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Optimizing lower extremity CT angiography: A prospective study of individualized vs. fixed post-trigger delays in bolus tracking

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ABSTRACT

Purpose: To compare the contrast media opacification and diagnostic quality in lower-extremity runoff CT angiography (CTA) between bolus-tracking using conventional fixed trigger delay and patient-specific individualized post-trigger delay.

Methods: In this prospective study, lower-extremity runoff CTA was performed in two cohorts, using either fixed or individualized trigger delay. Both cohorts had identical CT protocols, contrast media applications, and image reconstructions. Objective image quality (mean contrast opacification in HU), and subjective image quality (5-point Likert-scale), were assessed in six vessels: abdominal aorta (AA), common iliac artery (CIA), superficial femoral artery (SFA), popliteal artery (PA), posterior tibial artery (PTA), and dorsalis pedis artery (DPA) by one rater for objective and two raters for subjective image quality. Objective image quality was analyzed using Student t-tests, while subjective ratings were compared with Fisher's exact test.

Results: Overall, 65 patients were included (mean age: 71 ± 14; 39 men), 35 in the individualized cohort and 30 in the fixed cohort. No differences were found between the groups regarding demographics or radiation exposure. Individualized trigger delay ranged from 2 to 23 s (mean: 8.7 ± 4.0 s) and was 10 s in the fixed cohort. The individualized cohort showed higher opacification in the peripheral arteries (PTA: 479 ± 140 HU vs. 379 ± 106 HU; $p = 0.009$; DPA: 477 ± 191 HU vs. 346 ± 137 HU; $p = 0.009$). Overall subjective "image quality" was rated higher in the individualized group ("excellent" or "good" in Rater 1: 97 % vs. 57 %; $p < 0.001$; and Rater 2: 89 % vs. 53 %; $p = 0.002$).

Conclusion: Individualized post-trigger delay enhances diagnostic quality, by improving vessel opacification in peripheral arteries and increasing subjective image quality in lower extremity runoff CTA.

1. Introduction

CT angiography (CTA) is essential for diagnosing various vascular diseases such as peripheral arterial disease (PAD) and assessing the therapeutic outcomes [1–3]. Recent advancements in computed tomography have improved image quality and acquisition speed [4–9]. However, optimizing scan timing remains challenging due to the rapid scans and inter-individual cardiovascular variability, which affects contrast agent transport and subsequent enhancement of the examined vessels [9,10].

Currently two main-methods for scan timing prevail: Fixed delay and bolus-tracking. Fixed delay, where scanning starts after a set time post-contrast injection, is easy to implement but does not account for inter-individual patient differences such as cardiovascular output [11]. Bolus-tracking triggers the scan once a contrast threshold is reached in a region of interest [9,12], but thereafter still uses a fixed post-trigger

Abbreviations: AA, abdominal aorta; CI, confidence interval; CIA, common iliac artery; CT, computed tomography; CTA, computed tomography angiography; DPA, dorsalis pedis artery; FOV, field of view; HU, Hounsfield unit; PA, popliteal artery; PAD, peripheral arterial disease; PTA, posterior tibial artery; PTD, post-trigger delay; SD, standard deviation; SFA, superficial femoral artery; (T)EVAR, (thoracic) endovascular aortic repair.

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delay, also failing to accommodate individual cardiovascular dynamics. This can result in suboptimal contrast enhancement, particularly in the peripheral arteries during lower-extremity runoff CTA [13,14]. Scan timing errors, such as initiating the scan before contrasting of the desired vessels due to reduced cardiac output or vascular obstruction, or scanning too late and hence experiencing an overlay of contrasting veins, pose challenges in diagnostic interpretation [15,16].

Recognizing these challenges, previous studies have suggested computer-based intelligent methods to personalize scan timing [9,17]. Previous studies have demonstrated the benefits of individualized trigger delay over conventional fixed delay in other vascular territories, such as the abdominal aorta [18], in coronary angiography [19], or in carotid angiography [20]. Potential advantages of individualized post-trigger delay methods include reducing non-diagnostic scans, reduction in required contrast agent volume or injection rate, thereby mitigating risks for patients, saving costs and even environmental benefits by minimizing contamination of drinking water [16,21].

Therefore, we hypothesize that bolus tracking using individualized post-trigger delay improves contrast enhancement of peripheral arteries during runoff CTA compared to conventional bolus tracking, which uses a fixed delay. To investigate this, we performed a prospective study using fixed and individualized post-trigger delay in lower extremity CTA and evaluated objective and subjective image quality.

2. Materials and methods

2.1. Ethics approval

This study was approved by the institutional review board of the Ludwig Maximilian University, Munich (approval number: 22-0959) and complies with the declaration of Helsinki in its latest revision (2024). All patients provided written informed consent prior to study participation.

2.2. Patient cohorts

This prospective study analyzed patients receiving lower-extremity runoff CTA, acquired between October 2022 and February 2023. Consecutive selection was used resulting in two cohorts receiving either CTA with fixed or individualized post-trigger delay.

Inclusion criteria for the study were clinical indication for a lower-extremity run-off-CTA, age over 18 years, age-adjusted normal serum creatinine or creatinine clearance >30 ml/min/1.73 m^2 for safe contrast agent administration and written informed consent. Exclusion criteria for patients were contraindications against CT, known iodine contrast media allergy, age-adjusted reduced creatinine clearance <30 ml/min/1.73 m^2 as a contraindication for safe administration of contrast agent, or refusal to participate in the study.

2.3. Imaging protocol

All scans for both cohorts were performed using the same 128-slice Dual Source CT scanner (SOMATOM Drive, Siemens Healthineers) in single-source mode with identical data acquisition parameters (detector collimation: 2x96 mm; section acquisition: 2x192 mm under usage of z-flying focal spots; pitch: 1.2; table feed: 69 mm/s; gantry-rotation-time: 250 ms; tube voltage: 100 kVp; quality reference tube current–time product: 90 mAs per rotation under usage of automatic exposure control [CareDose4D; Siemens Healthineers]). Scans were performed in craniocaudal direction including a section from the diaphragm until the soles of the feet for all study participants.

2.4. Contrast agent application

Uniform contrast agent application protocols were followed for both cohorts. After testing flow with 10ml of 0.9 % saline solution, 70 ml of pre-warmed, non-ionic iodinated contrast agent (Iomeprol, 400 mg/ml, Imeron, Bracco Imaging) was injected, then followed by 15 ml of saline solution, all at a flow rate of 4 ml/s.

2.5. Bolus tracking

Aortic contrasting was monitored at the abdominal aorta at the level of the celiac trunk, with a threshold of 120 HU at 120 kVp for all scans. The individualized cohort utilized a noncommercially available prototype software (SOM7/VB30, Siemens Healthineers), to calculate the patient-specific post-trigger delay in real-time just during the acquisition of the bolus-tracking scans, as previously described [18]. In short, data acquisition from bolus tracking scans was commenced based on predicted local contrast over time (in HU), calculated from the contrast agent injection protocol (in gram iodine per second) and arterial impulse response function (IRF) in HU per gram of iodine. Once the threshold was surpassed and at least four bolus-tracking enhancement values were recorded, the contrast information was utilized to calculate the individual arterial impulse response in real-time through online-adjustment based on a population-averaged set of parameterized arterial flow curves, considering individualized post-trigger delay, monitoring position, scan area and scanner pitch. The predicted optimal individual delay time in seconds was then automatically set by the scanning software and additionally the set delay time was recorded for the purpose of this study. Because the software only depends on information from the bolus-tracking CT images, it is not depended on a specific contrast media injector. For the fixed cohort, conventional bolus tracking was used, with a post-bolus trigger delay set at 10 s.

2.6. Image reconstruction

All images in both cohorts were reconstructed with a slice thickness of 2 mm and an increment of 2 mm using a smooth edge-enhancing vascular convolution kernel (Bv38) and advanced modeled iterative reconstruction at a strength level of 3.

2.7. Objective image quality

Objective image quality was evaluated by one author (L.N., a final year medical student with extensive training and 1 year of experience in cardiovascular imaging), who was blinded to the group allocation of each case and any demographic or clinical information. Vessel opacification was measured in Hounsfield units (HU) at six different vessel locations for every patient: abdominal aorta (AA), common iliac artery (CIA), superficial femoral artery (SFA), popliteal artery (PA), posterior tibial artery (PTA) and dorsalis pedis artery (DPA). Regions of interest (ROI) were placed intraluminal to be as large as possible without including arteriosclerotic plaques or stents, and mean opacification in HU and standard deviation were recorded. At every location, two ROIs in adjacent axial images for the right and left side (four in total) were measured and averaged to increase robustness. Furthermore, we calculated signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR), as described before [20].

$$SNR = \frac{HUvessel}{SDvessel}$$

$$CNR = \frac{HUvessel - HUmuscle}{SDvessel}$$

HU_{vessel}: CT opacification of vessel lumen (in HU)
SD_{vessel}: standard deviation of vessel lumen opacification
HU_{muscle}: Opacification of the psoas muscle (measured at the level of the lower lumbar spine)

2.8. Subjective image quality

Subjective image quality was evaluated by two independent raters (B.O.S., a radiology attending with 12 years of experience in cardiovascular imaging, and L.N., a final year medical student with extensive training and 1 year of experience in cardiovascular imaging), who were blinded to the group allocation and all demographic or clinical information for each case. Quantitative image quality was scored on a 5-point Likert scale, as described before [18–20]: 5, excellent; 4, good; 3, moderate; 2, poor; 1, non-diagnostic. Consensus among readers regarding scale usage was established beforehand, based on data from ten randomly selected patients not included in the study.

2.9. Statistical analysis

Normally distributed variables were summarized by mean and standard deviation, while non-normally distributed variables were summarized by median and interquartile range, and categorical variables were summarized as frequencies and percentages.

Demographics of both cohorts were compared by using Fisher's exact test for categorical variables and by using Student's *t*-test for continuous variables. Objective image quality was compared using Student's *t*-test on the mean opacification values of both groups, with Benjamini-Hochberg correction for multiple testing. Subjective image quality on Likert scales was compared using weighted Cohen's κ for inter-rater agreement, where $\kappa < 0$ was interpreted as indicating no agreement, $0.0 < \kappa \leq 0.2$ as poor, $0.2 < \kappa \leq 0.4$ as fair, $0.4 < \kappa \leq 0.6$ as moderate, $0.6 < \kappa \leq 0.8$ as substantial, and $0.8 < \kappa \leq 1.0$ as excellent agreement. A difference in combined ratings across groups was tested with Fisher's exact test. All statistical analysis and visualizations were performed using GraphPad Prism (version 10.2.3, GraphPad) with a two-sided significance level of $p < 0.05$.

3. Results

3.1. Study participants

Patient characteristics shown in Table 1. Demographics did not differ between the two cohorts, including patients' age, sex, height, weight, body mass index (BMI), and previous vascular interventions. Likewise, no differences were found between the groups regarding use of contrast media, scan parameters, or radiation dose.

3.2 Delay after bolus tracking

For the individualized cohort, delay times ranged from 2 to 23 s (mean: 8.7 ± 4.0 s), which indicates considerable inter-individual differences of the predicted delay times based on real-time modulation (Fig. 2).

3.3. Objective image quality

In the individual cohort, mean vessel opacification was significantly higher for the distal arteries below the knee, in the PTA (479 ± 140 HU vs 379 ± 106 HU, $p = 0.009$) and the DPA (477 ± 191 HU vs 346 ± 137 HU, $p = 0.009$) (Fig. 1), with a mean difference in contrast of around 100 HU (PTA: +100 HU, DPA: +131 HU; full data shown in Table 2). SNR and CNR improved as well (Fig. 1; Full data provided in supplemental Tables S1 and S2). At the proximal locations, no significant differences in opacification were detected (AA, CIA, SFA, and PA, all $p \geq 0.815$).

3.4. Subjective image quality

Over all cases, the evaluations of the two independent readers resulted in a weighted Cohen's κ of 0.748, thereby indicating substantial agreement. Only in three cases their ratings differed a maximum of two points on the Likert-scale.

Both readers rated images from the individualized group as significantly higher quality (Fig. 3), classified as "excellent" or "good" in 97 % of the cases versus 57 % from the fixed cohort (Rater 1, $p < 0.001$), and 89 % versus 53 % (Rater 2, $p = 0.002$), respectively. Rater 1 rated no scan "poor" from the individualized group, but 9 cases from the fixed group, whereas Rater 2 rated only 1 scan "poor" in the individualized group, but 7 in the fixed group. In both groups, no scan was rated "non-diagnostic". Representative cases of both groups are shown in Fig. 4.

Table 1
Patient characteristics and scanning parameters.

Variables	Fixed PTD	Individualized PTD	*p*	
No. of participants	30	35	–	–
Age (years)	70.63 ± 12.29	70.83 ± 16.15	> 0.999	ns
Sex (female)	11 (37 %)	15 (43 %)	0.799	ns
Height (m)	1.71 ± 0.12	1.72 ± 0.10	0.709	ns
Weight (kg)	79.03 ± 14.81	78.60 ± 21.41	0.926	ns
BMI (kg/m^2)	27.05 ± 4.73	26.33 ± 5.91	0.594	ns
Tube Voltage (kV)	77.33 ± 7.85	76.57 ± 9.73	0.715	ns
Tube Current (mAs)	154.70 ± 25.88	160.86 ± 30.49	0.388	ns
CTDIvol (mGy)	2.40 ± 0.79	2.47 ± 1.34	0.820	ns
DLP (mGy·cm^{-1})	295.95 ± 96.04	311.92 ± 191.06	0.680	ns
ED (mSv)	1.51 ± 0.49	1.59 ± 0.91	0.680	ns
Contrast Volume (ml)	128.17 ± 6.50	122.94 ± 14.77	0.078	ns
Contrast Flow Rate (ml/s)	2.93 ± 0.05	2.93 ± 0.04	0.706	ns
Delay Time (s)	10.00	8.71 ± 3.97	–	–
Vascular interventions	14 (47 %)	16 (46 %)	> 0.999	ns
Stent	6 (20 %)	9 (26 %)	0.769	ns
Bypass	3 (10 %)	2 (6 %)	0.655	ns
(T)EVAR	1 (3 %)	2 (6 %)	> 0.999	ns
Prosthesis	1 (3 %)	1 (3 %)	> 0.999	ns
Occluder / Plug	0 (0 %)	1 (3 %)	> 0.999	ns
Limb Amputation	3 (10 %)	1 (3 %)	0.328	ns

(*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; ns = not significant).
Note. — Unless otherwise specified, data are means ± standard deviation.

4. Discussion

In this study, we evaluated the use of a patient-specific individual trigger delay derived from contrast media bolus tracking scans in patients undergoing lower extremity runoff CTA. We prospectively compared this method with conventional fixed delay and found that the novel approach led to objectively higher opacification in the peripheral below-the-knee arteries, and to subjectively higher image quality overall and better delineation of atherosclerotic lesions.

Diagnostic quality was not only rated higher, but also more stable using individual delay times with fewer outliers and no scans being rated as poor quality. The high variability of different delay times (2–23 s) underlines the vast inter-individual differences, which can be accounted for by our approach.

Over the last years, numerous approaches have been proposed to increase the diagnostic quality of CT angiography, such as empirically determined injection protocols, different radiation dosages, new technologies such as dual-energy CT or photon-counting detector CT, or even the acquisition of additional time-resolved scans [8,16,22,23]. However, these heavily rely on the operator, on new hardware, or come at the expense of an increased radiation dose or contrast media consumption.

Furthermore, the most influential factor for vascular contrast remains the cardiac output. The novel software we evaluated can estimate

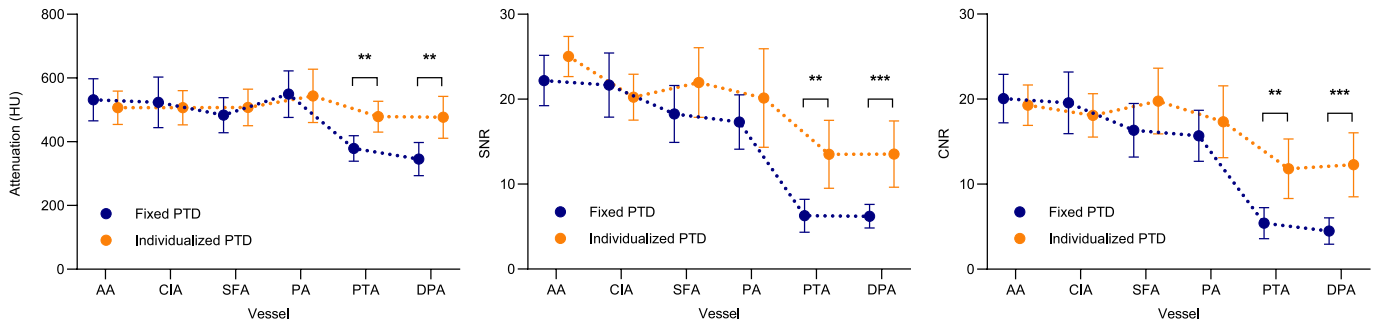

Fig. 1. Comparison of mean opacification (HU) at different vessels, from proximal to distal: abdominal aorta (AA), common iliac artery (CIA), superficial femoral artery (SFA), popliteal artery (PA), posterior tibial artery (PTA) and dorsalis pedis artery (DPA). (Data are shown as means; error bars indicate 95 % CI; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

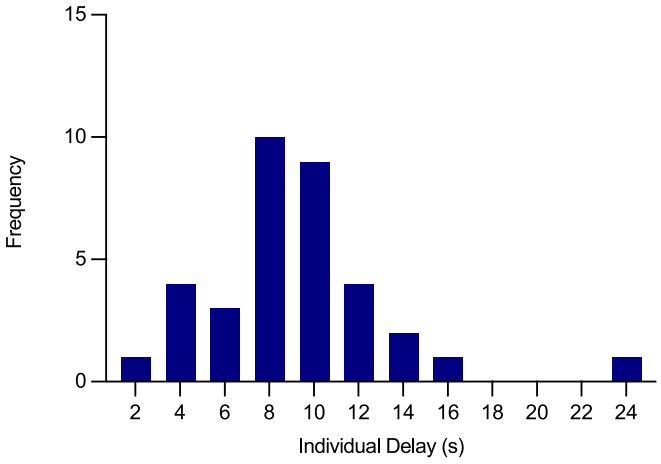

Fig. 2. Histogram shows distribution of delay times in the individual cohort (mean: 8.7 ± 4.0 s; range: 2–23 s). Standard delay time was 10 s in the fixed cohort.

the cardiovascular dynamics from the bolus-tracking scans and the opacification curve just in time, hence making it independent from operators or additional hardware. Furthermore, optimal scan timing prevents repetitive scanning, which has been recommended by numerous authors [11,13,15]. Thereby, a limitation of radiation dose and contrast media use can be achieved, not only for patient safety but also for environmental concerns such as contamination of drinking water [21].

While rising technologies such as photon-counting detector CT [23] or even novel contrast agents with higher and prolonged contrast [24] may further increase diagnostic quality, these technologies are still not available everywhere and new contrast media are still in an experimental pre-clinical phase. In the future, a combination of techniques may yield the best results for physicians and patients and further studies are encouraged.

Our study is subject to limitations. Firstly, our study was from a single-center institution and the sample size is limited. Secondly, we could not directly control for possible confounders such as cardiac output, however, we found no significant differences regarding age, sex, BMI, and previous vascular interventions. Third, most patients had advanced vascular disease, which may influence arterial contrasting. However, these patients are the most challenging to examine, require the highest possible diagnostic confidence, and showed high inter-individual differences in the calculated delay times. Lastly, we did not implement further technical optimizations, such as performing reconstructions of each limb separately with the smallest possible field of view (FOV), which might improve image resolution even before the analysis.

In conclusion, our study demonstrates that individualized trigger delay increases objective and subjective image quality over conventional fixed trigger delay in lower extremity runoff CTA. This approach enhances diagnostic accuracy, reduces the need for repeated scans, and potentially decreases radiation and contrast agent exposure, which should be examined in further studies.

Guarantor

The scientific guarantor of this publication is L.N.

Statistics and biometry

A.T.S. has significant statistical expertise.

Study subjects or cohorts overlap

Methodology:

- prospective
- diagnostic or prognostic study

Table 2
Objective image quality measured in vessel enhancement (HU).

Location	Fixed PTD	Individualized PTD	Difference*	95 % CI	*p*	
AA	532 ± 177	507 ± 152	−24.92	−56.63; 106.50	0.815	ns
CIA	524 ± 212	507 ± 156	−16.87	−74.53; 108.30	0.856	ns
SFA	483 ± 148	508 ± 166	24.34	−102.90; 54.20	0.815	ns
PA	550 ± 196	544 ± 237	−5.53	−104.50; 115.60	0.920	ns
PTA	379 ± 106	479 ± 140	99.86	−163.00; −34.72	0.009	**
DPA	346 ± 137	477 ± 191	131.10	−216.00; −46.24	0.009	**

AA = abdominal aorta; CIA = common iliac artery; SFA = superficial femoral artery; PA = popliteal artery; PTA = posterior tibial artery; DPA = dorsalis pedis artery; HU = Hounsfield units.
(*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; ns = not significant).
Note. — Unless otherwise specified, data are means ± standard deviation.
*Difference in mean opacification values between cohorts (Individual Delay – Fixed Delay) at every location and 95%-confidence interval (CI).

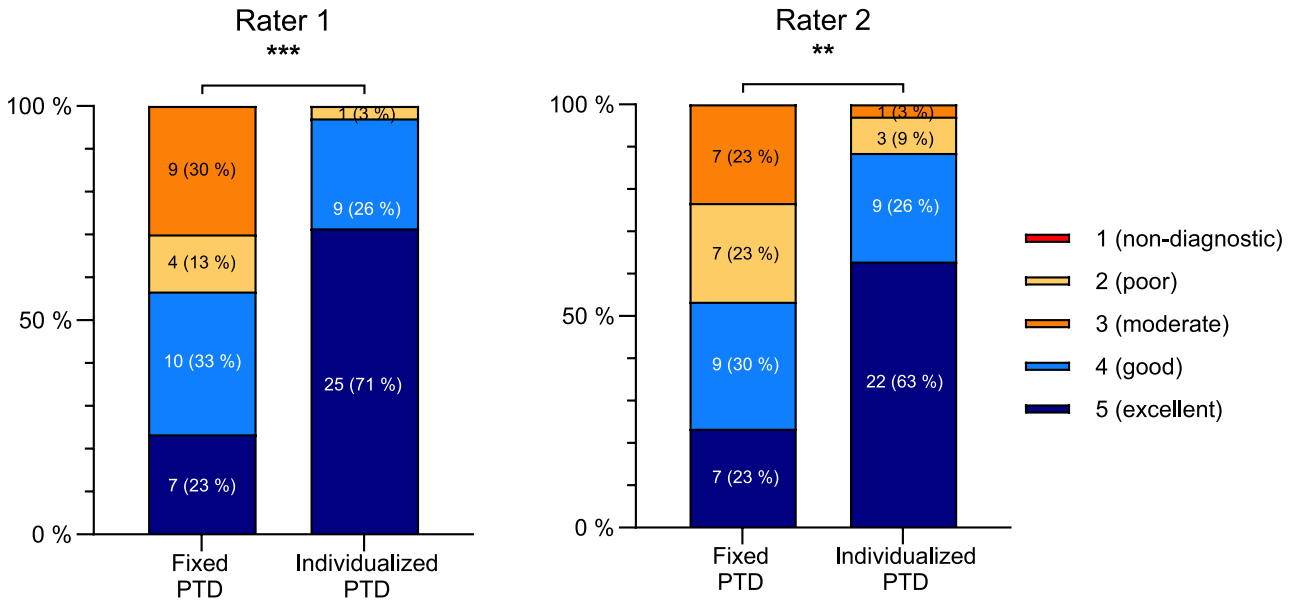

Fig. 3. Subjective quality ratings for overall "Image Quality" (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

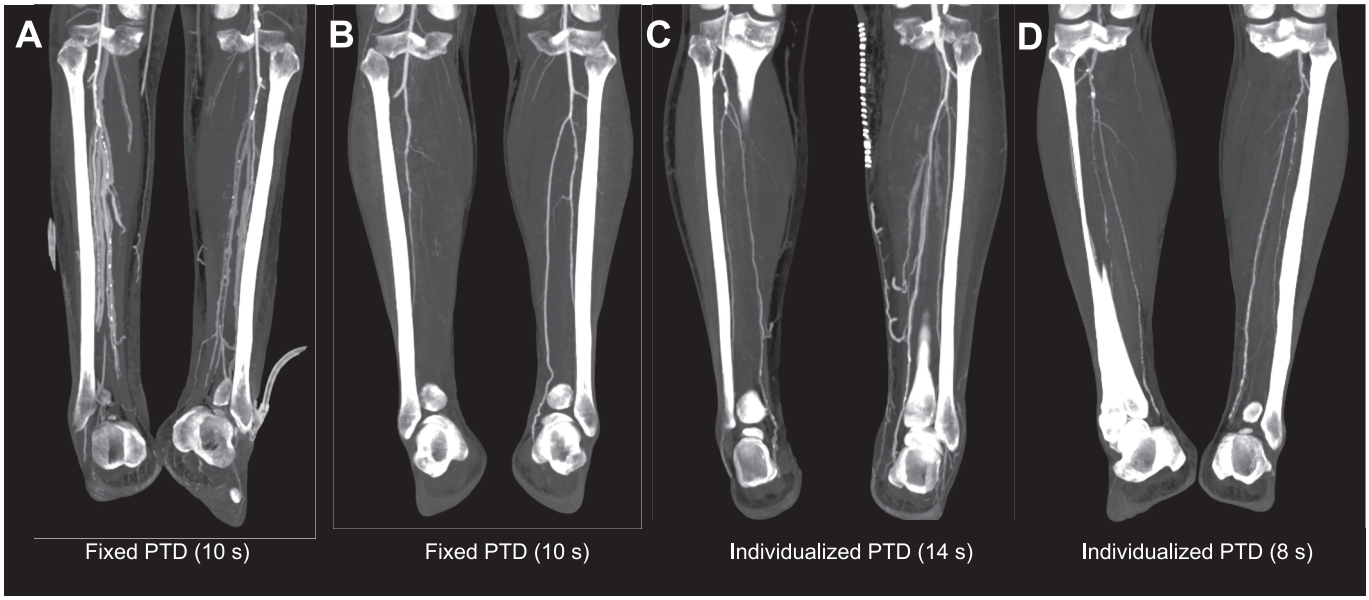

Fig. 4. Below the knee coronal maximum intensity projection (MIP), with identical scanning parameters,other than post-trigger delay (PTD) times: (A) Fixed PTD (10 s) in a 76-year-old female patient resulted in overlay of contrasting veins, both raters assigned subjective quality "2 (poor)". (B) Fixed PTD (10 s) in a 77-year-old male patient, with suboptimal contrast on the right, rated as "4 (good)" and"3 (moderate)" quality. (C) Individualized PTD (14 s) in a 73-year-old female patient; prolonged delay resulted in sufficient peripheral contrast on the right and only some venous overlay on the left side, after femoro-popliteal bypass; both readers rated quality as "5 (excellent)". (D) Individualized PTD (8 s) in a 58-year-old male patient resulted in clear in the periphery, even though atherosclerosis is present, rated as"5 (excellent)" by both raters.

- performed at one institution

Editor conflict of interest statement

Given their role as Section Editor Nicola Fink had no involvement in the peer-review of this article and has no access to information regarding its peer-review.

Ethical approval

Institutional Review Board approval was obtained.

Conflict of interest

B.O.S. received compensation by Siemens Healthineers for lectures at conferences.

CRediT authorship contribution statement

Loran Nas: Writing – original draft, Visualization, Investigation, Formal analysis, Data curation, Conceptualization. **Boj F. Hoppe:** Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Anna T. Stüber:** Writing – review & editing, Visualization, Formal analysis. **Sergio Grosu:** Writing – review & editing. **Nicola**

Fink: Writing – review & editing. **Alina von Fragstein:** Writing – review & editing. **Jan Rudolph:** Writing – review & editing. **Jens Ricke:** Writing – review & editing. **Bastian O. Sabel:** Writing – original draft, Visualization, Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

Informed consent

Written informed consent was obtained from all patients for this study.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Bastian Oliver Sabel reports financial support was provided by Siemens Healthineers. Bastian Oliver Sabel reports a relationship with Siemens Healthineers that includes: speaking and lecture fees. Co-author Nicola Fink is member of the editorial board of European Journal of Radiology. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejrad.2025.112009.

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