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The impact of iterative reconstruction algorithms on dynamic computed tomography myocardial perfusion parameters

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ABSTRACT

Objectives: Dynamic myocardial CT perfusion (CTP) enables the functional assessment of coronary artery disease. We aimed to assess the impact of iterative reconstruction using hybrid- (HIR) and model-based iterative reconstruction (IMR) – as compared to filtered back projection (FBP) on CTP-derived myocardial blood flow (MBF).

Methods: In our observational study we analyzed 35 patients who underwent dynamic myocardial CTP for the assessment of myocardial ischemia. Images were reconstructed using FBP, HIR and IMR algorithms. Qualitative and quantitative analysis of myocardial perfusion was performed by visual assessment and measurement of MBF on all reconstructed datasets. Image quality and interobserver variability were also assessed.

Results: Mean MBF was 105.61 $\pm$ 27.54 mL/100 g min^{-1} for FBP, 105.07 $\pm$ 27.72 mL/100 g min^{-1} for HIR and 103.69 $\pm$ 27.62 mL/100 g min^{-1} for IMR, without significant differences between the algorithms ($P = 0.49$). Image noise was significantly lower using novel iterative reconstructions compared to FBP (mean SDaorta: 48.3 $\pm$ 19.7 for FBP, 30.4 $\pm$ 13.3 for HIR and 19.5 $\pm$ 5.9 for IMR, $P < 0.001$ for all). Intraclass correlation coefficient for MBF was 0.96, while kappa value was 0.45 for visual assessment.

Conclusion: Iterative reconstruction techniques reduce noise without altering MBF values of dynamic myocardial CTP. Therefore, further dose reduction may be achieved for dynamic myocardial CTP imaging.

KEYWORDS

dynamic CT perfusion, myocardial blood flow, coronary computed tomography angiography, iterative reconstruction

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1. Introduction

Coronary computed tomography angiography (CCTA) is a reliable non-invasive imaging modality with high diagnostic accuracy for the exclusion of obstructive coronary artery disease (CAD) [1]. Advances in CT scanner technology, such as improvements in spatial and temporal resolution, dual-energy imaging, and wide detector panels, along with the implementation of iterative reconstruction algorithms, aids the detection of CAD and myocardial perfusion deficit [2]. However, a major limitation of CCTA is that it tends to overestimate the severity of stenosis, especially in the case of intermediate to severe stenosis, multivessel disease and extensive calcification, thus decreasing its specificity and positive predictive value [3].

In addition, CTA has evolved into a comprehensive imaging tool that allows for the simultaneous visualization, characterization, and quantification of coronary atherosclerosis, along with the assessment of myocardial ischemia. Dynamic myocardial CT perfusion (CTP) provides a quantitative assessment under pharmacological stress based on serial CT imaging measuring the inflow of contrast medium into the myocardium over time [4]. In recent studies, the addition of dynamic myocardial CTP has shown incremental diagnostic value over CCTA alone for the detection of hemodynamically significant CAD [5, 6]. CTP holds the potential to refine risk assessment in stable chest pain patients and can also assist in identifying residual ischemia after coronary interventions, as recent trials suggest that CTP is valuable especially in patients with known CAD or following coronary revascularization [2].

Radiation exposure during dynamic myocardial CTP is a non-negligible concern, as the effective dose values of this method have been shown to range between 3.8 and 12.8 mSv, yielding an average radiation dose of 5.3–9.2 mSv [6, 7]. Therefore, dose-reduction methods are of utmost importance. Radiation dose reductions can be achieved by reducing the tube potential (kV) or tube current (mAs). However, this results in increased image noise, which affects diagnostic image quality [8, 9]. It has been shown that iterative reconstruction (IR) is an effective post-processing method for maintaining the quality of CT images at lower radiation exposure [10, 11]. Therefore, it may represent a valuable method for radiation dose reduction in addition to other dose reduction strategies [8]. Data on the effect of image reconstruction algorithms on qualitative and quantitative myocardial perfusion parameters are scarce and somewhat controversial [9, 12, 13].

We hypothesized that hybrid iterative reconstruction (HIR) and novel model-based iterative reconstruction (IMR) could influence the measured myocardial perfusion parameters and visual assessment of perfusion defects, ultimately altering the result of the examination. Therefore, we aimed to further elucidate the effect of HIR and IMR on myocardial perfusion assessment compared to traditional filtered back projection (FBP) reconstruction. We also aimed to assess the reproducibility of qualitative and quantitative image quality parameters using novel IR techniques.

2. Materials and methods

2.1. Study population

Patients were screened and prospectively enrolled in our study. Inclusion criteria were intermediate CAD detected on CCTA (presence of a 50–69% stenosis in at least one of the major branches) or extensive calcification (>400 coronary artery calcium score) detected on non-enhanced CT images and the patient provided informed consent to perform CTP imaging ($N = 43$). Exclusion criteria were contraindications for receiving pharmacological vasodilator stress agents ($N = 2$). A total of 41 patients underwent dynamic myocardial CTP examination. Patients with insufficient image quality – one due to shortage of scan coverage and five due to significant artefacts caused by a suboptimal contrast flow curve which led to falsely altered values at the quantitative assessment – were also excluded. Therefore, 35 patients were included in our final analysis.

The study was approved by a national ethics committee (OGYÉI/719/2017) and was performed in accordance with the Helsinki declaration. Written informed consent was obtained from all patients.

2.2. Dynamic myocardial CTP acquisition and reconstruction

Dynamic myocardial CTP was performed using a 256-slice multi detector-row CT system (Brilliance iCT 256, Philips Healthcare, Best, The Netherlands). Images were acquired using pharmacological stress induced by regadenoson (Rapiscan®, GE Healthcare). We administered 400 µg of regadenoson intravenously via a 18G cannula in a single dose, followed by 30 mL of saline bolus. Data acquisition was started during peak stress approximately 1 min after the administration of the regadenoson bolus. Then, 50–60 mL of iodinated contrast agent (Iomeron 400, Bracco Imaging SpA, Milan, Italy) at a flow rate of 5.0 mL s^{-1} with dual-syringe automated mechanical injector was injected, followed by a saline chaser (5.5 mL s^{-1} for 7 s). Scanning was performed under a single breath-hold in the inspiration position. We performed stress dynamic CTP using a prospective ECG-gated dynamic mode targeting a phase at 35% of the RR interval (systolic phase). CT data were acquired at every alternate cardiac cycle, with a total of 18–25 dynamic datasets collected. Scan parameters for CTP were the following: tube voltage: 80–100 kV and tube current: 100–250 mAs [based on body mass index (BMI)]; gantry rotation time: 0.27 s; detector collimation: 128 × 0.625 mm; z-axis coverage: 8 cm; 360-degree acquisition. Axial images of dynamic myocardial CTP were reconstructed with 2 mm slice thickness. Besides reconstructing regular images with FBP, images were also reconstructed using hybrid iterative reconstruction (HIR) (iDose4 Level 4; Philips Healthcare, Best, The Netherlands) and model-based iterative reconstruction (IMR) (Body Routine Level 1, Philips Healthcare, Best, The Netherlands). Temporal filtering was performed on all three above mentioned datasets (IntelliSpace Portal, Philips Healthcare, Best, The Netherlands). Radiation dose was calculated from the dose-length product from the dose report, using a conversion factor of 0.014 $mSv^{*}mGy^{-1*}cm^{-1}$.

2.3. Quantitative image quality analysis

Objective image quality parameters were obtained using previously described methods [14]. Image noise was determined across different IR algorithms and FBP as the standard deviation of the attenuation value in a single circular region of interest (ROI) (200 mm^2) placed in the aortic root at the level of the left main coronary ostium. For all measurements, the size, shape and position of the ROIs were kept constant among the three datasets. The measurements were performed using a dedicated workstation (IntelliSpace Portal, Philips Healthcare, Best, The Netherlands). Furthermore, ROIs were placed in the myocardium and the epicardial fat as well in order to be able to determine the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR).

2.4. Dynamic myocardial perfusion CT analysis

Dynamic myocardial CTP images were analyzed using a semiautomated software on a dedicated workstation (IntelliSpace Portal, Philips Healthcare, Best, The Netherlands). We performed qualitative assessment of visual perfusion defects on contiguous short-axis sections of the left ventricle. Each LV myocardial segment was categorized as no perfusion defect, subendocardial perfusion defect or transmural perfusion defect using a 16-segment model of the left ventricle excluding the apex [15]. Window width and level were set in 300/150 or 200/100 Hounsfield units (HU) [16].

Quantitative myocardial perfusion analysis was performed by assessing myocardial blood flow (MBF) on all reconstructed datasets. Time-attenuation curves were created in the left ventricular outflow tract and were used as arterial input function. For a segment-based analysis, ROIs were set on short-axis images in the middle layer of each myocardial segment by one experienced radiologist trainee with 5 years of experience in cardiac imaging. The ROI was at least 50 mm^2 in size, endo- and epicardial borders, papillary muscle and artefacts were aimed to be avoided. (Fig. 1) MBF was computed applying a hybrid deconvolution method [17]. Qualitative and quantitative image analysis was also performed in a randomly selected group of patients (10 patients, 160 myocardial segments) by another reader with 4 years of experience in cardiac imaging to evaluate interobserver variability.

2.5. Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as numbers and percentages. Repeated measures ANOVA and Bonferroni post-hoc tests were performed to detect differences among the reconstruction algorithms and between image noise parameters (SD of the aorta). Kappa value was calculated to define differences in qualitative assessment of perfusion deficits across different IR techniques. Furthermore, intraclass correlation coefficient and kappa value was used to test interobserver variability on HIR reconstructed images. A P value of <0.05 was considered as significant. We used SPSS v.23 (IBM Corp., Armonk, NY, USA) for all calculations.

3. Results

3.1. Patient characteristics

Mean age was 62.7 ± 8.1 years, mean BMI was 28.5 ± 3.8 kg m^{-2} and 20% were female. Mean effective radiation dose of dynamic myocardial CTP examination was 7.88 ± 3.22 mSv. The demographical and clinical data of the 35 enrolled patients can be seen in Table 1.

3.2. Image quality assessment

Image noise in the aorta was significantly lower using HIR and further reduced with IMR as compared with FBP (P < 0.001 for all comparisons: mean image noise was 48.3 ± 19.7 for FBP, 30.4 ± 13.3 for HIR and 19.5 ± 5.9 for IMR). Noise reduction achieved by HIR and IMR was 36.9 and 60.0% as compared to FBP, respectively. Signal-to-noise ratio was 3.0 ± 1.1 for FBP, 5.0 ± 1.7 for HIR and 6.8 ± 2.1 for IMR, respectively (P < 0.001 for all comparisons). Contrast-to-noise ratio was 5.9 ± 1.7 for FBP, 9.1 ± 2.4 for

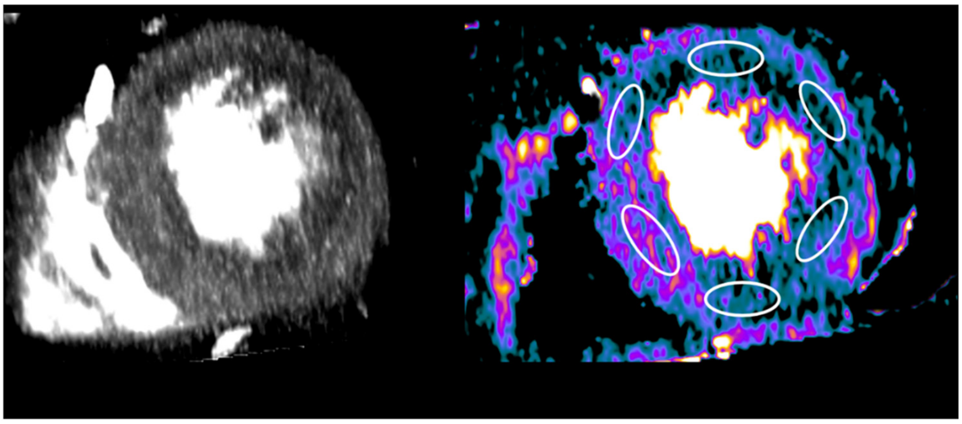

Fig. 1. A representative example of myocardial blood flow (MBF) measurement on the dynamic myocardial computed tomography perfusion (CTP) images. Circular regions of interest (ROIs) measuring 50 mm^2 were placed within the mid anterior, anterolateral, inferolateral, inferior, inferoseptal, and anteroseptal segments.
CTP: computed tomography perfusion; MBF: myocardial blood flow; ROI: region of interest

Table 1. Patient characteristics

N = 35		
Demographics	Male gender, n (%)	28 (80)
	Mean age, years	62.7 ± 8.1
	BMI, kg m^{-2}	28.5 ± 3.8
Clinical Characteristics	Hypertension, n (%)	29 (83)
	Dyslipidemia, n (%)	30 (86)
	Diabetes mellitus, n (%)	8 (23)
	Prior PCI, n (%)	3 (9)
	Former/current smoking, n (%)	16 (46)
	Cerebrovascular disease, n (%)	3 (9)
	Peripheral arterial disease, n (%)	14 (40)
	Family history of premature CAD, n (%)	10 (29)
	Ca-score	777.4 [89.0–1045.8]
Medication	OAC, n (%)	6 (17)
	Statin, n (%)	23 (66)
	ACE-I, n (%)	16 (46)
	ARB, n (%)	8 (23)
	β-blocker, n (%)	18 (51)

BMI: Body mass index, PCI: Percutaneous coronary intervention, CAD: Coronary artery disease, OAC: oral anticoagulant, ACE-I: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker.

HIR and 13.0 ± 3.9 for IMR, respectively ($P < 0.001$ for all comparisons).

3.3. Qualitative evaluation of perfusion defects

A total of 560 segments were evaluated using 3 different reconstruction algorithms (1,680 measurements). 75.9% of all segments showed no perfusion deficit, 20.0% showed subendocardial and 4.1% transmural perfusion defect on visual assessment.

The rate of segments without visible perfusion deficit was higher using HIR (454 segments) and IMR (425 segments) as compared with FBP (405 segments), although showed no significant difference: $X2$ $P = 0.14$. The kappa value showed moderate reproducibility for the assessment of visual perfusion deficits on the iDose images ($\kappa = 0.45$).

3.4. Hemodynamic parameters of dynamic myocardial CTP

We detected no significant difference in MBF values across IR algorithms: mean MBF was 105.61 ± 27.54 for FBP, 105.07 ± 27.72 for HIR and 103.69 ± 27.62 for IMR, $P = 0.49$. The reproducibility was excellent for the measurement of MBF with an ICC of 0.96.

A representative case is demonstrated in Fig. 2.

4. Discussion

In this present study, we aimed to assess whether model-based and hybrid iterative reconstruction algorithm alter MBF values and visual assessment of perfusion defects using a dynamic myocardial CTP protocol. We found no significant difference in MBF values using different IR algorithms. Furthermore, qualitative evaluation showed moderate reproducibility for the assessment of perfusion deficits whereas excellent reproducibility was detected for the measurement of MBF on quantitative evaluation. The utilization of novel IR algorithms significantly improved image quality reducing image noise.

Previous studies have already shown noise reduction after applying iterative reconstruction in multiple settings [9, 12, 13, 18, 19]. Eck et al. found that FBP and HIR both overestimated flow at low doses, making ischemia detection much more difficult, whereas model-based iterative reconstruction provided more accurate flow measurements even at low dose settings [19]. Tao et al. found that iterative reconstruction reduced image noise and mitigated streaking artefacts caused by photon starvation in dynamic myocardial CTP data sets acquired in porcine models at a low dose and improved perfusion map quality, in comparison to FBP reconstruction at the same dose [12]. In the study of Gramer et al. the application of IR reduced image noise and improved signal-to-noise ratio and contrast-to-noise ratio in dynamic myocardial CTP in animal models. However, the improvements were accompanied by lower subjective image quality ranking, due to visual misperception of over-smoothed images. Therefore, their suggestion is to adapt levels of iterative reconstructions carefully, with respect to altering image quality [9]. Improved image quality was observed in patients with iterative reconstructions in a study of Bhave et al., both signal-to-noise and contrast-to-noise ratios were increased with iterative reconstruction, indicating improvement in image quality compared to FBP. A lower standard deviation in x-ray attenuation values could be measured in normally perfused myocardium, which led to an improved differentiation between normal and hypo-perfused myocardial tissue using quantitative 3D analysis, which resulted in detecting perfusion defects better [13].

In our study we did not detect significant difference in quantitative parameters of myocardial perfusion among all three reconstructions assessed on dynamic myocardial CTP images. Reproducibility was excellent for quantitative assessment of the MBF and rather low for visual assessment of perfusion deficits, endorsing the clinical value of quantitative evaluation when interpreting dynamic myocardial CTP scans. To the best of our knowledge, the only study in this field, comparing the hemodynamic parameters measured by different reconstructions, conducted on human patients was carried out by Tanabe et al. They observed no difference among the hemodynamic parameters using FBP, HIR and IMR reconstructions, while our study with a larger sample size supported this finding. Additionally, our study included patients from a highly relevant patient cohort with intermediate stenosis, whereas the study by Tanabe et al. excluded patients with >50% stenosis on CCTA [18]. On the other hand, Eck et al. observed in porcine model that blood flow measurements increased for FBP when reducing radiation dose, while this phenomenon is not as pronounce using HIR, and even less marked using IMR, resulting in

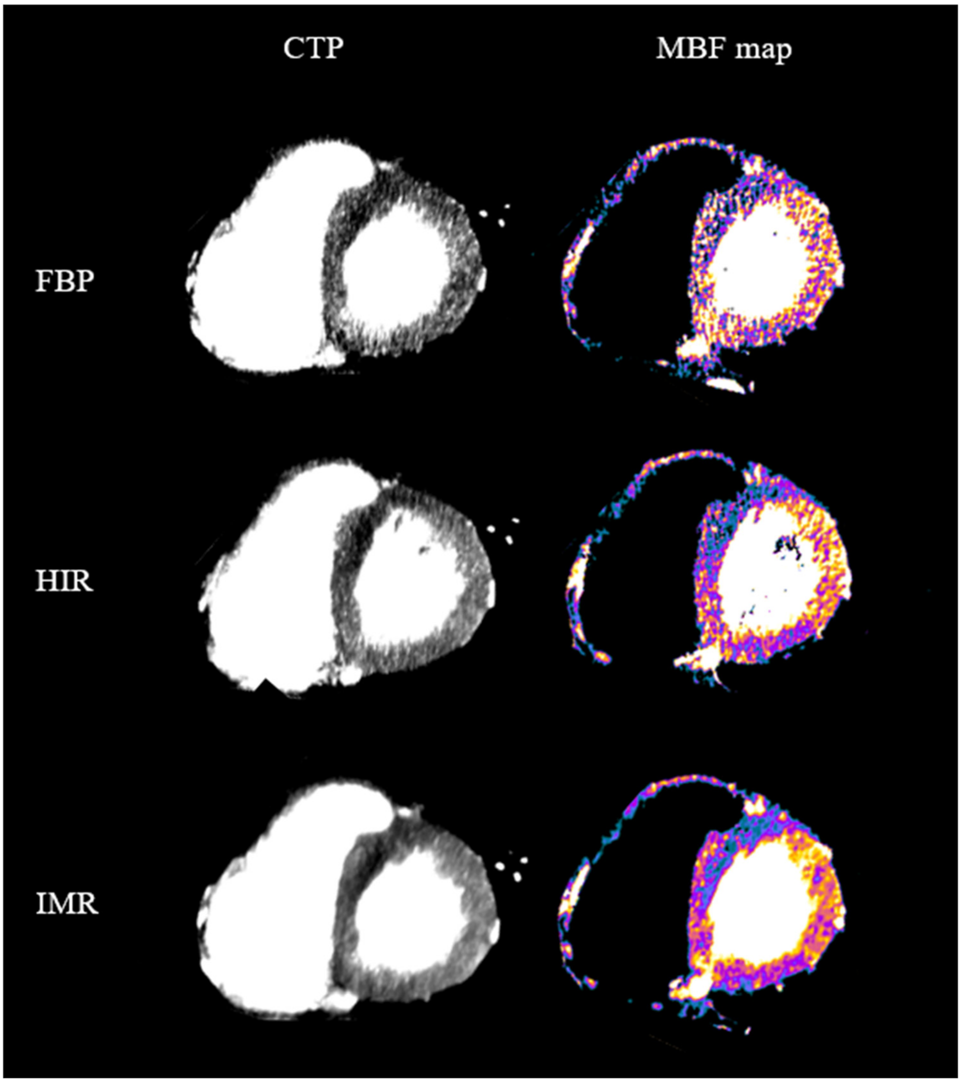

Fig. 2. Computed tomography perfusion (CTP) images and myocardial blood flow (MBF) maps reconstructed using three different techniques: filtered back projection (FBP), hybrid iterative reconstruction (HIR), and model-based iterative reconstruction (IMR). IMR provides the lowest image noise in CTP images compared to FBP and HIR.
FBP: filtered back projection, HIR: hybrid iterative reconstruction, IMR: model-based iterative reconstruction, MBF: myocardial blood low CTP: CT perfusion

more consistent flow measurements in model-based iterative reconstruction [19].

There is a substantial discrepancy between anatomical and functional information of CAD in recent trials. Therefore, functional assessment of CAD by using CT perfusion has been introduced to improve diagnostic accuracy and to complement traditional assessment of coronary atherosclerosis. A meta-analysis by Pontone et al. demonstrated that adding the functional information of a myocardial CT perfusion to anatomical data increased the specificity of coronary CTA from 64 to 91% in detecting flow-limiting coronary stenosis [20]. Their findings also highlighted the feasibility and the robustness of stress CTP, which is an imperative step before widespread clinical implementation [21]. The CRESCENT II (Comprehensive Cardiac CT With Myocardial Perfusion Imaging Versus Functional Testing in Suspected Coronary Artery Disease) trial showed that the implementation of dynamic myocardial CTP in the diagnostic work-up of patients with chronic coronary syndromes reduced the number of negative invasive coronarographies compared with standard care [22]. In patients with stable angina, it is also useful in patients with extensive calcification (as blooming artefacts heavily impact CCTA images, limiting their diagnostic value). Dynamic myocardial CTP also helps to select the vessel(s) for revascularization in pa-tients with multivessel CAD. The method may also facilitate patient management in a number of other specific settings, e.g. identification of global ischemia in extensive non-obstructive CAD or early detection of microvascular dysfunction and impaired myocardial perfusion in patients with diabetes mellitus or arterial hypertension [2].

Despite the known and undoubted advantages of dynamic myocardial CTP, its use has been limited to a few centers and mainly to the research environment, with a slow transition to clinical care. This might be the results of several factors, including the relatively high radiation dose, the lack of standardization in acquisition protocols and image analysis, lack of an accepted myocardial blood flow (MBF) cutoff to identify myocardial ischemia, logistical challenges, and reimbursement issues [23]. In our clinical practice, we used the criteria established by Pontone et al., where segmental myocardial ischemia was defined as an MBF of less than 101 mL/100 g min^{-1}. [6] Our data suggest that the use of novel IR algorithms could result in improved image quality without altering the results of dynamic myocardial CTP examinations, that may enable its reliable utilization using lower radiation exposure.

4.1. Limitations

We acknowledge the limitations of our study. First, the sample size is limited therefore different kV settings could not be analyzed separately. Additionally, the small sample size limits the statistical power of the study and affects the generalizability of the findings. Second, the subjective component of the analysis introduces the possibility of bias into the study. The visual assessment of perfusion defects has shown moderate interobserver variability ($\kappa = 0.45$), highlighting a limitation in subjective evaluation methods. Automated analysis techniques could be explored in future studies to minimize bias. During the past years, all major vendors have introduced hybrid and model type iterative reconstruction techniques to improve image quality. The results of our current study are derived from two different Philips iterative reconstruction algorithms (Philips, Best, The Netherlands), hence it might not apply for all other vendor's iterative reconstruction [24]. We used Level 1 IMR and we did not evaluate the effect of higher levels of iterative reconstruction. Furthermore, subjective parameters regarding the visual assessment cannot be ruled out as the noise textures allow experienced readers to differentiate the images reconstructed with FBP, HIR and IMR [25].

5. Conclusions

In conclusion, iterative reconstructions provide better image quality with lower noise levels without altering the quantitative measurements in dynamic myocardial CTP scans. Quantitative evaluation of perfusion deficits using MBF was highly reproducible. Therefore, the application of HIR and IMR might also provide an opportunity to perform lower dose examinations with excellent reproducibility, which is a major factor inhibiting the spread of dynamic myocardial CTP in clinical care.

Competing interest: Béla Merkely and Bálint Szilveszter are members of the Editorial Board of the journal, therefore they did not take part in the review process in any capacity and the submission was handled by a different member of the editorial board. The submission was subject to the same process as any other manuscript and editorial board membership had no influence on editorial consideration and the final decision.

Authors' contribution: All authors have read and agreed to the published version of the manuscript.

Ethical approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of OGYÉI (OGYÉI/719/2017, 02.11.2016.)

Consent to participate: Informed consent was obtained from all subjects involved in the study.

Consent to publish: Informed consent was obtained from all subjects involved in the study.

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