Published in final edited form as:

Proc SPIE Int Soc Opt Eng. 2015 February ; 9417: . doi:10.1117/12.2081547.

Dynamic Myocardial Perfusion in a Porcine Balloon-induced Ischemia Model using a Prototype Spectral Detector CT

Rachid Fahmi^a, Brendan L. Eck^a, Anas Fares^c, Jacob Levi^a, Hao Wu^a, Mani Vembar^b, Amar Dhanantwari^b, Hiram G. Bezerra^c, David L. Wilson^{a,d}

^aBiomedical Engineering Department, Case Western Reserve University, Cleveland, OH, 44106, USA

^bPhilips Healthcare, Cleveland, OH, 44143, USA

^cCardiovascular Imaging Core Laboratory, Harrington Heart & Vascular Institute, University Hospitals Case Medical Center, Cleveland, OH, 44106, USA

^dDepartment of Radiology, Case Western Reserve University, Cleveland, OH, 44106, USA

Abstract

Myocardial CT perfusion (CTP) imaging is an application that should greatly benefit from spectral CT through the significant reduction of beam hardening (BH) artifacts using mono-energetic (monoE) image reconstructions. We used a prototype spectral detector CT (SDCT) scanner (Philips Healthcare) and developed advanced processing tools (registration, segmentation, and deconvolution-based flow estimation) for quantitative myocardial CTP in a porcine ischemia model with different degrees of coronary occlusion using a balloon catheter. The occlusion severity was adjusted with fractional flow reserve (FFR) measurements. The SDCT scanner is a single source, dual-layer detector system, which allows simultaneous acquisitions of low and high energy projections, hence enabling accurate projection-based material decomposition and effective reduction of BH-artifacts. In addition, the SDCT scanner eliminates partial scan artifacts with fast (0.27s), full gantry rotation acquisitions. We acquired CTP data under different hemodynamic conditions and reconstructed conventional 120kVp images and projection-based monoenergetic (monoE) images for energies ranging from 55keV-to-120keV. We computed and compared myocardial blood flow (MBF) between different reconstructions. With balloon completely deflated (FFR=1), we compared the mean attenuation in a myocardial region of interest before iodine arrival and at peak iodine enhancement in the left ventricle (LV), and we found that monoE images at 70keV effectively minimized the difference in attenuation, due to BH, to less than 1 HU compared to 14 HU with conventional 120kVp images. Flow maps under baseline condition (FFR=1) were more uniform throughout the myocardial wall at 70keV, whereas with 120kVp data about 12% reduction in blood flow was noticed on BH-hypoattenuated areas compared to other myocardial regions. We compared MBF maps at different keVs under an ischemic condition (FFR < 0.7), and we found that flow-contrast-to-noise-ratio (CNR_f) between LAD ischemic and remote healthy territories attains its maximum (2.87 ± 0.7) at 70keV. As energies diverge from 70keV, we

noticed a steady decrease in CNR_f and an overestimation of mean-MBF. Flow overestimation was also noticed for conventional 120kVp images in different myocardial regions.

Keywords

Myocardial CT perfusion; spectral detector CT; beam hardening; mono-energetic images; FFR

1. INTRODUCTION

Cardiovascular disease accounted for one third of all deaths in 2007 and claims more lives each year in the US than cancer, respiratory disease, accidents, and diabetes combined^{1, 2} with a projected cost of 182 billion for 2015 and 322 billion in 2030. A reasonable percentage of this cost relates to efforts for imaging and screening for disease. Cardiac CT imaging provides comprehensive assessments, including the ability to image reliably coronary artery stenosis non-invasively. The correlation between anatomic stenosis, often detected by CT angiography (CTA), and functional myocardial ischemia is poor,³ leading to a large number of unnecessary invasive coronary angiographs (ICA) and coronary re-vascularization. One report estimates that less than 40% of patients who underwent elective ICA had confirmed significant CAD.⁴ Current guidelines for stable CAD recommend documenting ischemia with a non-invasive functional test (e.g., SPECT, stress echocardiography, or cardiac MRI) before ICA and re-vascularization are considered.

Computed tomography has the potential of becoming the modality of choice for a single non-invasive test targeting both the detection and exclusion of coronary stenoses and the assessment of myocardial perfusion. The feasibility of CTP has been demonstrated in several animal and clinical studies and its accuracy was compared to existing standard exams such as SPECT and MR.⁵⁻⁸ However, there are significant challenges to the clinical use of myocardial CTP, including high dose radiation from dynamic scanning; shading artifacts from fast imaging with partial angular coverage; and beam hardening (BH) artifacts arising from dense iodinated material in the aorta and heart chambers and the polychromatic nature of x-ray beam used in conventional single energy CT (SECT). If uncorrected, these artifacts, in particular BH artifacts, can significantly affect the accuracy of perfusion measurements.

New, evolving CT technologies address these challenges. Large multi-detector arrays and high-speed gantry rotation enable full 360 degree volumetric imaging of the heart. Different image-based methods have been proposed to correct BH artifacts in images acquired using conventional SECT scanners.⁹⁻¹¹ These methods rely on the segmentation of high (bone and iodine) and low (soft tissue) attenuating materials and on the estimation of iodine concentration. Since the reconstructed images are pre-corrected for water BH artifacts, neither the segmentation of high and low-attenuating materials nor the estimation of iodine concentration is accurate. This leads to suboptimal BH corrections. Dual energy CT has the potential to effectively address the BH artifacts by synthesizing monoE images either in the attenuation or in the projection space. Such an image depicts how the scanned object would appear if only a monochromatic x-ray beam was used for scanning. There exist different

technologies to acquire energy sensitive CT data, including single x-ray source with two switching kVps (e.g., 80kVp and 140kVp) and dual source systems with conventional CT detectors. Here, we used a prototype of a single source, dual-layer spectral detector system. This system uses a single kVp and detects radiation using dual-layer detectors which discriminate between high and low x-ray photons simultaneously. This simultaneous acquisition of high and low energy data results in accurate material decomposition and BH corrections in the projection space.¹²

In this work, we report the results of our initial investigation on the use of a prototype spectral CT detector (SDCT) system (Philips Healthcare, Cleveland, OH) for quantitative myocardial CT perfusion using an elegant percutaneous porcine model. This model was used to simulate low to high-grade stenoses guided by fractional flow reserve (FFR) measurements. We quantified myocardial blood flow using synthesized projection-based monoE images at different energies. We analyzed how BH artifact reduction and other monoE image characteristics (e.g., noise and iodine signal) affect the perfusion measurements. Results were compared against those obtained using conventional SECT images.

2. MATERIALS AND METHODS

2.1 SDCT system and generation of monoE images

The SDCT system is a single source dual-layer system which uses one x-ray source to expose two sandwiched scintillator layers directly placed on top of one another. The top layer absorbs low-energy x-ray photons, while the bottom layer detects the remaining higher-energy x-ray photons.^{13, 14} Hence, two signals are detected. Each one of these signals corresponds to an x-ray spectrum with a specific mean energy. Separation of the low and high-energy spectra is maximized using optimized atomic number and thickness of the top detector. The low and high-projection energy data acquired with the SDCT system are perfectly registered with each other both spatially and temporally. This allows for material decomposition and BH correction to be accurately performed in the projection domain. The prototype SDCT used in this study allows fast (0.27s) full 360 degree coverage which eliminates shading artifacts often arising from partial scans (180 degree+fan beam angle) that are usually adopted to improve temporal resolution.

Mono-energetic images can be generated either in the projection or in the image domain. In this work, only projection-based monoE images were used. In DECT, the contribution of the photoelectric and Compton scatter effects along each projection path is determined by collecting attenuation measurements at two different energies.¹⁵ Within the diagnostic x-ray energy range, this decomposition is equivalent to the two basis material decomposition which expresses the linear attenuation coefficient of a voxel, at a given energy, as a linear combination of the mass attenuation coefficients of two basis materials with distinct atomic numbers (e.g., water and iodine) at the same energy.¹⁶ The two collected set of attenuation measurements with the known relationship of mass-attenuation coefficients as a function of energy are used to solve for the densities of the two basis materials. The resulting sinograms are then de-noised and corrected for BH artifacts. Conventional reconstruction techniques are then used to reconstruct density maps for the two basis materials which are subsequently

used to synthesize monoE images through linear combinations.¹⁶ Examples of monoE images are shown on Fig. 1 for an ischemic pig scan at energies 60, 70, and 100keV. It is worth noting that the conventional images were obtained at precisely the same time by combining readings from the two detector layers, which facilitates CTP comparisons.

2.2 Animal model and Imaging protocol

The animal study was approved by the Institutional Animal Care and Use Committee. We created an elegant closed-chest pig model with a percutaneously delivered balloon in the left anterior descending (LAD) coronary artery used to obstruct blood flow. Young female country pigs (age: 12 weeks; weight: $40 \pm 4\text{kg}$) were procured from local vendors. During each experiment, the induced narrowing of the LAD artery was monitored by FFR measurements to achieve targeted levels of ischemia. Red and green colored fluorescent microspheres were injected into the LV cavity and a reference blood sample was collected at a constant rate, before balloon implantation for baseline flow, and with balloon inflated to the target $FFR \sim 0.7$, respectively. The animal was then transported to the CT facility under a portable ventilator in order to acquire dynamic CT scans under different hemodynamic conditions. At the end of the scanning process, we excised the heart and froze it for subsequent slicing and cryoimaging with the CryoVizTM fluorescent microscope in order to compute standard reference microsphere-based blood flow. These measurements will not be included in this paper. For each animal and each hemodynamic condition, 30-to-35 dynamic CT volumetric images were acquired once every heartbeat using prospectively ECG-triggering for a period of about 22–25sec. At least three hemodynamic conditions were considered: baseline ($FFR=1$), mild ischemia ($0.65 < FFR < 0.8$), and severe ischemia ($FFR < 0.4$). Contrast enhanced perfusion images were acquired at end systole (45% R-R) using 20mL of iodine (Omnipaque 350mgI/mL) flushed by 20mL of saline at 5mL/sec. Acquisitions are initiated 4–6sec post injection of the iodinated contrast. Full 360 degree acquisitions were used to eliminate shading artifacts. At least fifteen minutes were allowed between every two consecutive scans for a better iodine wash out from the heart chambers. Scans were acquired with 120kVp tube voltage and 100mAs tube current. The effective dose (mSv), for our dynamic CTP protocol, can be estimated using dose-length product (DLP) multiplied by a conversion coefficient for the chest ($k = 0.014 \text{ mSv.mGy}^{-1}.\text{cm}^{-1}$),¹⁷ where DLP (mGy.cm) was calculated as the product of CTD_{vol} by the z-coverage of the SDCT scanner (4cm). Depending on the number of acquired scans per sequence, the total dose radiation ranged from 15.2-to-17.6 mSv.

3. IMAGE PREPROCESSING AND MBF QUANTIFICATION

We designed and implemented a comprehensive image processing and blood flow quantification pipeline. Processing includes 3D elastic image registration, segmentation of the LV myocardium, and SVD-based deconvolution for MBF estimation.

*<http://www.bioinvision.com>

3.1 Motion artifact correction

In order to minimize motion artifacts due to breathing, CTP scans were acquired with the respirator turned off. However, misregistration between the acquired volumes per each cardiac cycle may occur due to irregular heartbeats and/or to poor ECG synchronization. Such misalignments between corresponding voxels over time result in inaccurate arterial and myocardial time attenuation curves (TACs) which in turn lead to inaccurate flow estimations. To correct these artifacts, we used a volumetric elastic registration method based on 3D cubic B-splines and normalized mutual information (NMI) to align the 3D volumes to a common reference time point. The NMI metric was chosen to cope with the dramatic change of the image intensity over time due to contrast kinetics. A multi-resolution approach and a multi-core implementation were adopted for speed.^{18, 19}

3.2 Left ventricular (LV) myocardium segmentation

For each condition, we used the registered 3d scans to create an average volumetric CT map and used it to segment the LV myocardium either manually or semi-automatically using a research version of the QMass software by Medis[†]. The average CT map volume has very low noise level and high contrast between the two ventricular chambers as can be seen on Fig.2-A. This renders the delineation of the LV myocardium easy and accurate. Since all volumes are aligned with each other, the same generated mask was used to isolate the LV myocardium in all volumes and all reconstructions. Different regions of interest (ROI) were manually or automatically selected on different myocardial segments (see Fig. 2-B) for analysis and comparisons of quantified blood flow.

3.3 Myocardial blood flow quantification

We used a model-independent deconvolution approach with block-circulant singular value decomposition (bSVD) to quantify MBF. For each animal and each hemodynamic condition, we obtained a series of *NECG*-triggered volumetric images of the heart. The mean time interval between successive scans is noted Δt . According to induction-dilution theory, the contrast concentration in the myocardial tissue, $C(t)$, and the arterial contrast concentration, $C_{art}(t)$, are related through the following convolution²⁰

$$C(t) = F \cdot C_{art}(t) * R(t), \quad (1)$$

where, F is the absolute blood flow, $R(t)$ is the impulse residue function (IRF) and $*$ denotes the convolution operator. The above equation is solved for the flow-scaled IRF, $R_F(t) = F \cdot R(t)$, through a deconvolution process and the absolute flow is determined as $F = \max_t(R_F(t))$. We discretized the integral equation 1 into a system of linear equations using the measured concentration-time curves $C(t)$ and $C_{art}(t)$ at time points $t_i = i \cdot \Delta t$ for $i = 1, \dots, N$. The discretized system can be written in a matrix form as $Ax = b$, where the N -element vector b is defined as $b_i = C(t_i)$ and the $N \times N$ matrix is given by²¹

[†]<http://www.medis.nl/>

$$a_{ij} = \begin{cases} \Delta t \cdot C_{art}(t_i - j - 1) & \text{for } 0 \leq j \leq i \\ 0 & \text{for } j > i, \end{cases}$$

In order to reduce the influence of the time shifts between the measured arterial and myocardial TACs, we used circular instead of linear discretization of equation 1. In this case, the matrix A above is transformed to a block-circulant matrix of size $M = 2N$ assembled using zero-padded time series $C_{art}(t)$ as was explained in.²¹

We used SVD decomposition of the matrix A as $A = U \cdot \Sigma \cdot V^T$ to determine the solution of the above discretized system, where the diagonal matrix $\Sigma = \text{diag}(\sigma_1, \dots, \sigma_N)$ contains the singular values σ_i in a non-increasing order and $U = [u_1, \dots, u_N]$ and $V = [v_1, \dots, v_N]$ are unique orthogonal matrices. The corresponding solution is given by

$$x = \sum_{i=1}^N \left(\frac{u_i^T \cdot b}{\sigma_i} \right) \cdot v_i.$$

This solution is equivalent to minimizing the following least-squares problem

$$x = \underset{x}{\operatorname{argmin}} \left(\|Ax - b\|_2^2 \right). \quad (2)$$

Note that the matrix A is ill-conditioned making the solution very sensitive to noise in the measured data. In order to reduce the effects of small singular values due to noise and to obtain a numerically stable solution, we used Tikhonov regularization.²² This consists of adding the L2-norm of the solution or that of its derivatives as a constraint to the minimization problem 2

$$x = \underset{x}{\operatorname{argmin}} \left(\|Ax - b\|_2^2 + \|Lx\|_2^2 \right),$$

where λ is the regularization parameter and the matrix L is either equal to the identity matrix or is an approximation of the 1st or 2nd order derivative operator.^{22–24}

The selection of an optimal value of λ is crucial since it directly affects the computed flow. A small λ will lead to a noisy solution and a large λ will result in a bad approximation of the solution. In this work, we used an automated approach to determine the optimal regularization parameter using the L-curve criterion (LCC).^{22–24} The L-curve is a log-log plot of the constraint norm $\|Lx\|_2$ versus the residual norm $\|Ax - b\|_2$ for various values of λ , as shown by the schematic plot on Fig. 3. The corner point of the corresponding curve (the point on the curve with maximum curvature) corresponds to the optimal λ .

4. RESULTS AND DISCUSSION

We compared CTP measurements using monoE and conventional images in pig perfusion experiments. Results are expressed as mean $\pm$ standard deviation and differences were compared using paired Student t-test in Matlab. A p-value ≤ 0.05 was considered to indicate statistical significance.

Figure 4 shows two different axial slices corresponding to the conventional 120kVp and the 70keV monoE average CT volume respectively, under the baseline condition (FFR=1). In this case, one should expect a relatively uniform enhancement on the non-ischemic myocardium. However, due to BH artifacts, clear hypoenhancements are noticed in the anterior and inferior walls in the conventional images as indicated by the black arrows on top row of Fig. 4. These artifacts can be mis-diagnosed as perfusion defects. On the other hand, these BH-induced hypoattenuations were significantly reduced on the 70keV images resulting in a relatively more uniform enhancement of the entire myocardium. Comparing attenuation in an anterior wall ROI, between the first time frame when iodine hasn't arrived yet in the LV and at peak iodine enhancement in the LV, we found that 70keV images effectively reduced the difference in mean attenuation in this ROI to less than 1 HU compared to 14 HU in conventional 120kVp images. Hyper-attenuation in the septal wall seen on the 120kVp image (red arrow on top row of Fig. 4) is also an effect of BH which was significantly minimized in the 70keV image. This effect was noticed in previous CT perfusion studies using a myocardium tissue phantom (see²⁵). BH artifacts in anterior and inferior walls in the 120kVp images lead to distorted tissue TACs. The deconvolution of these curves resulted in underestimation of flow as indicated by the red arrows on Fig. 5. For instance, for the baseline scan, mean relative flow over 15 adjacent slices measured as the mean flow ratio between an ROI in the LAD and an ROI in the lateral wall, was (0.98 ± 0.04) for 70keV vs. (0.88 ± 0.06) for 120kVp data. This shows clearly that 70keV-based flow is more uniform throughout the myocardium. The decrease in flow in BH-affected areas was also seen on the ischemic flow maps as shown on the bottom row of Fig. 5 (red arrow). One can also notice from these maps that on the septal and the lateral walls, flow is overestimated on conventional images compared to 70keV images (magenta arrows). This can be attributed to BH effects as well as to increased noise levels in the conventional data.

It is worth mentioning that we were able to detect MBF deficits in the correct LAD territory on both the 120kVp and the 70keV flow maps as shown on Fig. 5 (bottom row). However, there are clear flow differences in different myocardial walls between the conventional and the monoE maps. These differences are even exacerbated when we consider other keVs due in part to high noise levels and residual BH for lower keVs and to noise and low iodine signal for higher keVs. In order to evaluate these differences in flow as a function of monochromatic energy, we computed and compared the flow-contrast-to-noise-ratio, or CNR_f , between the ischemic and healthy myocardial regions as follows. Two equally sized ROIs were manually drawn in the ischemic LAD (e.g., anterior wall) and remote areas (e.g., mid- or inferolateral wall) and similarly used for all reconstructions. The flow-CNR is given by

$$CNR_f = \frac{\mu_{MBF}(LAD) - \mu_{MBF}(remote)}{\sigma_{MBF}(remote)}, \quad (3)$$

where, $\mu_{MBF}(roi)$ and $\sigma_{MBF}(roi)$ refer to mean and standard deviation of flow in selected ROI, respectively.

We computed CNR_f for energies ranging from 55keV-to-120keV and averaged the results over 15 adjacent slices of the heart. The corresponding results are shown on Fig. 6. As the monochromatic energy diverges from 70keV, we noticed a steady drop in CNR_f with a maximum mean value of (2.87 ± 0.70) attained at 70keV.

We also noticed steady overestimation of blood flow, both in LAD and remote myocardial tissue for higher energies. For instance, from a baseline scan (FFR=1) the mean MBF (in mL/min/100g) on an LAD ROI was (100.47 ± 19) for 70keV vs. $(120.15 \pm 28.16; p = 1.3e - 06)$ for 90keV and $(185.88 \pm 45.57; p = 3.8e - 15)$ for 120keV. This increase in flow mean and standard deviation with keV is mainly due to poor iodine signal at higher energies.

Results presented herein correspond to a single pig experiment. More data has been collected since the preparation of this manuscript and its analysis is underway and will be included in future publications. We will also validate the quantified flow against microsphere-based flow measurements.

5. CONCLUSION

We presented the first dynamic myocardial CT perfusion study using a percutaneous porcine model and a prototype dual-layer spectral detector CT scanner (Philips Healthcare). We showed how the SDCT scanner, through the synthesis of monoE images, helps reduce some of the artifacts often seen on perfusion scans acquired with conventional single energy CT scanners. In particular, we showed how beam hardening artifacts may lead to inaccurate flow measurements in the conventional data. We showed how myocardial blood flow quantification changes with monochromatic energy and how it compares to flow measurements using conventional CT data. A well designed image processing pipeline was implemented to quantify myocardial blood flow. Our preliminary results suggest that projection-based monoE images at 70keV offer optimal myocardial perfusion measurements compared with other monoE images as well as with conventional 120kVp images.

Acknowledgments

This research project is sponsored by an Ohio Third Frontier research grant from the state of Ohio to CWRU, University Hospitals of Cleveland, and Philips Healthcare. We would like to thank Dr. Steve J. Schomisch and Cassandra Cipriano from the department of Surgery at CWRU, for their tremendous help with the animal experiments, and Scott Esposito from Radiology for his help with the scanning process.

REFERENCES

1. Cook S, Walker A, Hügli O, Togni M, and Meier B, "Percutaneous coronary interventions in europe," *Clinical research in cardiology* 96(6), pp. 375–382, 2007. [PubMed: 17453137]

2. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, et al., "Heart disease and stroke statistics 2011 update a report from the American heart association," *Circulation* 123(4), pp. 18–209, 2011.
3. Tonino PA, Fearon WF, De Bruyne B, Oldroyd KG, Leeser MA, Ver Lee PN, McCarthy PA, van't Veer M, and Pijls NH, "Angiographic versus functional severity of coronary artery stenoses in the fame study: fractional flow reserve versus angiography in multivessel evaluation," *Journal of the American College of Cardiology* 55(25), pp. 2816–2821, 2010. [PubMed: 20579537]
4. Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, Brindis RG, and Douglas PS, "Low diagnostic yield of elective coronary angiography," *New England Journal of Medicine* 362(10), pp. 886–895, 2010. [PubMed: 20220183]
5. Blankstein R, Shturman LD, Rogers IS, Rocha-Filho JA, Okada DR, Sarwar A, Soni AV, Bezerra H, Ghoshhajra BB, Petranovic M, et al., "Adenosine-induced stress myocardial perfusion imaging using dual-source cardiac computed tomography," *Journal of the American College of Cardiology* 54(12), pp. 1072–1084, 2009. [PubMed: 19744616]
6. Schwarz F, Hinkel R, Baloch E, Marcus RP, Hildebrandt K, Sandner TA, Kupatt C, Hoffmann V, Wintersperger BJ, Reiser MF, et al., "Myocardial ct perfusion imaging in a large animal model: comparison of dynamic versus single-phase acquisitions," *JACC: Cardiovascular Imaging* 6(12), pp. 1229–1238, 2013. [PubMed: 24269264]
7. Rocha-Filho JA, Blankstein R, Shturman LD, Bezerra HG, Okada DR, Rogers IS, Ghoshhajra B, Hoffmann U, Feuchtner G, Mamuya WS, et al., "incremental value of adenosine-induced stress myocardial perfusion imaging with dual-source ct at cardiac ct angiography1," *Radiology* 254(2), pp. 410–419, 2010. [PubMed: 20093513]
8. Feuchtner G, Goetti R, Plass A, Wieser M, Scheffel H, Wyss C, Stolzmann P, Donati O, Schnabl J, Falk V, et al., "Adenosine stress high-pitch 128-slice dual-source myocardial computed tomography perfusion for imaging of reversible myocardial ischemia comparison with magnetic resonance imaging," *Circulation: Cardiovascular Imaging* 4(5), pp. 540–549, 2011. [PubMed: 21862731]
9. So A, Hsieh J, Li J-Y, and Lee T-Y, "Beam hardening correction in ct myocardial perfusion measurement," *Physics in medicine and biology* 54(10), p. 3031, 2009. [PubMed: 19398817]
10. Stenner P, Schmidt B, Bruder H, Flohr T, and Kachelriess M, "Partial scan artifact reduction (psar) for the assessment of cardiac perfusion in dynamic phase-correlated ct," in *Nuclear Science Symposium Conference Record*, 2008. NSS'08. IEEE, pp. 5203–5209, IEEE, 2008.
11. Hsieh J, Molthen RC, Dawson CA, and Johnson RH, "An iterative approach to the beam hardening correction in cone beam ct," *Medical physics* 27(1), pp. 23–29, 2000. [PubMed: 10659734]
12. Heismann BJ, Schmidt BT, and Flohr T, "Spectral computed tomography," *SPIE*, 2012.
13. Carmi R, Naveh G, and Altman A, "Material separation with dual-layer ct," in *Nuclear Science Symposium Conference Record*, 2005 IEEE, 4, IEEE, 2005.
14. Shefer E, Altman A, Behling R, Goshen R, Gregorian L, Roterman Y, Uman I, Wainer N, Yagil Y, and Zarchin O, "State of the art of ct detectors and sources: a literature review," *Current Radiology Reports* 1(1), pp. 76–91, 2013.
15. Alvarez RE and Macovski A, "Energy-selective reconstructions in x-ray computerised tomography," *Physics in medicine and biology* 21(5), p. 733, 1976. [PubMed: 967922]
16. Lehmann L, Alvarez R, Macovski A, Brody W, Pelc N, Riederer S, and Hall A, "Generalized image combinations in dual kvp digital radiography," *Medical physics* 8(5), pp. 659–667, 1981. [PubMed: 7290019]
17. Gramer B, Muenzel D, Leber V, von Thaden A-K, Feussner H, Schneider A, Vembar M, Soni N, Rummeny E, and Huber A, "Impact of iterative reconstruction on cnr and snr in dynamic myocardial perfusion imaging in an animal model," *European radiology* 22(12), pp. 2654–2661, 2012. [PubMed: 22752461]
18. Fahmi R, Eck BL, Vembar M, Bezerra HG, and Wilson DL, "Dynamic ct myocardial perfusion imaging: detection of ischemia in a porcine model with ffr verification," in *SPIE Medical Imaging*, International Society for Optics and Photonics, 2014.
19. Fahmi R, Eck BL, Vembar M, Bezerra HG, and Wilson DL, "Dose reduction assessment in dynamic ct myocardial perfusion imaging in a porcine balloon-induced-ischemia model," in *SPIE Medical Imaging*, International Society for Optics and Photonics, 2014.

20. Zierler K, "Indicator dilution methods for measuring blood flow, volume, and other properties of biological systems: a brief history and memoir," *Annals of biomedical engineering* 28(8), pp. 836–848, 2000. [PubMed: 11144667]
21. Fieselmann A, Kowarschik M, Ganguly A, Hornegger J, and Fahrig R, "Deconvolution-based ct and mr brain perfusion measurement: theoretical model revisited and practical implementation details," *Journal of Biomedical Imaging* 2011(14), pp. 1–20, 2011.
22. Hansen PC, "Deconvolution and regularization with toeplitz matrices," *Numerical Algorithms* 29(4), pp. 323–378, 2002.
23. Jerosch-Herold M, Swingen C, and Seethamraju RT, "Myocardial blood flow quantification with mri by model-independent deconvolution," *Medical physics* 29(5), pp. 886–897, 2002. [PubMed: 12033585]
24. Koh T. and Hou Z, "A numerical method for estimating blood flow by dynamic functional imaging," *Medical engineering & physics* 24(2), pp. 151–158, 2002. [PubMed: 11886835]
25. So A, Hsieh J, Li J-Y, Hadway J, Kong H-F, and Lee T-Y, "Quantitative myocardial perfusion measurement using ct perfusion: a validation study in a porcine model of reperfused acute myocardial infarction," *The International Journal of Cardiovascular Imaging* 28(5), pp. 1237–1248, 2012. [PubMed: 21800119]

Figure 1:

Examples of projection-based monoE images (60keV, 70keV, and 100keV). Shown is same slice corresponding to a mild ischemic case at peak enhancement in the LV chamber. W/L: 150HU/80HU.

Figure 2:

(A) Average CT map generated by averaging the aligned volumes in the corresponding 4D sequence. High contrast between the right and left heart chambers facilitates the delineation of the LV myocardium (enclosed by red and green contours). (B) Nomenclature of different myocardial walls shown on slice corresponding to an ischemic condition.

Figure 3:

Schematic illustration of the L-curve. A log-log plot of constraint norm $\|Lx\|_2$ vs. residual norm $\|Ax - b\|_2$ for different values of λ . A smooth spline (red curve) is then fitted to the obtained data points (black circles). The optimal regularization parameter λ , is identified by the location on the L-curve where the fitting spline has maximum curvature (red solid triangle).

Figure 4:

Two different slices from an average baseline (FFR=1.0) CT map. Top: 120kVp reconstruction, Bottom: 70keV monoE reconstruction. Dark areas due to BH clearly seen in 120kVp images (black arrows). Hyperenhancement in septal wall (red arrow) is also the result of BH effects.²⁵ The BH artifacts were significantly reduced on the 70keV images. Same W/L: 60/40.

Figure 5:
2D color-coded MBF maps in the LV myocardium overlaid on corresponding CT slice. Shown are maps corresponding to a baseline (Top) and an ischemic (Bottom) case for conventional 120kVp (Left) and 70keV (Right) data.

Figure 6:
Mean flow-CNR as a function of monochromatic energy for an ischemic condition with FFR 0.7.