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Impact of iterative reconstruction on CNR and SNR in dynamic myocardial perfusion imaging in an animal model

B. M. Gramer · D. Muenzel · V. Leber · A.-K. von Thaden · H. Feussner · A. Schneider · M. Vembar · N. Soni · E. J. Rummeny · A. M. Huber

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Abstract
Objectives To evaluate a new iterative reconstruction (IR) algorithm for radiation dose, image quality (IQ), signal-to-noise-ratio (SNR), and contrast-to-noise-ratio (CNR) in multidetector computed tomography (MDCT) dynamic myocardial perfusion imaging (MPI).
Methods ECG-gated 256-slice MDCT dynamic MPI was performed in six pigs after subtotal balloon occlusion of one artery. Two 100 kVp protocols were compared: high dose (HD): 150 mAs; low dose (LD): 100 mAs. HD images were reconstructed with filtered back projection (FBP), LD images with FBP and different strengths of IR (L1, L4, and L7). IQ (5-point scale), SNR, and CNR (ischemic vs. normal myocardium) values derived from the HD (FBP) images and the different LD images were compared.
Results Mean SNR values for myocardium were 16.3, 11.3, 13.1, 17.1, and 28.9 for the HD, LD (FBP), LD (L1), LD (L4), and LD (L7) reconstructions, respectively. Mean CNR values were 8.9, 6.3, 7.8, 9.3, and 12.8. IQ was scored as 4.6, 3.3, 4.4, 4.7, and 3.4, respectively. A significant loss of IQ was observed for the LD (L7) images compared to the HD (FBP) images ($P<0.05$).
Conclusion Appropriate levels of iterative reconstruction can improve SNR and CNR, facilitating radiation dose savings in CT-MPI without influencing diagnostic quality.
Key Points
- *Iterative reconstruction (IR) can reduce radiation dose in myocardial perfusion CT.*
- *Our study also demonstrated improvements in image quality (noise, SNR, and CNR).*
- *Dynamic CT-MPI could help determine the hemodynamic significance of coronary artery disease.*
- *With dynamic CT MPI, myocardial blood flow can be determined quantitatively.*

Keywords Dynamic myocardial perfusion · Radiation dose · Iterative reconstruction · MDCT · Ischemia

Abbreviations

CCTA	Coronary CT angiography
CNR	Contrast-to-noise ratio
CT	Computed tomography

B. M. Gramer (✉) · D. Muenzel · V. Leber · E. J. Rummeny · A. M. Huber
Institut für Radiologie,
Klinikum rechts der Isar der Technischen Universität München,
Ismaningerstrasse 22,
81675 München, Deutschland
e-mail: bettina.gramer@tum.de

A.-K. von Thaden
ZPF - Zentrum für präklinische Forschung des Klinikum rechts der Isar der Technischen Universität München,
Ismaningerstrasse 22,
81675 München, Deutschland

H. Feussner · A. Schneider
Research Group MITI des Klinikums rechts der Isar der Technischen Universität München,
München, Deutschland

M. Vembar
Clinical Science (Computed Tomography), Philips Healthcare,
Cleveland, OH, USA

N. Soni
Physics (Computed Tomography), Philips Healthcare,
Cleveland, OH, USA

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FBP	Filtered back projection
HD	High dose
IQ	Image quality
IR	Iterative reconstruction
LD	Low dose
MDCT	Multidetector CT
MPI	Myocardial perfusion imaging
ROI	Region of interest
SNR	Signal-to-noise ratio

Introduction

There are increasing apprehensions about diagnostic radiation exposure and the potential increased incidence of radiation-introduced carcinogenesis [1]. Manufacturers have developed several methods to reduce radiation exposure during CT examinations. For instance, in cardiac CT, ECG-based tube current modulation, prospectively ECG-triggered acquisition, and reduction of tube voltage are among the most commonly used methods for dose reduction [2].

Although radiation dose reductions can be achieved by reducing tube potential (kVp) or current (mAs), the limitations of the conventional reconstruction technique, i.e., filtered back projection (FBP), result in increased image noise and consequently impact diagnostic image quality (IQ) [3]. Recently, newer iterative reconstruction (IR) techniques have been developed that help address these shortcomings. First introduced in the field of nuclear medicine, IR techniques demonstrated an improvement of IQ, mostly demonstrated by an increased contrast-to-noise ratio (CNR) [4, 5]. These techniques have now been extended to CT and have facilitated noise reduction and improvements in CNR and signal-to-noise ratio (SNR) [3, 6–13].

A newer hybrid IR technique (iDose^4, Philips Healthcare, Cleveland, OH, USA) was recently introduced, the performance characteristics of which have been investigated in detail in previous papers [14]. Early clinical investigations using this IR have shown IQ improvements at reduced radiation dose in coronary CT angiography (CCTA) [15]. In this investigation, we aimed to study the impact of this IR technique on IQ and radiation dose in dynamic myocardial perfusion imaging (MPI) in an animal model using a 256-slice multidetector CT (MDCT). The aim was (1) to quantify the possible improvement in IQ by reduction of image noise and increase in SNR and CNR of normal and ischemic myocardium, (2) to assess subjective IQ by two readers, and (3) to examine radiation dose savings. We hypothesise that the use of IR in image reconstructions from a low-dose (LD) CT protocol provides image quality comparable to that of a high dose (HD) protocol with images reconstructed with FBP, while facilitating radiation dose reductions.

Materials and methods

Animal preparation and interventional induction of myocardial ischemia

Our prospective study was permitted by the regional governmental commission for animal protection. A total of six female Landrace pigs with a mean body weight of 38 kg (range 30–42 kg) were examined. In all animals myocardial ischemia was interventionally induced before CT perfusion analysis. A 7 F introducer (100 mm Radfocus Introducer II; Terumo, Tokyo, Japan) was positioned in the right carotid artery after surgical access by a veterinarian. The tip of the catheter was positioned in the proximal left main coronary artery. An undersized balloon was positioned in the middle segment of the LAD, the second diagonal branch, or the circumflex artery using a 0.014 inch guide wire. Subtotal occlusion of the coronary artery was induced by dilatation of a balloon (1.5–2.5 mm diameter) just before CT perfusion was started. CT examinations of the heart were performed with the animals under deep general anaesthesia with endotracheal intubation and controlled ventilation.

CT protocol

Myocardial perfusion imaging (MPI) was performed using 256-slice MDCT (Brilliance iCT, Philips Healthcare, Cleveland, OH) in order to visualise myocardial perfusion deficits. CT imaging was started within 10 s after balloon dilatation. Perfusion imaging was arranged during pharmacologically induced stress. Adenosine infusion (Adenoscan, Sanofi-Aventis Frankfurt, Germany) was started at least 3 min before the CT examination and continued during the CT data acquisition at a dose of 240 μg/kg/min. MPI was performed without table movement during an end-expiratory breath-hold in all pigs. A fixed volume of 40 mL of contrast agent (Imeron 400 MCT, Bracco Imaging Deutschland, Konstanz, Germany) was injected at a flow rate of 4 ml/s into an ear vein via an 18-gauge intravenous access using a dual syringe injection system (Stellant, MEDRAD, Indianola, PA). The contrast bolus was followed by 40 mL saline solution. Data acquisition was started in time with application of the contrast agent in order to obtain several unenhanced baseline images of the myocardium. ECG-gated dynamic CT images with zero table increment were acquired at end-systole centered at 40% of the RR interval. Images were acquired during 30 consecutive cardiac cycles covering an anatomical length corresponding to the full detector collimation of 80 mm in *z*-axis, sufficient to cover the left ventricle. The CT parameters were as follows: detector collimation of 64×1.25 mm; x-ray tube voltage of 100 kVp; tube current–time product of 150 mAs for HD acquisition and 100 mAs for LD acquisition; gantry rotation time of 0.27 s resulting in a standard temporal resolution of 135 ms; field of view (FOV) of 250 mm.

CT image reconstruction

Transverse images were reconstructed using conventional FBP for HD scans and FBP and a new IR technique for LD CT. The new IR technique used in this study is a hybrid implementation that uses multi-frequency noise removal techniques to help reduce noise uniformly across the entire frequency range, while at the same time maintaining the natural look of the image [14]. For a given tube output, this IR technique could reduce noise anywhere between 10 and 55% depending on the setting (level) used. Seven different levels of the IR setting (L1–L7) are provided by the manufacturer, which provide various levels of noise reduction for a given tube output [noise reduction ranging from 11% (L1) to 55% (L7)] [14].

In our study, we used the IR levels L1, L4, and L7 (1: lowest noise reduction, 4: medium noise reduction, 7: maximum noise reduction). All cross-sectional images were reconstructed with a slice thickness of 3.0 mm at 3.0 mm increments.

Quantitative image analysis

Data sets were transferred to a custom myocardial perfusion analysis postprocessing workstation (Extended Brilliance Workspace, version 4.5, Philips Healthcare, Cleveland, OH, USA). The time point of peak enhancement in normal myocardium was determined. The data set at this time point was selected for further evaluation. A region of interest (ROI) of 1 cm^2 was manually drawn in the ischemic area. Equally sized ROIs were drawn in two remote areas in the inter-ventricular septum and the lateral wall of the left ventricular chamber. The measurements were done identically for all reconstructions. To obtain quantitative parameters of image quality for the myocardial perfusion deficits, image noise as well as CNR and SNR were determined for each data set according to the previously described methods. Image noise was defined as the average standard deviation of the ROIs located in normal myocardium. CNR was determined by dividing the difference between the mean value obtained from the ROIs in the normal myocardium and the mean value obtained from the ROI in the ischemic myocardium by the image noise.

$$CNR = \frac{(Mean\ of\ the\ normal\ myocardium - Mean\ of\ the\ ischemic\ myocardium)}{Standard\ deviation\ of\ the\ normal\ myocardium}$$

SNR was determined by dividing the mean value of an ROI by the image noise of the same ROI.

$$SNR(for\ normal\ myocardium) = \frac{Mean\ of\ normal\ myocardium}{Standard\ deviation\ of\ the\ normal\ myocardium}$$

Qualitative image analysis

Qualitative image quality was evaluated by two radiologists using a 5-point Likert scale (modified according to Muenzel et al. [16]) for each different reconstructed data set comparing the normal myocardium, the septum, and the ischemic area on transverse images. All of the reconstructed data sets were de-identified without any designation of the iDose level. The rankings along with their definitions are shown in Table 1. After blinded review of all data sets, each reader assigned a Likert score for each data set on the basis of preferred image quality, with the focus on detail resolution and oversmoothing effects. The readers were instructed to ignore issues, such as motion or contrast, that could not be ascribed to the reconstruction algorithm. The mean score for all three areas was used as the final ranking for each animal. Both readers independently adjusted the optimum window setting for the assessment of the qualitative image quality.

Radiation dose

The effective dose (mSv) was estimated using dose-length product (DLP) multiplied by a conversion coefficient for the chest ($k=0.014\ mSv \cdot mGy^{-1} \cdot cm^{-1}$) [17].

Table 1 Grading scale for the qualitative image quality

Rating	Definition
5	Excellent image quality
4	Good image quality
3	Moderate image quality
2	Fair, evaluable
1	Not evaluable

Statistical analysis

All data are expressed as mean value ± standard deviation. Statistical analyses were performed using commercially available software (Microsoft® Excel® for Mac 2011, version 14.1.0 and Medcalc 7.2.0.2, MedCalc Software, Mariakerke, Belgium). Differences in quantitative IQ parameters (CNR and SNR) between the different scanning protocols and reconstruction techniques were compared using a two-tailed, paired Student's *t*-test. Differences in the subjective IQ were compared using a Mann-Whitney-Wilcoxon test. A *p*-value ≤ 0.05 was considered to indicate a statistical significance.

Results

Comparison of quantitative image quality

Image noise

Mean image noise was 11.2±4.1 HU for the HD (FBP) reconstructions. The mean image noise values for the different reconstructions of the LD protocol were 14.8±4.3 HU LD (FBP), 13.2±4.2 HU LD (L1), 10.4±3.9 HU LD (L4), and 7.5±3.4 HU LD (L7). Figure 1 shows four images acquired with the LD protocol and reconstructed with different FBP and different strengths of IR (L1, L4, and L7). Figure 2 is a plot showing a progressive reduction in mean image noise in all the animals with increasing strengths of IR (L1, L4, and L7). Significant differences were found for the comparison of LD (FBP) and LD (L7) with the HD (FBP) reconstruction ($p<0.05$).

SNR values

The SNR values of the ischemic areas in all animals were lower compared to normal myocardium in all reconstructions. The mean SNR values are shown in Fig. 3. The LD scans resulted in lower mean SNR values with FBP and IR reconstructions with lower strength [LD (L1)] for both ischemic and normal myocardium compared to HD (FBP) reconstructions ($p<0.05$). The mean SNR values are shown in Fig. 3.

The mean SNR values of LD (FBP) (11.3±2.1, $p=0.008$) and LD (L1) reconstructions (13.1±2.7, $p=0.002$) were lower compared to those of the HD (FBP) reconstructions (16.3±1.9) for normal myocardium ($p<0.05$).

Likewise, the SNR values for LD (FBP) (5.6±2.0) and LD (L1) reconstructions (5.7±3.0) were significantly lower for ischemic myocardium ($p<0.05$). The LD (L4) reconstructions showed a similar mean SNR value (8.3±3.4, $p=0.8$) compared to the HD (FBP) reconstructions for the ischemic myocardium (7.9±4.2) ($p=0.8$). A significant difference was found for the mean SNR value LD (L4) (17.1±3.0, $p=0.0002$) compared to the HD (FBP) reconstructions for the normal myocardium

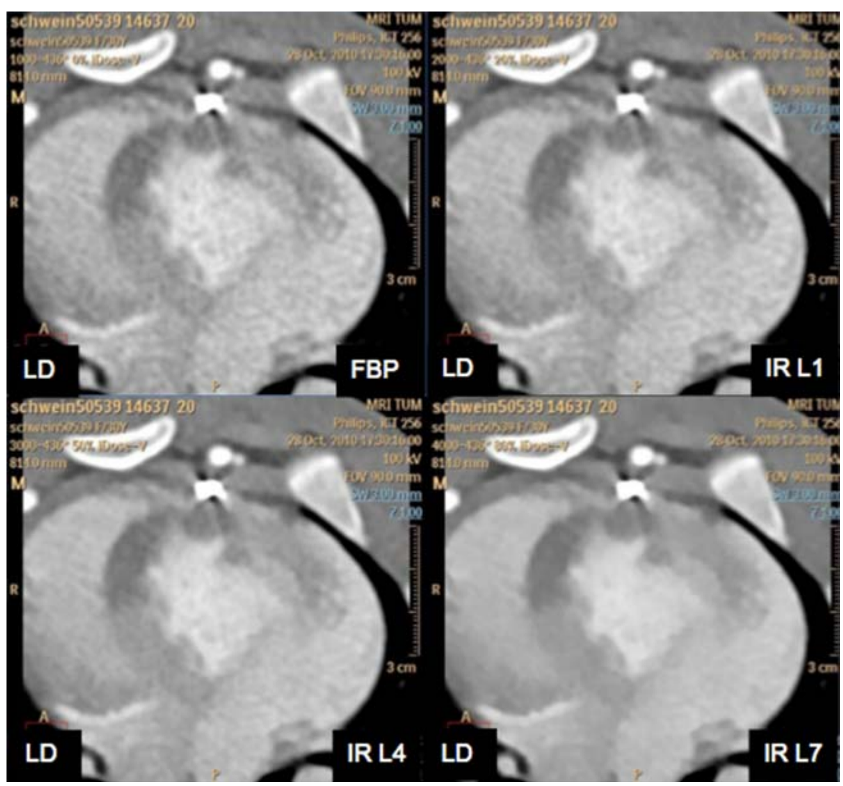

Fig. 1 The images in the *upper row* present LD (FBP) reconstruction and IR (L1) reconstruction and in the *lower row* IR (L4) reconstruction and IR (L7) reconstruction. All images were acquired with the LD protocol

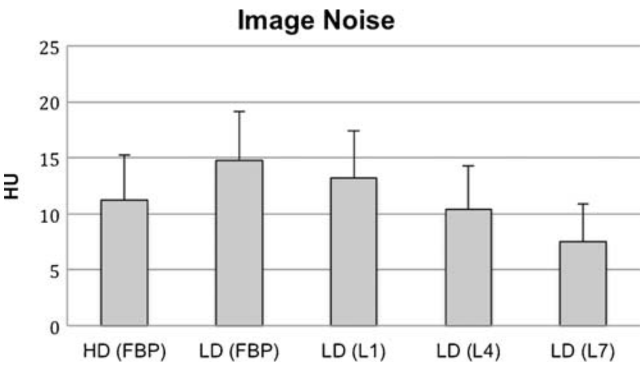

Fig. 2 Mean image noise values in all animals. Dose reduction causes higher image noise, when reconstructed with FBP. A comparable noise level is observed for IR LD (L4). The highest IR level causes less noise on images acquired with the LD protocol compared to the HD (FBP) images

(16.3±1.9) (p<0.05). Lastly, SNR values were significantly higher for the IR [L7 reconstructions, both for ischemic (10.2±5.6, p<0.04) and normal myocardium (28.9±7.4, p=0.0005)] compared to HD (FBP) reconstructions (p<0.05).

CNR values

A positive contrast between normal and ischemic myocardium was found for all animals and all reconstructions. The relative differences between the different reconstruction methods and protocols were lower compared to the mean SNR values. The mean CNR values are shown in Fig. 4. The mean CNR value of the LD (FBP) reconstructions (6.3±1.4, p=0.8) and LD (L1) (7.8±2.1, p=0.5) reconstructions were lower compared to the HD (FBP) reconstruction (8.6±4.1) (p=0.8 and 0.5, respectively). The LD (L4) reconstructions showed similar mean CNR values (9.3±2.5) compared to the HD (FBP) reconstructions (p=0.08). Significantly higher CNR values were measured from the IR (L7) reconstructions (12.8±3.3, p=0.01) compared to HD (FBP) reconstructions (p<0.05).

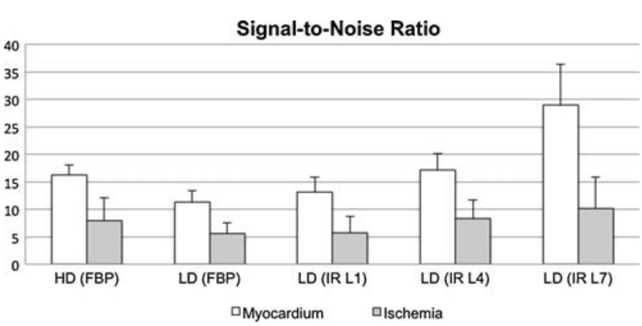

Fig. 3 Mean SNR values for normal and ischemic myocardium of the six pigs, which increase with the IR level

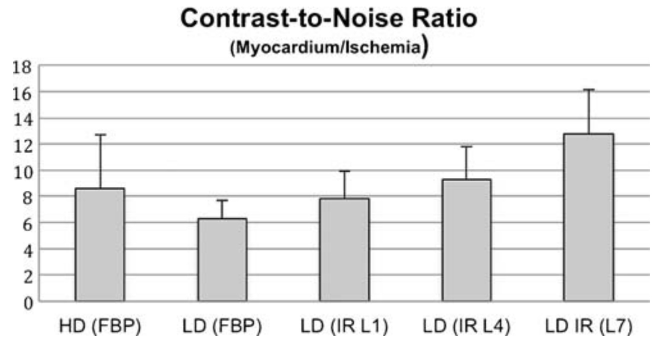

Fig. 4 Mean CNR values of normal myocardium and ischemic myocardium in six animals. The LD values increase with the strength of the IR levels

Comparison of qualitative image quality

In all included animals, a perfusion defect was clearly visible in the expected perfusion territory at the time of peak enhancement on all reconstructions of both protocols. The results are summarised in Table 2. In general, there was a decrease in the subjective IQ in LD (FBP) reconstructions (mean score of 3.3±0.6) compared to HD (FBP) reconstructions (mean score: 4.6±0.8) (P<0.05), attributable to image noise caused by the lower tube output. In contrast, there was no significant difference in the mean subjective IQ from the LD (L1) reconstructions (mean score: 4.4±0.7) or LD (L4) reconstructions (mean score: 4.7±0.8) compared to the original HD (FBP) reconstructions (p>0.05 for L1 as well as for L4). Further increase in strength of IR also tended to negatively affect the IQ, with IR (L7) resulting in a lower mean score of 3.4±0.6 compared to HD (FBP) (p<0.05), owing to the perception of a reduction in spatial resolution. Figure 5 shows an image acquired with the HD protocol (FBP) compared to images acquired with LD protocol and reconstructed with different reconstruction methods [FBP, IR (L1), IR (L4), and IR (L7)].

Radiation dose

Mean DLP for the HD protocol was 1,709.37 mGy·cm, resulting in an estimated radiation dose of about 23.9 mSv.

Table 2 Evaluation of qualitative image quality. Mean values of two radiologists. No significant differences were found for the comparison of the LD protocols with the HD protocol using IR

Protocol	Reader 1	Reader 2	Mean of 2 readers	p-value
HD (FBP)	4.5	4.7	4.6	
LD (FBP)	3.5	3.2	3.3	0.03
LD (IR, L1)	4.5	4.3	4.4	>0.05 (n.s.)
LD (IR, L4)	4.5	4.8	4.7	>0.05 (n.s.)
LD (IR, L7)	3.5	3.3	3.4	0.04

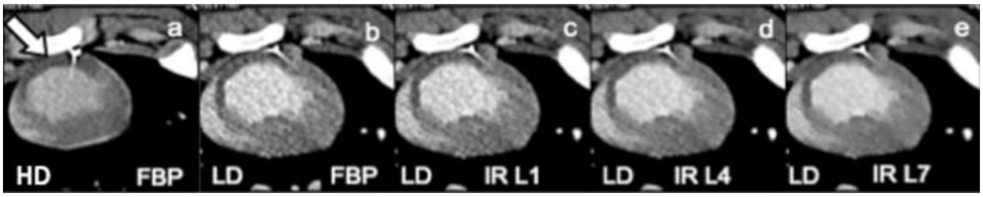

Fig. 5a–e Pig with subtotal balloon occlusion in the left anterior descending artery. A perfusion defect is visible in the apex of the heart (**a**, *arrow*). **a** was acquired with HD protocol and reconstructed with FBP. **b**–**e** Axial slices acquired with the LD protocol and reconstructed with FBP and IR L1, L4, and L7. The extent of image noise is reduced stepwise from FBP to IR L7)

Mean DLP for LD protocols was 1,140.75 mGy·cm, for an estimated radiation dose of about 15.9 mSv. $CTDI_{vol}$ for HD protocols was 183 mGy, for LD protocols 123 mGy.

Discussion

A wide detector CT system allows for total or subtotal coverage of the left ventricular myocardium without table movement in contrast to standard detectors, which require table movement for brain or myocardial perfusion scans [18–20]. By avoiding table movement, a higher temporal sampling can be achieved and motion artifacts may be reduced. Since dynamic CT MPI involves repetitive scans at a given location, care must be taken to address concerns regarding radiation dose. One method to reduce radiation dose is to use only a stress protocol instead of two separate CT data acquisitions (stress and rest), which may be sufficient if a quantitative evaluation of myocardial blood flow is available. With dynamic CT MPI, myocardial blood flow can be determined quantitatively [20–22]. Therefore, we used a stress protocol without a rest examination, as we plan to apply it in patients. Subtotal occlusions of one coronary vessel cause clearly detectable perfusion defects in the myocardium, which appear suitable for comparison of different protocols and reconstruction methods.

Various strategies have been utilised with the intention of reducing radiation dose in CT [23]. In cardiac CT, the commonly used approaches include ECG-controlled tube current modulation [24, 25], noise reduction filters [26], adjustment of tube voltage (kVp) and tube current (mAs) [27], and different ECG-gating methods (prospective vs. retrospective gating) [28, 29]. The use of prospective gating allows for radiation reductions of up to 80% in cardiac CTA [30, 31], with the adjustment of tube voltage allowing up to 40% reduction in radiation exposure for a constant tube current [26, 32]. Specifically for perfusion imaging of the brain and the myocardium, usually a lower tube voltage is used [33, 34]. The introduction of IR techniques in CT has opened up new possibilities of improving image quality while at the same time reducing radiation dose [3, 6–13]. Some studies in the past have demonstrated the advantages of IR techniques, for example, in CCTA [9, 15] or in chest computed tomography [35], either by significantly improving the IQ for a given tube output (compared to FBP) or maintaining IQ in low-dose protocols.

In our study, we evaluated the feasibility of the new IR technique (iDose^4) in CT MPI to assess its impact on IQ and radiation dose in low-dose CT acquisitions compared to the conventional FBP reconstruction technique from a routine-dose CT acquisition. Our results show that with the use of IR, a radiation dose reduction of 33% is feasible when the LD protocol is employed. The application of IR reduces image noise and improves SNR and CNR. The degree of improvement increases with the aggressiveness of the applied IR. Image reconstructions obtained using a moderate strength of IR [LD (L4)] from scans with tube output reduced by 33% exhibited image noise, SNR, CNR, and IQ comparable to those obtained from HD (FBP) reconstructions. However, the improvements were accompanied by a lower subjective IQ ranking (i.e., moderate) at the maximum strength of IR applied [LD (L7)], attributed to a visual impression of over-smoothed images that could affect quantification of myocardial perfusion.

Previous implementations of IR techniques have been known to alter the “look and feel” (texture) of images, resulting in images with blurred borders compared to FBP reconstructions [3, 36]. Other work found that noise reduction may also increase the perception of artificial over-smoothing of the images [13]. From our experience, even though images were subjectively ranked by the expert readers as moderate (average ranking of 3.3) at aggressive IR levels from LD CT [IR (L7)] we did not observe any deviations in the “look-and-feel“ and texture of the images. Likewise, Funama et al. [37] used the same implementation of IR as used in our study and achieved similar results with objective measurements of quantitative metrics (CNR, SNR, etc.); in addition, the authors also showed that the IQ can be maintained while at the same time achieving radiation dose reductions of up to 76% compared to standard protocols using FBP reconstructions. One reason for these different results could be that the IR technique used in our study uses a combination of processing in the projection and image domain, with correlated noise removed in the projection domain and multifrequency components in the image domain, unlike other image-based techniques. Similar IQ improvements using this IR technique have also been reported in CCTA, with radiation dose savings of up to 75% [15].

Additionally, we took a conservative approach, reducing the tube output by 33%. Our results showed consistent improvement in subjective and objective IQ using a moderate level of IR (L4) compared to HD CT acquisitions. This indicates that the tube output could be reduced further with a moderate level of IR without negatively impacting the IQ.

Our results demonstrate the benefits of IR techniques in 256-slice dynamic CT MPI with regards to improvements in SNR, CNR, and overall IQ, while at the same time allowing radiation dose reductions (of about 35%) in an animal model. Further optimization of the protocol from a radiation dose perspective while maintaining the ability to extract quantitative information from dynamic CT MPI images could expand the role of cardiac CTA for the determination of the hemodynamic significance of coronary artery disease.

In conclusion, a new iterative reconstruction technique (iDose^4) can improve image quality while facilitating radiation dose reductions in dynamic myocardial perfusion imaging in animal models using a 256-slice multidetector computed tomography. Thus, a standard protocol may be replaced by a low-dose protocol with about 33% reduction in radiation dose, if the levels of iterative reconstruction are adapted carefully with respect to the resulting image quality.

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