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Effect of Beam Hardening on Transmural Myocardial Perfusion Quantification in Myocardial CT Imaging

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Abstract

The detection of subendocardial ischemia exhibiting an abnormal transmural perfusion gradient (TPG) may help identify ischemic conditions due to micro-vascular dysfunction. We evaluated the effect of beam hardening (BH) artifacts on TPG quantification using myocardial CT perfusion (CTP). We used a prototype spectral detector CT scanner (Philips Healthcare) to acquire dynamic myocardial CTP scans in a porcine ischemia model with partial occlusion of the left anterior descending (LAD) coronary artery guided by pressure wire-derived fractional flow reserve (FFR) measurements. Conventional 120 kVp and 70 keV projection-based mono-energetic images were reconstructed from the same projection data and used to compute myocardial blood flow (MBF) using the Johnson-Wilson model. Under moderate LAD occlusion (FFR~0.7), we used three 5 mm short axis slices and divided the myocardium into three LAD segments and three remote segments. For each slice and each segment, we characterized TPG as the mean “endo-to-epi” transmural flow ratio (TFR). BH-induced hypoenhancement on the ischemic anterior wall at 120 kVp resulted in significantly lower mean TFR value as compared to the 70 keV TFR value (0.29 ± 0.01 vs. 0.55 ± 0.01 ; $p < 1e-05$). No significant difference was measured between 120 kVp and 70 keV mean TFR values on segments moderately affected or unaffected by BH. In the entire ischemic LAD territory, 120 kVp mean endocardial flow was significantly reduced as compared to mean epicardial flow (15.80 ± 10.98 vs. 40.85 ± 23.44 ml/min/100g; $p < 1e-04$). At 70 keV, BH was effectively minimized resulting in mean endocardial MBF of 40.85 ± 15.3407 ml/min/100g vs. 74.09 ± 5.07 ml/min/100g ($p = 0.0054$) in the epicardium. We also found that BH artifact in the conventional 120 kVp images resulted in falsely reduced MBF measurements even under non-ischemic conditions.

Keywords

Myocardial CT perfusion; beam hardening; transmural perfusion gradient; myocardial blood flow; spectral detector CT; dual energy CT

1. INTRODUCTION

Detection of abnormal transmural blood flow gradient and the measurement of endocardial-to-epicardial flow ratio may be of clinical importance for predicting hemodynamically significant coronary artery disease (CAD) and for identifying patients with subendocardial ischemia^{1, 2}. It has been observed that the subendocardial layer of the left ventricular (LV) myocardium is more vulnerable to ischemia than the outer layers³. Noninvasive perfusion imaging may be capable of evaluating spatial distributions of myocardial blood flow. Using magnetic resonance imaging to obtain quantitative myocardial blood flow, Muehling et al.⁴ have noted regional heterogeneity in myocardial perfusion for healthy volunteers at rest and hyperemia. Computed tomography perfusion (CTP) imaging has also been used in previous studies to detect and quantify transmural differences in myocardial perfusion. George et al.⁵ used attenuation density in the subendocardial and subepicardial layers to describe transmural perfusion ratio (TPR) and showed that TPR is inversely correlated with the stenosis diameter. Hosokawa et al.⁶ computed the transmural perfusion gradient as the difference between epi- and endo-cardial attenuation normalized by the LV wall thickness and showed that it has great potential to evaluate the severity of myocardial ischemia, similarly to myocardial perfusion scintigraphy score. The ability to reliably evaluate transmural defects could better inform clinical decisions and improve the positive predictive value of myocardial perfusion imaging.

When using conventional myocardial CT imaging, beam hardening (BH) artifacts can negatively affect the accuracy of perfusion estimates^{7, 8}. BH artifacts arise due to the polychromatic nature of the x-ray beam and preferential absorption of low energy x-rays by high attenuating materials, such as bone and iodinated contrast agent, which appear as cupping or streaks in the image. The use of spectral CT imaging may improve perfusion estimates by effectively reducing BH artifacts in monoenergetic (keV) images^{7, 9}. In this paper we used a prototype spectral detector CT (SDCT) scanner (Philips Healthcare) to acquire dynamic myocardial CT perfusion images in a porcine ischemia model¹⁰. The SDCT system uses two detector layers to acquire energy sensitive projection data which, after material decomposition, can be used to generate an array of images including projection-based monoenergetic CT images, and iodine and water density images. Conventional single energy (kVp) images can also be generated from the same SDCT acquisition by combining data in the two detector layers, giving a unique opportunity to compare keV and kVp perfusion estimates.

We have developed an advanced myocardial perfusion imaging pipeline and used it to assess transmural perfusion gradient with conventional and synthesized monoenergetic CT images. We selected 70 keV as the optimal processing energy to compare conventional and monoenergetic-based results, based on our previous work⁷, due to its balance between iodine contrast-to-noise ratio and BH artifact reduction.

We were able to detect TPG with partial occlusion of the left anterior descending (LAD) artery using both conventional 120 kVp and projection-based monoenergetic 70 keV images. However, at 120 kVp, we found that BH introduced false ischemic regions and accentuated TPG under baseline and ischemic conditions, respectively.

2. MATERIALS AND METHODS

2.1 Animal model and image acquisition

We used a porcine ischemic model (female Yorkshire pigs: 40–50 kg, 13–15 weeks of age) with percutaneously induced ischemia guided by fractional flow reserve (FFR). Under fluoroscopy, a balloon catheter was implanted in the LAD coronary artery and an FFR wire placed with one pressure sensor proximal and the other distal to the balloon to measure the extent of ischemia in real-time. Prior to scanning, the balloon was inflated to induce the desired level of stenosis as determined by FFR. Prospective-ECG-triggered images were acquired at end systole (45% R-R) using a prototype SDCT scanner with an injection of 20 ml of iodinated contrast agent flushed by 20 ml of saline at 4 ml/s. The SDCT scanner is a single source, dual-layer detector system¹¹, which allows simultaneous acquisitions of low- and high-energy projections, hence enabling accurate projection-based material decomposition and effective reduction of BH-artifacts. During each experiment, dynamic CTP images were acquired under baseline (FFR=1) and ischemic (FFR≤0.75) conditions. At least a 15-to-20 minute interval was allowed between consecutive scans to ensure contrast wash out from the heart, and scanning was initiated 3–4 s into iodine injection. Full 360 degree scans were acquired to avoid partial scan shading artifacts. We used a tube potential of 120 kVp and 100 mA tube current. Conventional single energy (kVp) images and projection-based monoenergetic (keV) images at 70 keV were reconstructed from the same projection data. Perfusion estimates were compared between keV and kVp images. Reconstructed slices were 2 mm thick with no overlap.

2.2 CT Image processing

For a given hemodynamic condition, the reconstructed 4D CTP sequences underwent a series of processing steps¹⁰ prior to quantifying the myocardial blood flow. The main steps are summarized below:

4D image registration: Spatial misalignment between the acquired volumes per each cardiac cycle may occur due to breathing and/or poor ECG synchronization. If not corrected, these misalignments result in inaccurate arterial and myocardial time attenuation curves (TAC) which lead to inaccurate flow quantifications. Hence, for each hemodynamic condition, we applied an elastic registration method based on 3D cubic B-splines and normalized mutual information¹² to align the 3D volumes to a common reference time point.

Short axis reformatting and segmentation of the myocardium: For every 4D sequence, we generated a low noise, high contrast average 3D average CT image using the registered 120 kVp volumetric images. Short axis reformatting of the myocardium was performed on the average CT volume using a research version of the QMass software by Medis using 5 mm thick slices. Delineation of left ventricular (LV) myocardium was easily and accurately performed on the reformatted high contrast average CT volume and to generate a corresponding 3D binary mask of the myocardial wall. Two dimensional tracing of the epi- and endo-cardial contours was manually performed on the average CT map in the short axis plane using an interactive contour tracing tool (Figure 1). The short axis

reformatting geometry and myocardial mask was applied to all registered volumes in the 4D dataset.

Transmural perfusion gradient analysis: We characterized TPG as the as the mean endo- to epi-cardial transmural flow ratio (TFR). In order to assess and compare TPG between the two reconstructions, we divided the LV myocardium into six segments in the short axis plane. Three of these segments (anterior, antero-lateral, and antero-septal) are in the ischemic LAD region, and the remaining three segments (infero-lateral, inferior, and infero-septal) are located in remote non-ischemic territories (see Figure 1). Epi and endocardial contours were traced as the outer and inner thirds of the myocardial wall using an interactive contour tracing tool (Figure 2). For each slice and each myocardial segment, we computed mean endocardial and epicardial MBF from the inner and outer thirds of the segment respectively (Fig.2), and took their ratio to get the corresponding TFR:

$$TFR = \frac{\text{mean}(MBF_{\text{endo}})}{\text{mean}(MBF_{\text{epi}})}.$$

We quantified the effect of BH artifact on the TFR in conventional images as compared to keV images.

2.3 Myocardial blood flow (MBF) quantification

We developed a myocardial CT perfusion software and used it to analyze both conventional and keV image sequences. For each sequence, tissue myocardial blood flow was computed by deconvolution of the myocardial TACs, $C(t)$, measured from 2×2 pixel regions, within the myocardial mask, with the arterial input function (AIF), $C_{\text{art}}(t)$, measured from an ROI traced inside of the LV chamber:

$$C(t) = 1/\rho_t F \cdot C_{\text{art}}(t) \otimes R(t),$$

where, F is the flow and $R(t)$ is the impulse residue function (IRF). The convolution operator in the above equation is denoted $\otimes$ and ρ_t refers to the tissue density.

We used the Johnson and Wilson parameter estimation model to solve for the flow-scaled impulse residue function as:

$$F \cdot R(t) = \begin{cases} 0 & \text{if } 0 \leq t < T_0 \\ F & \text{if } T_0 \leq t < T_0 + T_C \\ F \cdot E \cdot e^{-k(t - T_0 - T_C)} & \text{if } t \geq T_0 + T_C \end{cases}$$

where T_0 is the bolus arrival time, T_C is the intravascular transit time, E is the ejection fraction and k is the mono-exponential decay rate of the extracted contrast in the extravascular space.

3. RESULTS

The myocardial TACs measured within the anterior wall (indicated by red arrows on Figure 4) are severely affected by BH artifacts, especially when the contrast signal is high in the LV cavity as indicated by the peak of the AIF in Figure 3. These artifacts result in a noticeable dip in the mean HU value in the 120 kVp curves as compared to their 70 keV counterpart as illustrated by the black curve in Figure 3. Using the distorted 120 kVp TACs to compute the myocardial blood flow led to an underestimation of the blood flow in the BH-affected myocardium (see upper row of Figure 4).

In some of our animal studies, we found that subendocardial layers of the LV myocardial wall showed more ischemia than the mid- and epicardial layers. This was most evident in animals having a lower mean arterial pressure. In the ischemic example shown in Figure 4 with $\text{FFR} \sim 0.7$, we clearly see a ring of reduced endocardial flow in the 70 keV image flow maps in the LAD territory. With the BH fueled degradations in the 120 kVp images, the angular and radial extent of ischemia is distorted. Figure 4 shows conventional 120 kVp flow maps and their corresponding 70 keV maps. Both reconstructions allowed visualization of transmural perfusion gradient on the ischemic LAD territory. In particular, the 120 kVp blood flow was greatly underestimated in the endocardial layer and the tissue under-perfusion uniformly extends to mid- and epicardial layers. We characterized transmural perfusion in terms of ratio of mean blood flow in the endo- and the epicardial layers and assessed the effect of BH artifact in conventional 120kVp images as compared to monoenergetic 70 keV images.

First, we noticed that there was no significant difference between 120 kVp and 70 keV mean TFR values on the remote non-ischemic segments (infero-lateral, inferior, and infero-septal) and on the ischemic antero-lateral and antero-septal segments. However, on the ischemic anterior segment, mean TFR value across the three slices was significantly lower on the 120 kVp maps compared to the 70 keV maps (0.29 ± 0.01 vs. 0.55 ± 0.01 ; $p < 1e-05$). The significant decrease in mean MBF on the endocardium compared to the epicardium for 120 kVp (15.80 ± 10.98 ml/min/100g vs. 40.85 ± 23.44 ml/min/100g; $p < 1e-04$) was not all due to the induced ischemia but also due to BH artifacts presenting themselves as hypoenhancement that distort corresponding TACs as was shown in Fig. 3. On the other hand, with the effective reduction of BH in the 70 keV scans, mean MBF in the endocardium was 40.85 ± 15.34 ml/min/100g compared to 74.09 ± 5.07 ml/min/100g ($p = 0.0054$) in the epicardium. In the remote non-ischemic segments, the mean 120 kVp MBF across the three slices in the endocardium was 119.77 ± 8.04 and was not significantly different from that in the epicardium (126.56 ± 6.78 ml/min/100g; $p = 0.01$). Comparable results were obtained in these segments for the 70 keV maps (125.6 ± 5.9 ml/min/100g in the endocardial vs. 129.26 ± 5.2 ml/min/100g in the epicardial layer; $p = 0.007$).

Comparisons of mean TFR across different myocardial segments in the two reconstructions are summarized in Figure 5 where a p-value < 0.05 indicates statistical significance. Note that statistical difference between mean 120 kVp and 70 keV TFR is most significant in the anterior myocardial segment ($p < 1e-05$) which is most severely affected by BH in the conventional images as compared to 70 keV images. Due to BH reduction in the 70 keV

images, no difference was noticed between mean TFR across the entire LAD territories in the 70 keV flow maps as a result of a uniformly reduced MBF in these ischemic areas. However, mean 120 kVp TFR in the BH-affected anterior wall was significantly reduced than that in other less BH-affected LAD segments ($p=0.03$). As expected, mean TFR was closer to unity in remote healthy myocardium for both reconstructions with no significant difference ($p=0.27$).

4. DISCUSSION AND CONCLUSIONS

In this study, we demonstrated the ability to distinguish and quantify transmural perfusion gradient in a porcine ischemia model. We observed that BH artifacts in conventional 120 kVp images may negatively affect the quantification of transmural perfusion gradient compared to projection-based 70 keV images obtained from a prototype spectral detector CT scanner. This preliminary study presents findings from only one animal experiment. A larger study is underway, including 12 other pig data sets on the same scanner at both baseline and under mild ischemia ($FFR \leq 0.75$). Practically, the transmural ischemic effect was not always reproduced in all animals. Analysis of more data is warranted in order to confirm the presented results and potentially to reveal the hemodynamic conditions which can reliably reproduce the transmural ischemic effect. We believe that these initial findings are of great importance as BH artifacts in CTP can have a sizable impact on the assessment of myocardial transmural perfusion ratio in both attenuation-based analysis⁵ or in blood flow analysis, as performed in this work and translated from magnetic resonance imaging⁴.

While dual energy CT represents a viable and reliable hardware solution to BH artifacts in myocardial perfusion CT, conventional systems could gain from software corrections^{13, 14}. Future work could be performed to compare TPG in the BH corrected conventional scans to the 70 keV reference. If BH correction algorithms could reliably remove BH artifacts, this may reduce the need for dual energy scanners and enable confident measurements of myocardial blood flow or transmural perfusion gradients to support clinical decisions. Most importantly, elimination of BH artifacts could reduce false positives from CTP, making it a more effective gatekeeper exam for invasive coronary angiography.

We have recently developed a cryo-imaging method to serve as a reference for spatial assessment of myocardial blood flow¹⁵. This technique enables us to evaluate transmural perfusion gradient in CTP and compare to a reference. The ability to distinguish and quantify transmural perfusion gradient with CTP could provide additional information on physiologic myocardial blood flow distributions for clinical use, potentially improving the detection of hemodynamically significant coronary artery disease and identifying patients with subendocardial ischemia.

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Figure 1.

Average CT map generated from a registered 4D sequence. High contrast between the right and left ventricles facilitates the delineation of the LV myocardium (enclosed by red and green contours). Dissection, in the short axis plane, of the left ventricular myocardium into six segments: anterior (Ant), anteroseptal (Ant-S), anterolateral (Ant-L), inferior (Inf), inferoseptal (Inf-S), and inferolateral (Inf-L). Flow measurements and comparisons are made within these segments.

Figure 2. Interactive contouring of endo- and epi-cardial layers in the short axis plane. For each of the six myocardial segments (see Fig.1), ratio of mean myocardial flow in these two layers is used to characterize the transmural perfusion.

Figure 3.

Arterial and sample tissue time attenuation curves generated as mean HU value over time. Conventional 120 kVp (left) and corresponding 70 keV (right) curves. Curves are generated as mean HU value in an ROI within the left ventricular cavity (red), the anterior segment (black), and the lateral segment (blue), respectively.

Figure 4.

Transmurial flow gradient. Shown are myocardial flow maps on three conventional 120 kVp (upper row) and their corresponding monoenergetic 70 keV (bottom row) slices in the short axis plane. Color bar range goes from 0 to 150 ml/min/100g for all maps. Shown on middle upper row are names and locations of the six myocardial segments used for analysis. Similar segmentations are used for other slices. Red arrows show part of the anterior segment which lies between the sternum and the contrastfilled LV cavity.

Figure 5.

Transmural flow gradient. Comparison of 120 kVp and 70 keV mean transmural flow ratio on different myocardial segments. The only statistically significant difference in TFR was found in the BH affected anterior segment, where 120 kVp indicated much lower TFR as compared to 70 keV. In 70 keV, TFR was consistent across LAD segments, indicating effective removal of BH artifact. In the remote myocardium, TFR~1.0 as expected in healthy myocardium.