



Research article

Reproducibility and workflow efficiency of a novel software for quantitative coronary plaque characterization using photon-counting and energy-integrating detector computed tomography

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ABSTRACT

Introduction: The clinical adoption of quantitative coronary plaque characterization with coronary CT angiography (CCTA) is currently limited by time demands and lack of standardization across software platforms. This study aimed to evaluate the reproducibility and efficiency of a novel plaque quantification tool and to compare results between energy-integrating detector (EID-CT) and photon-counting detector (PCD)-CT.

Methods: In total, 170 patients were retrospectively enrolled in the current study: 86 patients were scanned using conventional EID-CT, while 84 using a dual-source PCD-CT. Quantitative plaque analysis was carried out using dedicated plaque analysis tools: syngo.CT Coronary Cockpit (Software 1, currently not commercially available) and MEDIS QAngioCT (Software 2) by three experienced readers. Total plaque volume (TPV) was quantified both automatically and manually.

Results: Among the 550 lesions analyzed, median TPV 67.0 mm³ [IQR: 31.4 to 148.7] using Software 1 and 50.8 mm³ [IQR: 23.7 to 110.0] using Software 2 ($p < 0.001$). Software1 demonstrated shorter measurement times than Software 2 (3.9 ± 2.5 vs. 22.9 ± 8.8 min; $p < 0.001$) and showed excellent intra- and inter-observer reproducibility for EID-CT and PCD-CT (ICC:0.995–0.998), whereas reproducibility using Software 2 was lower (ICC:0.845–0.880). PCD-CT showed improved agreement in TPV assessment, with a lower mean bias between software tools (PCD-CT:15.0 mm³ vs. EID-CT:45.3 mm³), and a smaller absolute difference between automated and manual measurements using Software 1, compared to EID-CT (PCD-CT: 2.5 ± 23.4 mm³ vs. EID-CT: 6.6 ± 28 mm³).

Conclusion: The prototype software offers a promising approach for rapid, reproducible quantification of coronary atherosclerosis, with PCD-CT technology further reducing manual corrections and inter-platform variability.

1. Introduction

Coronary CT angiography (CCTA) has emerged as a first-line modality for assessing coronary artery disease (CAD) by providing data on the degree of luminal narrowing, as well as the extent and characteristics

of coronary plaques [1,2]. Beyond qualitative evaluation, CCTA allows for quantitative assessment of CAD using coronary segmentation software, enabling a more robust analysis of coronary plaques. Several studies demonstrated the incremental prognostic value of quantitative plaque characterization using CCTA in predicting future major adverse

Abbreviations: CCTA, Coronary CT angiography; CAD, Coronary artery disease; QCT, quantitative CT; PCD-CT, Photon-counting detector CT; EID-CT, Energy-integrating detector CT; TPV, Total plaque volume; SCCT, Society of Cardiovascular Computed Tomography; ASIR-CV, Adaptive statistical iterative reconstruction algorithm for cardiovascular imaging; IQ, Image quality; UHR, Ultra-high resolution; QIR, Quantum iterative reconstruction; SD, Standard deviation; CAD-RADS 2.0, Coronary Artery Disease Reporting and Data System; VMI, Virtual monoenergetic image.

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cardiovascular events [3,4]. Furthermore, quantitative assessment has proven to be an effective method for detecting changes in both plaque composition and extent as a result of pharmacological treatments [5]. However, alongside the aforementioned advantages, the limitations of quantitative characterization techniques must also be acknowledged. The extensive variety of commonly used quantitative CT (QCT) software highlights the need to consider inter-platform variability. Additionally, manual editing required in semi-automated solutions raises concerns about inter-reader and intra-reader variability, as well as time-efficiency, while their accuracy and feasibility remain highly dependent on image quality [2,6].

Photon-counting detector CT (PCD-CT) offers improved spatial resolution and image quality compared to conventional energy-integrating detector CT (EID-CT) [7,8]. In recent years, technological advancements of PCD-CT and the optimization of its reconstruction settings have helped addressing the challenges of accurate assessment of coronary arteries [9,10]. Additionally, novel software tools have been developed to enhance both time efficiency and image quality, leading to a more effective solution for plaque quantification. Our study aims to evaluate the inter-platform and inter-observer reproducibility of a dedicated plaque quantification tool for total plaque volume (TPV) assessment using both EID-CT and PCD-CT images.

2. Methods

2.1. Study population

In this retrospective study, symptomatic patients with suspected CAD who were clinically indicated to undergo CCTA were enrolled between July 2023 and December 2023. CCTA was performed on either EID-CT or PCD-CT systems (Fig. 1). The study's inclusion criteria were an age of 18 years or older. Exclusion criteria were the following: 1) the absence of CAD 2) presence of coronary artery stents, 3) presence of coronary artery bypass grafts and 4) poor image quality due to motion, step, breathing or beam-hardening artefacts that could impair reliable coronary artery segmentation. Prior to the examination, demographic data, anthropometric measurements and medical history of the patients were documented.

Written informed consent was waived due to the retrospective nature of the analysis. The study was approved by the institutional and national

ethical committees (IV/655–3/2022/EKU and 28803–5/2020/EÜIG) and performed in accordance with the Declaration of Helsinki.

2.2. Coronary CTA acquisition protocol

CCTA was carried out following the guidelines set by the Society of Cardiovascular Computed Tomography (SCCT) [11]. For the EID-CT acquisition, a dedicated cardiac wide-detector CT scanner (GE Cardio-Grappe, GE Healthcare, Chicago, IL, USA) was applied with a rotation time of 240 ms. All patients without any contraindication were administered 0.8 mg of sublingual nitroglycerin prior to scans and received a maximum of 20 mg of intravenous beta-blockers to achieve a target heart rate of < 65 beats per minute. Patients received Iomeprol contrast material (Iomeron 400, Bracco Ltd., Milan, Italy) using a four-phasic injection protocol [12]. 85–95 ml of contrast media was administered via antecubital venous access at a flow rate of 4.5–5.5 ml/sec. Bolus tracking was applied in the left atrium to obtain accurate scan timing. Image reconstruction from the raw data was performed using the adaptive statistical iterative reconstruction algorithm for cardiovascular imaging (ASIR-CV level 70 and 90) [13].

PCD-CT examinations were performed using a first-generation clinical dual-source PCD-CT system (NAEOTOM Alpha, software version VA50, Siemens Healthineers, Forchheim, Germany) with a gantry rotation time of 250 ms. The following scan parameters were used, adjusted according to patients' anthropometric measurements: a tube potential of 120 or 140 kVp, automatic modulation of tube current set to image quality (IQ) level of 80 and collimation of 144 mm × 0.4 mm for standard resolution or 120 mm × 0.2 mm for ultra-high resolution (UHR) imaging. Prospective ECG-triggered sequential scan mode or retrospective ECG-gated helical mode was applied according to patients' heart rate and rhythm. All patients without contraindication received 0.8 mg of sublingual nitroglycerin and up to 20 mg of beta-blockers intravenously. Iodinated contrast agent (Iomeron 400, Bracco Ltd., Milan, Italy) was injected through antecubital venous access at a flow rate of 4.5–5.0 ml/sec, following a four-phasic injection protocol and using bolus tracking (10). CCTA standard resolution images were reconstructed using 0.6 mm slice thickness, using a quantum iterative reconstruction (QIR) algorithm at a strength level of 3, with a vascular, medium smooth kernel (Bv40).

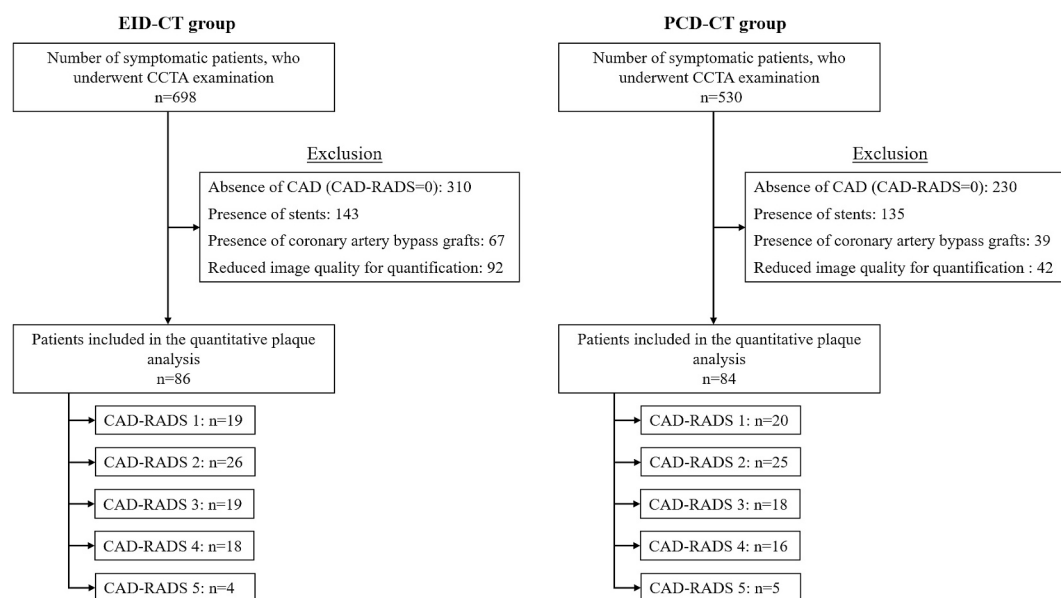


Fig. 1. Flowchart of the study. CT, computed tomography; EID, energy-integrating detector; PCD, photon-counting detector; CCTA, coronary computed tomography angiography; CAD-RADS, Coronary Artery Disease Reporting and Data System.

2.3. Quantitative plaque assessment

Quantitative plaque analysis was performed using two specialized software solutions (Software 1: syngo.CT Coronary Cockpit software (Siemens Healthineers, Forchheim, Germany, currently not commercially available); Software 2: QAngio CT, version 3.1 Medis Medical Imaging Systems) by three independent readers (B.S., M.B., B.V.) with at least 5 years of experience in cardiovascular CT imaging.

The main steps of quantitative plaque assessment were performed as follows (Fig. 2): First, the centerline of the selected vessel was semi-automatically extracted and subsequently manually adjusted to achieve alignment with the geometric center of the lumen, if needed. Therefore, proper curved and straight multiplanar reconstruction images were generated, that are essential for precise segmentation of the vessel wall. To ensure consistency in the evaluation, lesion start and end markers were defined once in Software 2 and transferred to Software 1. Inner and outer vessel wall were automatically delineated by the software, however manual adjustments were made if necessary. The lumen and vessel wall contours were identical (collapsed) for the segments without plaque. Segments or side branches with diameters less than 1.5 mm were excluded from the quantitative analysis. Plaques with a measured volume below 10 mm³ were excluded due to the limited reliability of quantification at small volumes resulting from partial volume effects and segmentation noise. With Software 1, coronary arteries were first segmented automatically and then manually adjusted, with TPV measured and recorded in both cases. Process and measurement time spent on the analysis was recorded for all cases with both software tools. Window-level display settings were kept constant.

2.4. Statistical analysis

Continuous variables are expressed as mean $\pm$ standard deviations

(SD) and as median and interquartile range depending on their distribution. Categorical variables are represented as counts with corresponding percentages in parentheses. Inter-platform agreement in TPV measurements between the two software tools was assessed using Bland-Altman analysis, for both CT scanner systems (EID-CT vs PCD-CT). Significant differences between TPV measures were determined using Wilcoxon signed-rank test. The discrepancy between automated and manual plaque volume measurements using Software 1 was assessed to evaluate how results differed when using EID-CT versus PCD-CT reflecting manual workload. To minimize potential bias, measurements were conducted in a randomized and anonymized fashion and intra- and inter-observer reproducibility was systematically evaluated (blinding period of 2 weeks was applied). Agreement for manual plaque quantification measurements was described using intraclass correlation coefficients (ICCs) in a randomly selected subset of 20 patients (51 lesions), consistent with sample sizes commonly used for reproducibility analyses in prior plaque quantification studies [14]. Measurement time was recorded by the readers. P-value < 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS Statistics, version 29.0 (IBM) and MedCalc Statistical Software version 23.0.8 (MedCalc Software Ltd).

3. Results

In total, we enrolled 170 patients with 550 coronary plaques in the study: 86 patients were scanned using EID-CT, while 84 using PCD-CT. The mean age was 62.4 ± 11.8 years, 34.7% were female and the mean BMI was 27.4 ± 4.1 kg/m². Median calcium score was 91 [IQR:7.0 to 300.8]. Effective radiation dose did not differ significantly between EID-CT and PCD-CT (3.85 ± 1.33 vs 3.85 ± 2.44 mSv, respectively, $p = 0.975$). Sequential acquisition was performed in 155 of 170 cases (91.2%). UHR mode was applied in 18 of 84 PCD-CT scans (21.4%). The

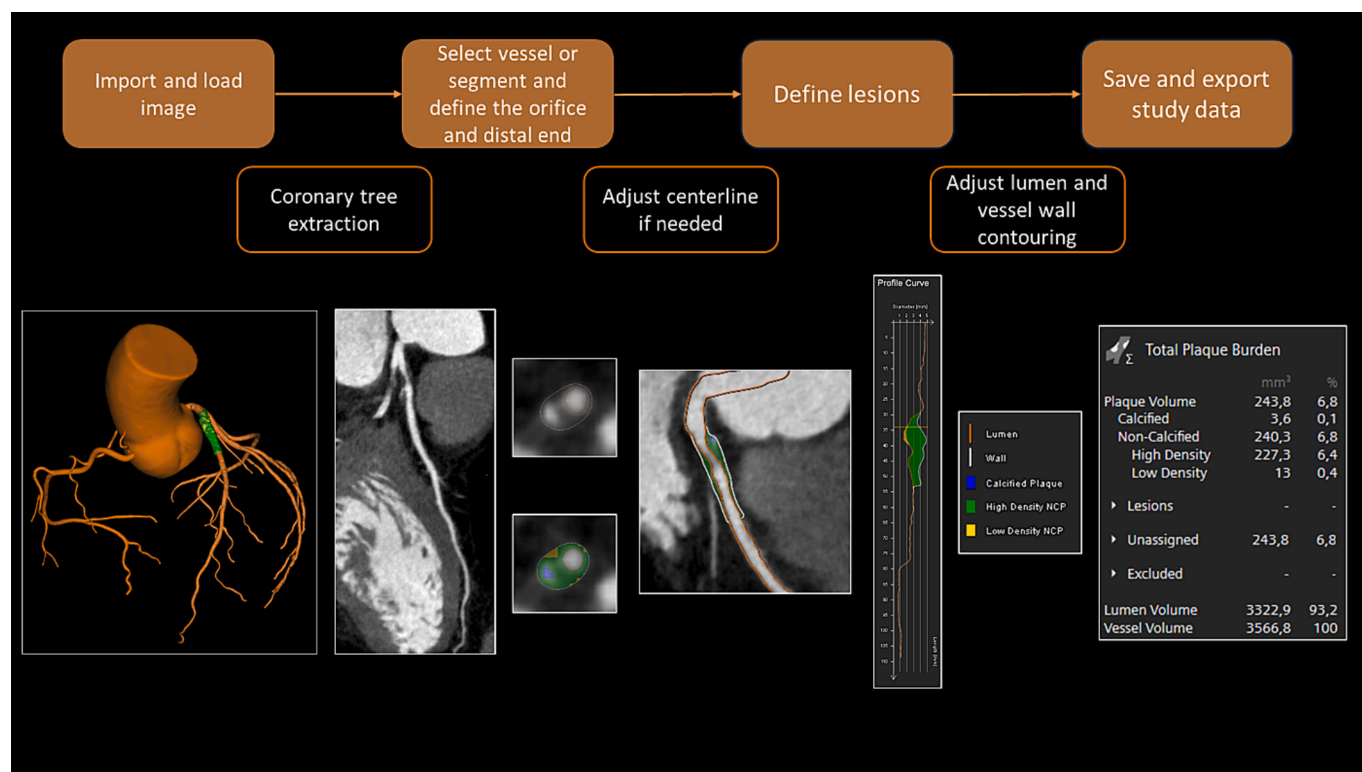


Fig. 2. Representative example and features of the novel software tool for plaque assessment. The figure illustrates a representative coronary CT angiography (CCTA) case analyzed using the novel plaque assessment software. After loading the CCTA dataset, the software automatically detects plaques and outlines the vessel contours. Lesions are then manually added by marking their borders, and contours are corrected if necessary to ensure accurate plaque quantification. The lower panel demonstrates the 3D visualization of the coronary tree, the color-coded mapping of plaque components, and the results table of the quantitative analysis.

mean heart rate was 60.0 ± 9.7 bpm. Table 1 summarizes the patient characteristics and comorbidities. Coronary Artery Disease Reporting and Data System (CAD-RADS 2.0) severity categories were similar between the EID-CT and PCD-CT groups ($p = 0.99$, see Fig. 1) [15].

Among the 550 lesions analyzed, median TPV was 67.0 mm^3 [IQR: 31.4 to 148.7] using Software 1 and 50.8 mm^3 [IQR: 23.7 to 110.0] using Software 2 ($p < 0.001$), the mean bias was 29.5 mm^3 between the two software with a lower limit of agreement (LoA) of -76.4 and an upper LoA of 135.4 (Fig. 3).

3.1. EID-CT versus PCD-CT for plaque quantification

In the PCD-CT group, analyzing 286 plaques, the median TPV was 60.2 mm^3 [IQR: 32.8 to 114.6] using Software 1, compared to 51.9 mm^3 [IQR: 28.4 to 88.5] with Software 2.

Among the 264 plaques assessed with EID-CT, the median TPV measured with Software 1 was 74.9 mm^3 [IQR: 38.0 to 175.5], while Software 2 yielded a median TPV of 49.1 mm^3 [IQR: 22.1 to 110.6].

Additionally, the discrepancy between automated and manual measurements using Software 1 was smaller with PCD-CT as compared with EID-CT, both in absolute terms and variability ($2.5 \pm 23.4 \text{ mm}^3$ vs. $6.6 \pm 28.0 \text{ mm}^3$ for EID-CT), indicating reduced volumetric variation in the PCD-CT group and better performance for higher resolution images.

The bias between the two software algorithms was notably smaller for PCD-CT (15.0 mm^3 with a lower LoA of -52.2 and an upper LoA of 82.2) compared to EID-CT (45.3 mm^3 with a lower LoA of -83.9 and an upper LoA of 174.6), suggesting greater agreement in plaque volume measurements using photon-counting CT despite higher CACS (Fig. 4). Only considering patients who underwent UHR PCD-CT with 95 lesions, inter-software agreement remained favorable, with a mean bias of 13.4 mm^3 and 95% limits of agreement of -85.7 to 59.0 mm^3 .

3.2. Time efficiency and reproducibility assessment

Software 1 demonstrated significantly shorter measurement times than Software 2 (3.9 ± 2.5 vs. 22.9 ± 8.8 min; $p < 0.001$). Software 1 demonstrated excellent intra- and inter-observer reproducibility for both conventional and photon-counting CT (ICC: 0.995–0.998), outperforming Software 2, which showed moderate reproducibility (ICC: 0.845–0.880).

Table 1

Patient characteristics, CT image acquisition parameters.

Demographics	N = 170
Age (years)	62.4 ± 11.8
Sex	
Female, n (%)	59 (34.7)
BMI (kg/m^2)	27.4 ± 4.1
Cardiovascular risk factors	
Hypertension, n (%)	106 (62.4)
Hyperlipidemia, n (%)	81 (47.6)
Diabetes mellitus, n (%)	26 (15.3)
Smoking history, n (%)	54 (31.8)
Positive family history, n (%)	43 (25.3)
CCTA protocol	
Mean effective dose, mSv	3.8 ± 2.0
Mean contrast dose, ml	82.9 ± 8.7
Spiral acquisition, n (%)	12 (7.1)
Mean heart rate, n (%)	60.7 ± 9.7
Coronary artery calcium score	91 (7.0–300.8)

BMI, Body mass index; CCTA, coronary computed tomography angiography.

Continuous variables are expressed as mean $\pm$ standard deviation or median and 25th–75th, while categorical variables as numbers and percentages.

4. Discussion

In our analysis, several main findings emerged: (1) The syngo.CT Coronary Cockpit demonstrated excellent inter-observer reproducibility for TPV measurements during expert-guided segmentation, regardless of whether the data were acquired using PCD-CT or EID-CT. (2) Inter-platform variability in TPV measurements was also observed between different semi-automated tools, with a smaller mean bias noted for PCD-CT compared to EID-CT. (3) Furthermore, the use of PCD-CT resulted in a smaller absolute difference between automated and manually edited segmentations when assessed with the novel quantitative plaque analysis tool, suggesting less manual workload for analyzing coronary lesions. (4) Finally, the novel software tool provides fast and robust automated plaque assessment when evaluating different severity stages of CAD.

In our current clinical practice, CCTA reports are often limited to qualitative or semi-quantitative assessments of CAD focusing on stenosis alone. However, this approach underutilizes the full potential of CCTA, which contains rich quantitative information on plaque burden, composition, and distribution. Dedicated plaque analysis software enables systematic extraction of this data, providing objective measurements that go beyond visual assessment. Quantitative imaging biomarkers have emerged as valuable tools for predicting future cardiac events by providing detailed information on coronary atherosclerosis, while also enabling precise follow-up of plaque progression and morphological changes [16]. The assessment of TPV may offer a clinically meaningful and easy-to-apply framework for CAD staging, while helping to clarify the complex relationship between functionally significant stenosis and plaque burden [17]. Owing to its potential clinical relevance, the quantification of CAD has attracted increasing attention in cardiovascular research. However, its clinical applicability has not yet been fully established. Semi-automated software tools often require manual adjustments, which can compromise both intra- and inter-observer reproducibility and are time-consuming, thereby limiting their integration into routine clinical practice. Another contributing factor is the emergence of several commercially available software solutions that utilize different segmentation algorithms and apply varying definitions and thresholds for plaque components, which, above all, underscores the necessity of assessing inter-platform variability [18]. We observed a systematic difference in TPV measurements between the two software platforms, with Software 1 yielding higher TPV values than Software 2. Both platforms provide semi-automated plaque quantification; therefore, this difference should not be interpreted as reflecting a lack of automation in Software 2. Rather, the observed offset and workflow differences likely reflect differences in default segmentation behavior, contour initialization, plaque definition criteria, interpolation between slices, and the handling of partial-volume effects and calcified blooming. In our expert-guided workflow, the initial output of Software 2 required more manual correction to align with the readers' assessment, which contributed to longer analysis times. However, further software optimization, vendor-specific tuning, or training of the algorithm on expert-annotated datasets may potentially improve its initial segmentation performance and workflow efficiency. Importantly, in the absence of an intravascular reference standard such as IVUS or OCT, we cannot determine which software provides measurements closer to the reference plaque volume. These findings emphasize that absolute TPV values from different software platforms should not be considered directly interchangeable, and that serial or comparative plaque assessment should ideally be performed using the same software environment.

The agreement of measurements may depend on the reader's level of experience and can also vary with plaque composition [19]. Reproducibility is generally greater for TPV and calcified plaque measurements than for non-calcified plaque assessment [20]. However, the accurate identification of non-calcified plaques is crucial, as they have been established as the strongest predictors of adverse coronary events, beyond stenosis severity and TPV [21]. Given the prognostic importance

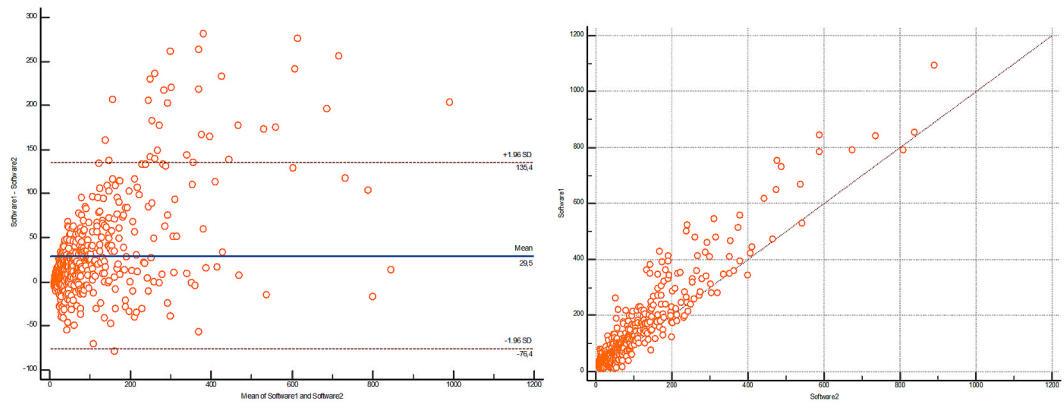


Fig. 3. Bland–Altman and correlation plots demonstrating the bias between the different software algorithms (Software 1 vs Software 2, all lesions). Bland–Altman plot (left panel) comparing total plaque volume measurements between Software 1 and Software 2 in the total study population. The solid line indicates the mean bias, and the dashed lines represent the 95% limits of agreement. The mean bias was 29.5 mm³ for TPV between the two software solutions. Strong correlation (right panel) was detected between the two softwares ($r = 0.983$, $p < 0.001$), while Software 1 measured systematically higher TPV values.

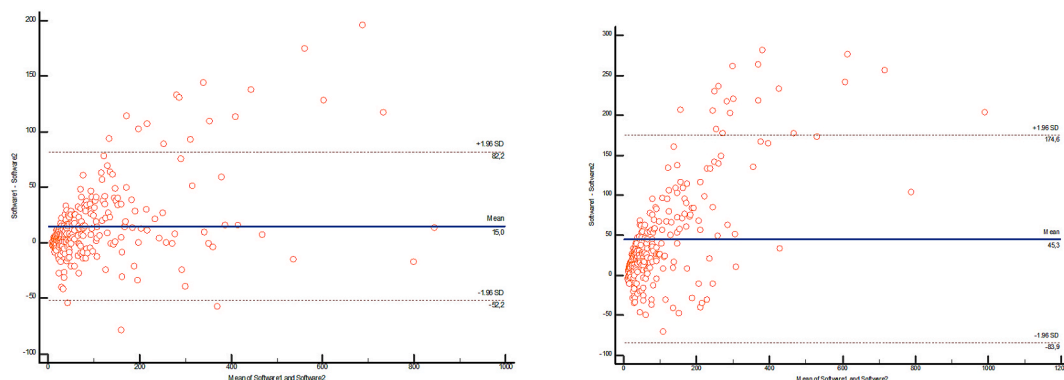


Fig. 4. Bland–Altman plots for the EID-CT and PCD-CT cohorts separately illustrate the bias between the two software algorithms in each group. In the comparison of software performance, the PCD-CT cohort demonstrated a markedly smaller bias than the EID-CT group, reflecting improved consistency across algorithms. The solid line indicates the mean bias, and dashed lines represent the 95% limits of agreement (LoA). Different y-axis scaling applied.

of plaque composition, recent studies have demonstrated that quantitative plaque assessment provides clinically relevant information, especially when integrated with patient-specific factors such as age and sex, to improve risk stratification and guide treatment decisions (e.g. lipid-lowering therapy or coronary intervention planning) [22]. Nevertheless, minimizing intra-reader and inter-reader variability is essential for the reliable clinical implementation of plaque quantification, thereby supporting the advancement of patient-centered treatment.

High-quality imaging is a prerequisite for both accurate and reproducible plaque analysis. In recent years, advances in detector technology have led to the development of PCD-CT [23]. By reducing electronic noise and artifacts, PCD-CT has demonstrated improved image quality in the evaluation of coronary arteries compared to conventional EID-CT [9,10,24]. The use of advanced energy-resolving x-ray detectors in PCD-CT enables superior spatial resolution, resulting in a more accurate evaluation of coronary artery luminal stenosis compared to conventional EID-CT [20]. This advantage is particularly beneficial in clinical practice for the visualization of heavily calcified coronary arteries, including the depiction of ring-shaped plaques [24]. Beyond its technical improvements, PCD-CT has recently been demonstrated to be cost-effective for CCTA compared to EID-CT, which may further support its global integration into routine cardiovascular imaging workflows [25]. This state-of-the-art detector technology also enables spectral imaging without compromising temporal resolution, allowing for more precise characterization of plaque composition and significantly mitigating

motion artifacts [26]. A recent study demonstrated that, compared to EID-CT, UHR PCD-CT yielded significantly lower measured plaque volumes – by approximately one-third – along with improved intra-reader and inter-reader reproducibility, particularly for low-attenuation plaque components [18]. Additionally, the spectral imaging capability of PCD-CT enables the generation of virtual monoenergetic images (VMIs), which can enhance CAD assessment by optimizing visualization and reducing blooming artifacts. However, the use of VMIs can also significantly affect plaque component characterization independently of detector technology, necessitating careful standardization of protocols [27]. In line with these findings, our results also confirm the high reproducibility of TPV quantification using PCD-CT. Nonetheless, achieving high inter-platform reproducibility in the quantification of non-calcified plaque volumes remains a challenge [28]. The advantages of this novel detector technology are evident in the reduced inter-platform variability observed during quantitative plaque assessment, further supported by the decreased need for manual corrections in PCD-CT image analysis versus the automated segmentation in our study and also by the substantially lower bias between different plaque quantification softwares using PCD-CT vs EID-CT.

The clinical utility of quantitative plaque assessment spans multiple domains, contributing to enhanced patient-centered care and improved risk stratification. Also, there are ongoing efforts within the U.S. healthcare system to establish reimbursement pathways for coronary plaque quantification, as recognition of its clinical value continues to grow. Several studies have demonstrated that plaque quantification

serves as a reliable tool for monitoring therapeutic response, as reflected by changes in plaque volume and composition [29,30]. Thereby, the integration of quantitative plaque assessment into clinical decision-making may support a precision medicine approach by facilitating tailored therapy selection based on individual atherosclerotic burden, potentially improving treatment efficacy while optimizing healthcare resource utilization [31]. A primary limitation of quantitative plaque analysis software in clinical practice is the relatively prolonged processing time, which largely depends on the level of automation and the need for manual adjustments. Nonetheless, in addition to time efficiency, maintaining high reproducibility through standardized and validated protocols remains essential for reliable quantitative assessment, which is still in the early stages of advancement [32,33]. Our findings demonstrated that the use of the novel prototype software enabled quantitative plaque assessment with high reproducibility in a more time-efficient manner, for both PCD-CT and EID-CT datasets.

5. Limitations

We acknowledge that this study had limitations. First, the PCD-CT and EID-CT study populations were not matched in terms of anthropometric characteristics; however, ensuring representation of all CAD-RADS severity levels was prioritized during patient selection. Second, the unique visual characteristics of PCD-CT compared to EID-CT may have enabled readers to infer the imaging modality, potentially introducing bias into the assessment despite the randomized order of case evaluation. A direct comparison between EID-CT and PCD-CT is challenging even at an intra-vendor level because quantitative plaque measurements are highly sensitive to acquisition and reconstruction settings. In an inter-vendor setting, additional confounders are introduced, including differences in tube potential selection and spectral sensitivity, ECG-gating and motion-correction approaches, iterative reconstruction and denoising algorithms, detector design, as well as effective slice thickness and z-axis resolution. These factors should be considered when interpreting inter-platform differences in plaque volume [32]. The better inter-software agreement observed with PCD-CT may be driven by improved image resolution, while software-specific algorithmic features and their interaction with acquisition settings likely also contribute. A key limitation of this study is the absence of an intravascular ultrasound (IVUS)-based reference standard, which is warranted in future investigations to validate plaque quantification. Only two commercially available software tools were used, potentially limiting the generalizability of our results across other platforms. Furthermore, analyses were performed at the lesion level, and multiple plaques were included per patient. As within-patient clustering was not modeled, lesion-level measurements may not be fully independent. Broader implementation will require further validation, standardization of analysis protocols – such as kernels, iterative reconstruction levels, and other post-processing parameters – which can alter plaque measurements. Lastly, the absence of prognostic follow-up data restricts the ability to assess the clinical impact of the quantitative findings.

6. Conclusions

This study demonstrates that the novel prototype software facilitates time-efficient, and highly reproducible quantitative plaque assessment across both PCD-CT and EID-CT datasets. Notably, inter-platform variability was lower and the need for manual adjustments was reduced when using PCD-CT data.

CRediT authorship contribution statement

B. Sipos: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation. **B. Vattay:** Writing – review & editing, Visualization, Data curation. **M. Boussoussou:** Writing – review &

editing, Visualization, Methodology. **M. Vecsey-Nagy:** Writing – review & editing, Methodology. **B. Nagy:** Writing – review & editing. **A. Kubovje:** Visualization, Data curation. **P. Maurovich-Horvat:** Writing – review & editing. **C. Schwemmer:** Writing – review & editing, Software. **V. Haase:** Writing – review & editing, Software. **M. Kiss:** Writing – review & editing, Software. **M. Schoebinger:** Writing – review & editing, Software. **B. Merkely:** Supervision, Resources, Project administration, Conceptualization. **B. Szilveszter:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors 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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