamic CT acquisitions can impart a prohibitively large radiation dose due the need for multiple CT acquisitions. This current work seeks to provide guidance on appropriate dynamic or static acquisitions that will allow for high fidelity myocardial blood flow estimates.

In this work, we perform a simulation study of numerous different dynamic cardiac CT acquisitions in order to assess myocardial blood flow (MBF) estimation performance across a range of patient and acquisition scenarios. Prior work by our group evaluated different MBF models applied to simple time-attenuation-curves, without the inclusion of the confounding effects in realistic CT data including beam-hardening errors and realistic quantum noise⁵. Recently, we presented preliminary results for MBF estimation with realistic CT simulation⁶. In this study, we extend former studies by evaluating a range of realistic CT data acquisitions and add to the quantitative methods additional evaluation of qualitative static perfusion performance as well as comparisons based on grading disease severity.

2. Methods

Ground truth iodine kinetic curves were generated with a realistic iodine delivery and exchange model, described in⁷. In brief, this model supported iodine exchange between the capillary and extravascular space. Myocardial blood flow is significantly heterogeneous within a capillary bed, and this is represented in the model by considering 20 different flow levels (F_1 - F_{20} , where the flow levels are spaced to cover the range of relative flows). The model also allowed for axial dispersion of iodine concentration along the capillary length. Using this model, curves were generated for a range of flow states (MBF = 0.5, 1, 2, 3 ml/g/min) and cardiac outputs (3, 5, 8 L/min).

These ground truth curves drove changes in the right ventricle, left ventricle, aorta, and myocardium in a custom version of a cardiac digital phantom⁸. CT acquisitions were simulated with our validated CT simulator incorporating beam hardening and realistic x-ray flux levels. CT acquisitions that reduce radiation exposure were varied with 1, 2, and 3 sec sampling as well as tube current reductions with 140, 70, and 25 mAs. For each flow and acquisition technique, 5 different phase shifts with 5 independent noise realizations each were generated leading to a total of 2,700 dynamic data sets. CT images were generated with conventional processing plus an additional beam-hardening correction method to account for iodine content⁹. Time attenuation curves were extracted for multiple regions around the

myocardium to estimate regional MBF. We compared A) three quantitative MBF estimation methods for all acquisitions (a two-compartment model, an axially-distributed capillary model, and the adiabatic approximation to the tissue homogeneous model ¹⁰); B) one semi-quantitative method (peak/slope ¹¹), and C) one qualitative method (static perfusion at three times post-injection).

To compare performance of static and dynamic assessments in a different way, we examined their classification accuracy in a task grading MBF reduction severity in 4 levels: none, mild, moderate, or severe. Classification thresholds were chosen near histogram intersections, and an overall accuracy was calculated as the mean of the accuracy in distinguishing severe from moderate, moderate from mild, and mild from no flow reduction. Accuracy on each binary distinction was calculated as the number correctly classified divided by the number classified.

3. Results

Results are presented in the following figures with descriptive captions. In brief, we present representative simulated time attenuation curves (figure 2). The myocardial blood flow (MBF) estimation performance is shown in figure 3. In this figure, estimates are combined across cardiac outputs, phases, time sampling schemes, noise realizations, and regions of interest. For the noise-free cases, each datum represents 180 estimates; for the others, 900 estimates contributed to the mean performance (because there were 5 noise realizations for each noisy scenario). In figure 4, the MBF estimation error is plotted versus temporal subsampling and tube current reductions. Data are combined across cardiac outputs, true MBF levels, phases, noise realizations, and regions of interest. Each noise-free data point is therefore the RMSE of 240 MBF estimates and each noisy data point is the RMSE of 1200 MBF estimates. This demonstrates that quantitative modeling methods (2-compartment, Distributed, and Adiabatic Approximation) all perform equally well, while the Slope method is sub-optimal with high residual error.

The comparison of quantitative to semi-quantitative to qualitative methods is shown in figure 5. Static perfusion CT is interpreted by evaluating the relative reduction in iodine enhancement around the myocardium to identify whether regional flow is impaired compared to “normal” regions. To compare model performance, we calculated the ratio of estimated MBF at a particular true flow to estimated MBF for the same conditions at a normal stress-state flow (true MBF=3 ml/min/g). This mimics comparing ischemic myocardium to healthy myocardium. A model could perform well on this measure if the estimated MBF was proportional to flow, even if quantitatively incorrect. Optimal performance for this measure is marked with the black dashed line; For example, if the flow to a region was 0.5 ml/g/min, this should present as an apparent value 17% of the value at 3 ml/g/min.

Finally, we evaluated the ability to distinguish different flow states with different acquisition techniques. This attempts to measure the performance of a classification task (detection of flow state), while the prior results show performance for an estimation task (measurement of

blood flow). Figure 6 presents representative histograms of the CT numbers for static acquisitions.

4. Discussion

Results demonstrate the selection of applied quantitative blood flow estimation methods (2-compartment, Distributed, and Adiabatic Approximation) is not as critical as the selection of appropriate acquisition techniques. For the simulated scenarios, we demonstrate that one-half dose reductions through reduced photon flux (reduced tube current) result in comparable estimates to reducing temporal sampling from a sample per second to a sample every other second. The Slope method has been frequently used because it is extremely straightforward to apply. However, this work shows that, while flow estimates from the Slope method are correlated with true flow, it should not be considered a quantitatively accurate methodology, since it consistently and significantly underestimates true flow, with an average error of 1.2 ml/min/g. Unlike the Slope method, the quantitative blood flow estimation methods have very little bias, and the increases in error at lower tube current or temporal subsampling are due to increases in variability rather than bias.

Static perfusion assessment is becoming more common as a simple additional read of current CT angiography (CTA) study or as a fairly easy additional acquisition to CTA. This work confirms that the timing of the static acquisition post-injection is critical and that relative enhancement information (comparing hypo-enhanced to “normal” reference regions) should be used with caution, especially if information about severity of ischemia is needed.

Our preliminary work examining the ability of static and dynamic perfusion assessment methods to distinguish flow reductions of different grades (no reduction and mild, moderate, or severe ischemia) suggests that both methods are very proficient at this task for ~ 1 cc myocardial ROIs, with dynamic perfusion assessment outperforming static (96.9% vs 94% overall classification accuracy). For static assessment, the HU thresholds for grading perfusion deficit severity will vary with the volume of contrast injected, and to a lesser extent, with the bolus shape. In contrast, the dynamic method allows thresholds to be set in meaningful units (ml/min/g) and is effective regardless of bolus size or shape (Fig 6B combines data from a 50cc contrast injection with data from a 100cc contrast injection, and still outperforms the static method at a single contrast volume).

Our future work will seek to provide guidance on appropriate static perfusion acquisition techniques and timing as well as continue to compare classification and estimation performance against dynamic CT perfusion assessments.

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Figure 1.

Schematic of major components of two region models for estimation of myocardial blood flow. Iodine concentration is a function of time and distance along capillary. Dispersion of iodine contrast can occur along the capillary length via diffusion, with coefficient in each region D_{tissue} & D_p . For an axially distributed two region model (denoted Distr), $D_{\text{tissue}} = D_p = 10^{-6} \text{ cm}^2/\text{s}$. For the adiabatic approximation to the tissue homogenous model (denoted Adia), $D_{\text{tissue}} = \infty$ (perfect mix/homogenous in tissue). For the 2-compartment model (denoted 2Comp), $D_{\text{tissue}} = D_p = \infty$ (perfect mixing in both compartments).

Figure 2.

Representative time attenuation curves (TAC). (A) Ground truth noise free curves for MBF=[0.5, 1, 2, 3] ml/g/min. Panels (B) and (C) show TAC's for four 0.06 cc regions around myocardium for MBF= 1 mg/g/min. (B) plots CT acquisition at 140 mAs with scans every 1 second, representing highest radiation dose acquisition in this study. (C) plots TAC for CT acquisition at 25 mAs with scan every 3 seconds, representing the lowest radiation dose acquisition in this study.

Figure 3.

MBF estimation performance showing the MBF estimate from each model's fit to the processed TAC. Data are presented subdivided by tube current and by true MBF.

“Noisefree” indicates TACs where the simulated CT acquisition does not have quantum noise (but still shows beam hardening effects). Error bars are standard deviations of all estimates for that particular combination of true MBF and tube current. Dashed lines are placed at each of the true MBF values for reference; a perfectly predictive model would have one point on each dashed line and no error bars.

Figure 4.

Effect of Temporal Subsampling and Tube Current Reductions on MBF Estimation Error.

The root mean square error (RMSE) of the estimates compared to the true MBF, subdivided by tube current and temporal sampling rate.

Figure 5.

Apparent Reductions in Flow Estimates. Static perfusion CT is interpreted by evaluating the relative reduction in iodine enhancement around the myocardium to identify whether regional flow is impaired compared to “normal” regions. Model flow estimates are plotted for the compartmental-based models (panel A) and the slope model (panel B). For comparison to a static perfusion style estimate (panel C), iodine enhancement is assumed proportional to MBF. (C) The ratio of iodine enhancement at one MBF to MBF=3 ml/min/g varies considerably with time; results are shown for 10, 15 and 20 seconds after the right ventricular cavity iodine peak. Data is presented subdivided divided by true MBF and tube current, and combines estimates across cardiac outputs, phases, noise realizations, regions, and, for the non-static data, time sampling schemes.

Figure 6.

Distinguishing flow states. One of the essential tasks of perfusion assessment is to successfully distinguish between grades of ischemia. Here we examine example representative distributions of attenuation values (for static perfusion assessment) or estimated MBF values (for dynamic perfusion assessment) for known true flow states representing (from right to left) normal stress MBF (3 ml/min/g), mildly reduced (2 ml/min/g), moderately reduced (1 ml/min/g) or severely reduced (0.5 ml/min/g) perfusion, in order to evaluate whether these states can be distinguished. A) Via static perfusion assessment. Plots of frequency of observation of mean attenuation for each myocardial ROI for true MBF of 0.5 (blue), 1 (green), 2 (red), or 3 (cyan) ml/min/g. Data is combined across 2 tube currents, 5 noise realizations, 4 time samples, and 10 ROIs, yielding 400 mean attenuation values contributing to each curve. In general, separation is quite good. Overall mean classification accuracy based on three simple HU thresholds is 94.0%. B) Via dynamic perfusion assessment. Plots of frequency of observation of MBF estimate for each myocardial ROI for true MBF of 0.5 (blue), 1 (red), 2 (green), or 3 (magenta) ml/min/g. Data is with 1 second sampling and is combined across 3 tube currents, 2 injection volumes, 5 noise realizations, and 10 ROIs, yielding 300 estimated MBF values per curve. Separation between flow levels is even better than for static assessment, with mean overall classification accuracy of 96.9%