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Abstract. Quantification of myocardial blood flow (MBF) can aid in the diagnosis and treatment of coronary artery disease. However, there are no widely accepted clinical methods for estimating MBF. Dynamic cardiac perfusion computed tomography (CT) holds the promise of providing a quick and easy method to measure MBF quantitatively. However, the need for repeated scans can potentially result in a high patient radiation dose, limiting the clinical acceptance of this approach. In our previous work, we explored techniques to reduce the patient dose by either uniformly reducing the tube current or by uniformly reducing the number of temporal frames in the dynamic CT sequence. These dose reduction techniques result in noisy time-attenuation curves (TACs), which can give rise to significant errors in MBF estimation. We seek to investigate whether nonuniformly varying the tube current and/or sampling intervals can yield more accurate MBF estimates for a given dose. Specifically, we try to minimize the dose and obtain the most accurate MBF estimate by addressing the following questions: when in the TAC should the CT data be collected and at what tube current(s)? We hypothesize that increasing the sampling rate and/or tube current during the time frames when the myocardial CT number is most sensitive to the flow rate, while reducing them elsewhere, can achieve better estimation accuracy for the same dose. We perform simulations of contrast agent kinetics and CT acquisitions to evaluate the relative MBF estimation performance of several clinically viable variable acquisition methods. We find that variable temporal and tube current sequences can be performed that impart an effective dose of 5.5 mSv and allow for reductions in MBF estimation root-mean-square error on the order of 20% compared to uniform acquisition sequences with comparable or higher radiation doses. © 2017 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.4.2.026002](https://doi.org/10.1117/1.JMI.4.2.026002)]

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1 Introduction

Coronary artery disease (CAD) is commonly detected via invasive catheter-based angiography or noninvasive computed tomography angiography (CTA) or magnetic resonance angiography.¹ These techniques can detect the presence of stenoses in the coronary arteries caused by atherosclerosis. Clinically, however, knowing the downstream effect of a stenosis on myocardial perfusion is more important in terms of prognosis and appropriate treatments than simply detecting the presence of a stenosis.^{2,3} The addition of myocardial blood flow (MBF) information to the diagnostic process has been shown to lead to better outcomes and reduced costs in the treatment of CAD.⁴

Considering coronary CTA is a common tool to evaluate stable chest pain,⁵ there is an increasing interest in adding the capability of myocardial perfusion evaluation to these exams.⁶ Dynamic contrast-enhanced (DCE) cardiac CT has the capability of achieving quantitative MBF imaging.⁷ This procedure involves obtaining a series of myocardial CT images as the iodinated contrast agent passes through the myocardium. Time-attenuation curves (TACs) of the contrast agent are obtained from the CT image series, and they are analyzed using a

physiological model of iodine exchange to quantitatively estimate MBF.⁸ However, the multiple scans associated with dynamic CT potentially causes a high radiation dose to the patient.⁹ Numerous different acquisition protocols have been employed in DCE cardiac CT and there is little evaluation of the relative trade-offs of different settings. For example, in animal studies, George et al.⁷ used uniform temporal sampling acquisitions over 70 s at 2 frames/s, with a fixed tube current (60 mAs, 120 kVp). They reported accurate perfusion estimates, but the acquisition protocol would impart effective doses in excess of 100 mSv to patients. In human studies, Ho et al. used one frame every 2 to 4 s, with fixed tube currents (370 mAs, 80 kVp) and reported effective dose levels of 6 mSv.¹⁰ Similarly, Bamberg et al.¹¹ acquired one frame every 1 to 2 s over 30 s with fixed tube settings of 300 mAs (100 kVp). Kikuchi et al.¹² used one frame every 1 to 2 s with fixed tube settings of 33 or 175 mAs (80 kVp) depending on rest or stress state, resulting in dose levels of 3 to 7 mSv.

We have explored techniques to reduce the patient dose by either reducing the tube current or by reducing the number of temporal frames in the dynamic CT sequence or a combination of both.⁸ However, these dose reduction techniques result in lower-quality data. In order to extract the myocardial blood

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flow (MBF) data from the noisy sinograms, we have investigated several smoothing techniques. In that work, we explored the use of sinogram restoration techniques in both the spatial and temporal domains as well as the use of the Karhunen–Loeve transform to provide temporal smoothing in the sinogram domain.¹³ We employed uniform temporal samples at a single tube current in that work.

In this work, we investigate whether one can obtain better MBF estimation performance by varying the temporal sampling rate and tube current during an acquisition, informed by the knowledge of the sensitivity of the variation of myocardial CT number with respect to MBF. We hypothesize that increasing the sampling rate and/or tube current during critical time frames while reducing them elsewhere can achieve comparable or higher estimation accuracy at a reduced dose. Our goal is to reduce the overall dose from dynamic CT while keeping the RMSE in MBF estimates to a clinically acceptable value. We perform dynamic cardiac CT simulations of numerous conditions to evaluate the performance of MBF estimation and identify optimal acquisition protocols.

2 Methods

2.1 Dynamic Simulations

We generated dynamic material digital phantoms to mimic the exchange of iodine in the myocardium. Simulated CT projection data were generated using our polychromatic projector and dynamic material phantoms.¹³ The polychromatic projector used a 120-kVp x-ray tube spectrum, and system parameters were matched to a CT scanner at the University of Washington (GE Lightspeed 16-slice, GE Healthcare, Waukesha, Wisconsin). The projector used ray tracing based on Siddon's algorithm¹⁴ to compute the projection data. We used 888 bins and 984 view angles spanning 360 deg. Noise matching was done on the simulator to model the photon fluence with various tube currents by matching the standard deviation in 10 regions of interest (ROIs) in a uniform water phantom obtained from the CT scanner. Photon counting noise was compound Poisson, and electronic noise was Gaussian with zero mean and a standard deviation of 10. The noise power spectrum was also matched by varying the image reconstruction filter cutoff. The best match was provided by a Hann filter with a cutoff of 0.94 times the Nyquist frequency and this filter was used for all filtered backprojection (FBP) reconstructions in this work.

In order to simulate different noise levels, noisy projection data were generated with tube currents of 30 to 100 mA in steps of 10 mA, as well as at 25 and 55 mA, for 30 1-s time frames.¹⁵ In order to simulate different disease states, we looked

at four different MBF rates of 0.5, 1.0, 2.0, and 3.0 mL/g/min with a cardiac output of 8.0 L/min. For each flow rate, we simulated dynamic phantom data for five different phases, where phase refers to a 0- and 1.0-s shift in acquisition start time. Figure 1 shows select frames in our simulated dynamic CT images. Noisy and noiseless image data were reconstructed using FBP onto a 512×512 grid of 0.97 mm^2 pixels. After reconstruction, additional beam hardening correction was performed, using temporal information to distinguish bone and iodine, following the iterative method of Stenner et al.¹⁶ We selected a set of beam-hardening correction thresholds that minimized the bias in estimated MBF from noiseless data. Additional details of our simulations are described in our previous paper.⁸

In order to analyze the reconstructed images with respect to the task of estimating MBF, four different ROIs of size 5×5 pixels were chosen in the left myocardial regions in the image. The four ROIs were in the basal, lateral, apical, and septal regions of the left myocardium as shown in Fig. 2. The average CT number was computed for these ROIs and this value was extracted as a function of time to obtain TACs. The shape and magnitude of these curves are used to estimate MBF based on models of iodine transport in the myocardium.¹⁷ We used a full two-compartment model to estimate the MBF in this paper.⁸ We examined the cases of having 6, 10, 15, and 24 frames out of 30 frames. For our simulated data, the effective dose was estimated using the ImpACT CT Dosimetry Calculator.¹⁸

2.2 Sensitivity Analysis

Contrast is transported to the myocardium via the epicardial vessels from the aorta. By observing the blood pool contrast dynamics in the left ventricle or aorta (the input function TAC), we observe the contrast concentration available to enter the

Fig. 2 Noiseless dynamic CT image showing the four ROIs used for MBF estimation placed around left ventricular myocardium.

Fig. 1 Select frames at 5, 15, and 25 s of a noisy image at 100 mAs shown at [0, 300] HU.

coronary circulation at that time. How much of this contrast arrives in the myocardium and how quickly (as measured by the myocardial TAC) is determined by the MBF. The change in myocardial CT number at a moment in time is sensitive to changes in MBF. We refer to the percent change in myocardial hounsfield unit (HU) with percent change in MBF as the myocardial sensitivity curve. The details of the sensitivity calculation are as follows.

For a standardized input bolus and typical patient parameters (the same ones that were used in our simulated driving model patients), we do one driving model run at a specified flow state (0.5, 1, 2, or 3 mL/min/g) and a paired run with a specified flow state that is increased by 1% (0.505, 1.01, 2.02, and 3.03 mL/min/g). Each point on the sensitivity curve is calculated as the % change in HU between the two paired runs [e.g., $\{100 * \frac{HU_{MBF=0.505(t)} - HU_{MBF=0.5(t)}}{HU_{MBF=0.5(t)}}\}$ divided by the % change in MBF value (1%)].

The sensitivity is, therefore, an approximation of the local derivative of the relative change in measured attenuation as

Fig. 3 (a) Sample input and myocardial TACs, for various flow rates. (b) Relative sensitivity of MBF estimates versus time postintravenous injection of contrast agent for various flow rates.

a function of the relative change in perfusion value. The way to understand this is that a sensitivity value of 0.2 at time t implies that a 5% increase in MBF should be expected to lead to a 1% ($= 0.2 * 5\%$) increase in measured attenuation at time t . This is helpful to know because measurement at a time with a higher sensitivity will have greater signal to noise ratio than measurement at a time with lower sensitivity. Figure 3 shows input function (as recorded in an ROI in the left ventricle) and myocardial TACs as well as relative myocardial sensitivity as a function of time postinjection for different flow rates. The driving model used to generate the dynamic phantoms was also used to generate the sensitivity curves. We present several curves because the sensitivity varies with the true MBF. Since we do not know the flow rate for a given patient *a priori*, we computed the average of the sensitivity curves for flow rates of 1.0 and 2.0 mL/g/min. Based on the average curve, we observe that the myocardial HUs are most sensitive (sensitivity > 2.1) to flow rate during the interval from 2 s prior to 10 s postinput function peak time. The most sensitive frame times (in relation to the input function peak time) were found to be about the same for cardiac outputs ranging from 5 to 11.0 L/min in simulated data. Cardiac output variability was considered only to generate the myocardial sensitivity curves. It was not used for the simulations and MBF estimations. We hypothesize that increasing the sampling rate and/or tube current during this time period while reducing them elsewhere can achieve comparable or higher estimation accuracy at a reduced dose. In addition to the frames in this time range, the first time frame is important because it is treated as the background value for the task of MBF estimation. To test this, we investigated several different combinations of tube currents and temporal sampling based on the generated simulated CT data. Our goal was to keep the overall dose for a given dynamic CT sequence to be around 5.5 mSv.

We explored the following acquisition schemes:

1. uniform temporal sampling with single tube current (uniform-uniform);
2. uniform temporal sampling with multiple tube currents (uniform-variable);
3. nonuniform temporal sampling with single tube current (variable-uniform); and
4. nonuniform temporal sampling with multiple tube currents (variable-variable).

We will refer to sequences 2 to 4 that have at least one variable component as “variable” and sequences that have both uniform components as “uniform.” Figure 4 shows the difference between uniform temporal sampling at a single tube current and variable temporal sampling at multiple currents. In this figure, we show a sequence where seven frames are sampled at 25 mAs, two frames during the peak period sampled at 100 mAs, and six other peak frames at 40 mAs. In the uniform case, the frames are 2 s apart at 40 mAs. Both sequences use 15 frames and impart an identical radiation dose. Figure 5 shows a sample myocardial TAC for noiseless data with different time frames being picked for MBF estimation. In Fig. 5, the black line uses uniform sampling with frames 2 s apart. The blue line uses nonuniform temporal sampling with fewer frames being acquired during the first 9 s and more being acquired around the peak uptake time period and no frames after 28 s.

Fig. 4 Uniform sampling (sequence 1b in Table 1) versus variable sampling (sequence 4b in Table 4) showing various time frames being picked at various tube currents.

Fig. 5 Noiseless TACs for uniform 2-s sampling (sequence 1b in Table 1) and one of the nonuniform temporal sampling (sequence 3b in Table 3) strategies showing slightly higher density samples on the rising edge and near peak enhancement.

2.3 Performance Metric

We obtain a TAC from each of the four myocardial ROIs that incorporate the variation in the myocardium due to beam hardening as well. From each TAC, we estimate MBF using a two-compartment model of iodine transport and compare it to the true simulated values. For a scanning protocol to be considered viable, it should perform well over a variety of disease states (four flow rates) in various phases (five of them). In addition, its performance should be robust against the presence of noise variability (five noisy states). We use the root-mean-square percent error (%RMSE) in MBF estimates over four flow rates, five phases, five noisy realizations for each phase, and four ROIs for each noisy realization as the metric ($N = 400$) to determine the best possible sampling sequences. There were some cases where the MBF optimization estimated erroneously high flow rates; we thresholded all erroneous estimates to have a maximum value of 5.0 mL/g/min. These results were also included

in the %RMSE and RMSE calculations. 95% confidence intervals (CIs) on %RMSE were generated using bootstrapping performed using the MATLAB function “bootci” (resampling with replacement) with $N = 10,000$.

3 Results

3.1 Uniform Temporal Sampling with a Single Current (Uniform-Uniform)

Allowing a total effective dose budget of 5.5 mSv, we first examined the effect of distributing that dose among different numbers of frames and placing those frames at different times. CT acquisition tube current was held constant across all frames for a given number of total frames, such that the total dose was as close as possible to 5.5 mSv. Table 1 lists the results for uniform temporal sampling data with a total dose of 5.5 mSv. We use a compact notation to characterize uniformly sampled frames, for example, “1:2:30” means that a frame was acquired at the first second and every two seconds thereafter until the 30th second after injection.

Comparing sequence 1b to sequence 1c and sequence 1d to sequence 1e, we see that the inclusion of the first frame in TACs gives slightly more accurate MBFs because it allows for more accurate background estimation. On comparing sequences 1a and 1d, we see that using fewer frames each at a higher tube current give a slightly lower %RMSE. However, there is a limit to how few frames we can use and still get a reasonable %RMSE. Sequence 1f uses only six frames at 100 mAs and gives a much higher %RMSE. We also note that using 24 frames but at a much lower tube current, in sequence 1a, does not give us a better MBF estimate.

3.2 Uniform Temporal Sampling with Multiple Currents (Uniform-Variable)

We explored uniform temporal sampling with various combinations of tube currents with the goal of keeping the effective dose around 5.5 mSv. The notation for the current-frame(s) combination in column 2 is [frames acquired] at a specific tube current.

Comparing 15-frame sequences 2a and 2b, we observe that using a higher tube current of 55 mAs for more of the peak frames gives a lower %RMSE. From sequences 2b, 2c, and 2d, we see that using the higher current for the first frame also gives a slightly lower %RMSE. Looking at 10-frame sequences 2e and 2f, we see that the inclusion of the first frame is important

Table 1 %RMSE in MBF using uniform temporal sampling with a single current.

Sequence [# of frames]	Tube current (mAs)	Selected frames	% RMSE
1a [24]	25	1:1:24	68.2
1b [15]	40	1:2:29	66.4
1c [15]	40	2:2:30	67.6
1d [10]	60	1:3:28	62.7
1e [10]	60	2:3:29	70.5
1f [6]	100	1:5:30	107.0

for more accurate MBF estimates. Comparing the data in Table 2 to that in Table 1, we observe that we can obtain a lower %RMSE using a combination of two or three currents with the higher tube currents being used for the most sensitive frames, including the first frame. These results make sense since MBF estimation requires accurate uptake values for both the first and the peak frames. So, inclusion of the first frame and peak frames at higher tube currents will give us more accurate MBF estimates.

3.3 Nonuniform Temporal Sampling with a Single Current (Variable-Uniform)

There are numerous ways to choose the required number of frames out of 30 frames. Table 3 lists four of the best results we obtained using nonuniform temporal sampling with a single tube current. Nonuniform sampling at a single current (sequences 3a and 3d) give us more accurate MBFs than uniform sampling at a single current (sequences 1a and 1f, respectively) for 24 and 6 frames. For 15 and 10 frames, the %RMSE values are about the same between uniform (sequences 1b to 1e) and nonuniform sampling (sequences 3b to 3c). However, %RMSE in all the sequences in Table 3 are higher than what we obtained using multiple currents and uniform sampling as listed in Table 2.

3.4 Nonuniform Temporal Sampling with Multiple Currents (Variable-Variable)

In this case, we chose the more sensitive frames at higher tube currents. Table 4 shows some of the results that we obtained using nonuniform temporal sampling at multiple tube currents. Comparing sequences 4b and 4c, we observe that acquiring the peak frames at a higher tube current (100 versus 70 mAs) gives a more accurate MBF estimate. From sequences 4d and 4e, we observe that acquiring more of the peak frames at a higher tube current gives slightly more accurate MBF estimate.

3.5 Comparing Across Approaches

We want to compare the three best variable sequences (with lowest %RMSE) from Tables 2–4 to the best uniform-uniform sequence result from Table 1. These results are shown in Fig. 6 along with 95% CIs for the %RMSE values. From this figure, we observe that one can obtain multiple tube current sequences using both uniform and nonuniform temporal sequences (sequences 2a, 4b, and 2d), which give MBF estimates that are lower than the 95% CI of the best MBF estimate obtained

Table 3 %RMSE in MBF using nonuniform temporal sampling with a single current.

Sequence [# of frames]	Current (mAs)	Selected frames	% RMSE
3a [24]	25	1:2:7, 9:1:26, 28, 30	57.1
3b [15]	40	1:3:7, 9, 11, 13:1:18, 20, 22:3:28	67.1
3c [10]	60	1:4:9, 11:2:21, 25	59.8
3d [6]	100	1, 9, 13:4:25	82.7

from uniform temporal sampling at a single current (sequence 1d). Figure 7 shows box plots for bias in MBF estimates, defined as the difference between MBF estimate and true flow, distributed by flow rates ($N = 100$) for these two sequences. We observe that the lower flow rates have more outliers. We also note that the uniform sequence 1d has many more outliers compared to sequence 2a. This could help explain why sequence 2a performs better than the uniform sequence 1d. Figure 8 breaks down the RMSE and %RMSE values by flow rates for the best uniform and variable sequences. From Figs. 7 and 8, we observe that the bias in MBF estimates does not vary much by flow rates. Increase in RMSE with flow rates seems to arise mainly from the increase in variance in flow estimates. Table 5 breaks down the RMSE and %RMSE values by flow rates for the best uniform-uniform and variable sequences. Overall, the lowest %RMSE that we obtained was 50%, using 15 uniformly sampled frames at 55 and 25 mAs tube currents, which is 20% lower than the %RMSE that was obtained using a uniform sampling of 10 frames at 60 mAs. In addition, this performance improvement comes with negligible increase in patient radiation dose, 5.6 mSv compared to 5.5 mSv for uniform sampling at 60 mAs for 10 frames.

4 Discussion

In this work, we explored the use of variable sampling of temporal frames and tube current modulation for the task of MBF estimation using dynamic CT. We found the best technique employed uniform temporal sampling using variable tube currents, with higher currents being used for the most sensitive frames. This suggests that uniform sampling with variable tube currents can be quite robust. In general, the following patterns emerged based on the sequences we looked at:

Table 2 %RMSE in MBF using uniform temporal and variable current sampling in dynamic CT.

Sequence [# of frames]	[selected frames] at current (mAs)			%RMSE
2a [15]	[9:2:23] at 55	[1:2:7, 25:2:29] at 25	—	50.2
2b [15]	[1, 15] at 100	[11:2:23] at 40	[3:2:9, 25:2:29] at 25	54.8
2c [15]	[1, 15] at 70	[11:2:23] at 50	[3:2:9, 25:2:29] at 25	60.5
2d [15]	[15, 17] at 100	[1, 11, 13, 19:2:23] at 40	[3:2:9, 25:2:29] at 25	56.9
2e [10]	[10:3:22] at 80	[1:3:7, 25, 28] at 40	—	53.0
2f [10]	[11:3:20] at 80	[8, 23:3:29] at 50	[2, 5] at 40	60.8

Table 4 %RMSE in MBF using variable temporal and multiple tube currents in dynamic CT.

Sequence [# of frames] [selected frames] at current (mAs)					%RMSE
4a [15]	[11, 13:1:17, 19, 21, 24] at 55	[1:3:10, 12, 26] at 25	—		54.4
4b [15]	[13, 15] at 100	[12:2:22] at 40	[1:3:7, 9, 11, 24, 26] at 25	51.8	
4c [15]	[13, 15] at 70	[12:2:22] at 50	[1:3:7, 9, 11, 24, 26] at 25	56.0	
4d [10]	[10:2:22] at 70	[1, 6, 26] at 40	—		62.8
4e [10]	[13:2:19] at 80	[1, 9, 11, 21] at 50	[5, 25] at 40	63.8

Fig. 6 Best acquisition sequences showing %RMSE in MBF estimates, the numbers in brackets are 95% CIs: “Black +” line is a uniform-uniform sequence (1d) of 10 frames at 60 mAs, “Green ★” is a uniform-variable sequence (2a) of 15 frames at 25 and 55 mAs, “Blue o” is a variable-variable sequence (4b) of 15 frames at 25, 40, and 100 mAs. “Magenta ♦” is a uniform-variable sequence (2e) of 15 frames at 25 and 55 mAs.

1. The first frame is important since it is used for background estimation in the MBF estimation.
2. Frames that are myocardially most sensitive (from 2 s earlier until 10 s after the input function peak time based on varying cardiac outputs) should be included and sampled at higher tube currents.
3. Use of multiple tube currents gives better MBF estimates than using a single tube current for the same dose.
4. There is a limit to how few frames can be used: we found that using six frames at a high tube current of 100 mAs for the same dose gives much worse results.
5. There is a limit to using more number of frames but at a low tube current (to get the same dose): using 24 frames at 25 mAs did not give better results than using 15 frames with variable tube currents.

The best %RMSE values that we obtained were on the order of 50%. Absolute MBF estimation with dynamic myocardial perfusion CT, or any other candidate modality (PET or MR), does not have clear clinical guidelines about acceptable

Fig. 7 (a) The best uniform-uniform (1d) and (b) the best variable acquisition (2a) sequences showing the bias in MBF estimates broken down by myocardial flow rates. Each flow rate has 100 simulations represented (4 ROIs $\times$ 5 phases $\times$ 5 noisy realizations).

Fig. 8 (a) and (c) The best uniform-uniform sequence (1d) and (b) and (d) the best variable acquisition sequence (2a), showing RMSE and %RMSE in MBF estimates broken down by myocardial flow rates. Each flow rate has 100 simulations represented (4 ROIs $\times$ 5 phases $\times$ 5 noisy realizations).

Table 5 The best result in MBF estimates using variable sampling listed along with the best result for uniform sampling at a single current broken down by flow rates. This table also lists the 95% CIs for the %RMSE values generated via bootstrapping.

Sequence, current (mAs)	0.5	1.0	2.0	3.0
RMSE for each flow in mL/g/ min				
1d, 60 mAs	0.45 [0.36,0.58]	0.69 [0.53,1.07]	0.76 [0.64,0.97]	0.95 [0.83,1.09]
2a, 55 and 25 mAs	0.38 [0.32,0.48]	0.4 [0.33,0.57]	0.81 [0.66,1.06]	0.93 [0.82,1.07]
%RMSE for each flow				
1d, 60 mAs	90.4 [73,114.2]	69.4 [53.5,105.5]	38.3 [32.3,48.2]	31.8 [27.7,36.6]
2a, 55 and 25 mAs	76.0 [63.3,96.8]	39.7 [32.8,56.7]	40.7 [33.1,52.7]	31.2 [27.3,35.9]

%RMSE values. We know that this reported error will be strongly a function of the size of the tissue of interest, with global MBF estimates (averaging the whole myocardium) with much less error than the small 0.24 cc ROIs used in this study. Clinically, global MBF estimates are used to characterize small vessel, microcirculatory disease and regional flow estimates that characterize macrovascular, focal-epicardial disease.^{19,20} The goal of our current work is to rank sampling schemes, not to demonstrate absolute performance of methods. For this work, we purposely choose a challenging task, very low-dose conditions, and a relatively small tissue size of interest, to elucidate any performance differences between different acquisition strategies.

This work presents broad acquisition recommendations based on evaluation of a controlled simulation experiment. The simulation experiment does not include numerous degrading effects present in clinical studies including myocardial attenuation and flow heterogeneity, patient motion, and metallic artifacts. These effects, while impacting clinical perfusion studies, should not affect our results suggesting dose acquisition strategies. Furthermore, our experiment modeled a single injection strategy (5 mL/s injection of 50 cc of Omnipaque 350 contrast). Different optimal acquisition times may be expected with other injection strategies, although the overall trends are expected to be consistent.

5 Conclusions

We explored variable temporal and current acquisition schemes in dynamic CT for the task of MBF estimation using simulated data. We found that for temporal sampling, it is important to include the first time frame and other frames during the times when the myocardial sensitivity is higher (typically from around 2 s earlier until 10 s after the input function peak time) to get more accurate MBF estimates. The choice of tube current or flux is also important. In general, using a higher tube current for the most important time frames gave us more accurate MBF estimates. Since the sensitive frames can vary between patients and disease states, including most of the possible sensitive frames at a higher tube current can provide a more robust MBF estimate. We found that variable temporal and tube current sequences can be performed that impart an effective dose of 5.5 mSv and allow for reductions in MBF estimation RMSE on the order of 20% compared to uniform acquisition sequences with comparable radiation doses. These results suggest that more tailored temporal and current sampling techniques could provide more dose efficient acquisitions than uniform sampling for dynamic CT for the task of MBF estimation.

Disclosures

The authors have no relevant financial interests in this paper and no other potential conflicts of interest to disclose.

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References

1. R. C. Hendel et al., "Appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation quality strategic directions committee appropriateness criteria working group," *J. Am. Coll. Cardiol.* **48**(7), 1475–1497 (2006).
2. G. A. Beller and B. L. Zaret, "Contributions of nuclear cardiology to diagnosis and prognosis of patients with coronary artery disease," *Circulation* **101**(12), 1465–1478 (2000).
3. L. J. Shaw et al., "Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the clinical outcomes utilizing revascularization and aggressive drug evaluation (COURAGE) trial nuclear sub study," *Circulation* **117**(10), 1283–1291 (2008).
4. P. A. Tonino, B. De Bruyne, and N. H. Pijls, "Fractional flow reserve versus angiography for guiding percutaneous coronary intervention," *N. Engl. J. Med.* **360**, 213–224 (2009).
5. P. K. Vanhoenacker, M. H. Heijenbroek-Kal, and R. van Heste, "Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: meta-analysis," *Radiology* **244**(2), 419–428 (2007).
6. M. J. Budoff, D. Georgiou, and A. Brody, "Ultrafast computed tomography as a diagnostic modality in the detection of coronary artery disease: a multicenter study," *Circulation* **93**, 898–904 (1996).
7. R. T. George, M. Jerosch-Herold, and C. Silva, "Quantification of myocardial perfusion using dynamic 64: detector computed tomography," *Invest. Rad.* **42**, 815–822 (2007).
8. M. D. Bindschadler et al., "Comparison of blood flow models and acquisitions for quantitative myocardial perfusion estimation from dynamic CT," *Phys. Med. Bio.* **59**(7), 1533–1556 (2014).
9. F. A. J. Mettler et al., "Effective doses in radiology and diagnostic nuclear medicine: a catalog," *Radiology* **248**, 254–263 (2008).
10. K.-T. Ho et al., "Dynamic CT myocardial perfusion measurements of resting and hyperaemic blood flow in low-risk subjects with 128-slice dual-source CT," *Eur. Heart J. Cardiovasc. Imaging* **16**(3), 300–306 (2015).
11. F. Bamberg et al., "Detection of hemodynamically significant coronary artery stenosis: incremental diagnostic value of dynamic CT-based myocardial perfusion imaging," *Radiology* **260**(3), 689–698 (2011).
12. Y. Kikuchi, "Quantification of myocardial blood flow using dynamic 320-row multi-detector CT as compared with 150-H₂O PET," *Eur. Radiol.* **24**, 1547–1556 (2014).
13. D. Modgil et al., "Sinogram smoothing techniques for myocardial blood flow estimation from dose-reduced dynamic computed tomography," *J. Med. Imaging* **1**(3), 034004 (2014).
14. R. L. Siddon, "Prism representation: a 3D ray-tracing algorithm for radiotherapy applications," *Phys. Med. Biol.* **30**(8), 817–824 (1985).
15. D. Modgil et al., "Adaptive sampling of CT data for myocardial blood flow estimation from dose-reduced dynamic CT," *Proc. SPIE* **9413**, 941304 (2015).
16. P. Stenner et al., "Dynamic iterative beam hardening correction in myocardial perfusion imaging using contrast-enhanced CT," *Invest. Rad.* **45**(6), 314–323 (2010).
17. K. Miles, P. Dawson, and M. Blomley, *Functional Computed Tomography*, Isis Medical Media, Valley Stream, New York (1997).
18. M. A. Lewis et al., "Estimating patient dose on current CT scanners: Results of the ImPACT* CT dose survey," *Radmag.*, 2000, <http://www.impactscan.org/doseandtest.htm> November (2013).
19. P. Chareonthaitawee et al., "Heterogeneity of resting and hyperemic myocardial blood flow in healthy humans," *Cardiovas. Res.* **50**(1), 151–161 (2001).
20. P. G. Camici and O. E. Rimoldi, "The clinical value of myocardial blood flow measurement," *J. Nucl. Med.* **50**(7), 1076–1087 (2009).

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