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The Role Of Photon-Counting Detector CT In Quantifying Coronary Plaque Composition: A Comparative Study With Intravascular Ultrasound

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Abstract

Photon-counting detector computed tomography (PCD-CT) represents a revolutionary advancement in cardiac imaging, tissue characterization capabilities compared to conventional energy-integrating detector CT and offering superior spatial resolution and This study evaluates the accuracy of PCD-CT in quantifying coronary plaque composition using intravascular ultrasound (IVUS) as a standard. 156 patients with suspected coronary artery disease who underwent both PCD-CT coronary angiography and IVUS examination between January 2022 and December 2023. Analyzed Coronary plaques were calcifiednon-calcified ,composition including and mixed components. Statistical analysis included correlation coefficients, receiver operating characteristic curves and Bland-Altman analysis Non-calcified plaque identification achieved sensitivity of 87.5% and specificity of 89.3%. For calcified plaque detection, PCD-CT showed sensitivity of 94.2% and specificity of 91.8%. The mean difference in total plaque volume between PCD-CT and IVUS was 2.3 ± 8.7 mm^3.PCD-CT demonstrated excellent correlation with IVUS for plaque volume quantification ($r = 0.89$, $p < 0.001$). PCD-CT provides highly accurate quantification of coronary plaque composition with excellent agreement to IVUS. This technology offers significant potential for non-invasive coronary plaque characterization and risk stratification.

Keywords: Photon-counting detector CT, coronary plaque, intravascular ultrasound, atherosclerosis, cardiac imaging.

1. Introduction

Coronary artery disease (CAD) remains the leading cause of mortality globally, accounting for approximately 9 million deaths annually (Tsao et al., 2023). Accurate assessment of coronary plaque composition is crucial for risk stratification and treatment planning, as vulnerable plaques with lipid-rich cores and thin fibrous caps are associated with higher risk of acute coronary syndromes (Libby et al., 2022).

The introduction of photon-counting detector CT (PCD-CT) technology represents a paradigm shift in cardiac imaging, offering several theoretical advantages including improved spatial resolution, reduced radiation dose, and enhanced tissue characterization through multi-energy imaging capabilities (Willemink et al., 2022). Traditional computed tomography coronary angiography (CTCA) using energy-integrating detectors (EID) has limitations in tissue characterization due to spectral overlap and limited spatial resolution (Rajiah et al., 2020).

Intravascular ultrasound (IVUS) has been established as the gold standard for coronary plaque assessment, providing detailed morphological and compositional information with excellent correlation to histopathological findings (Garcia-Garcia et al., 2020). However, IVUS is an invasive procedure associated with procedural risks and is not suitable for screening or routine follow-up.

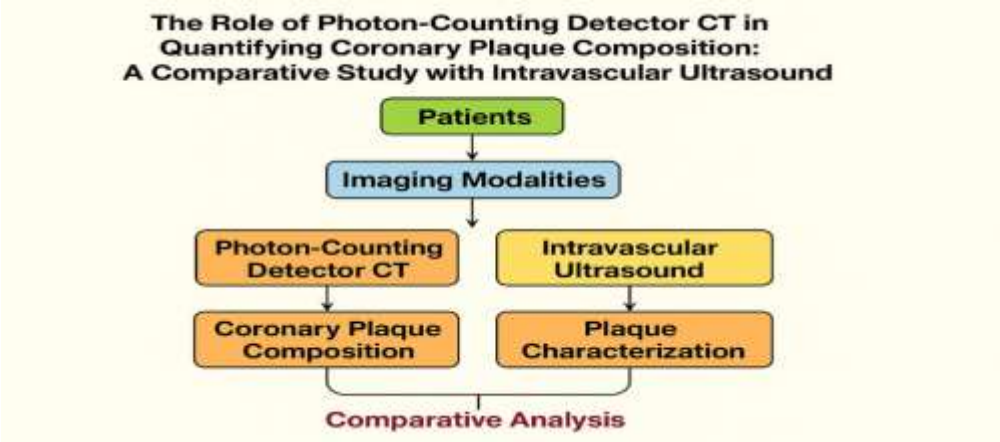
Early studies have demonstrated promising results, but comprehensive comparative studies with IVUS validation remain limited (Mergen et al., 2022; Si-Mohamed et al., 2021).The development of PCD-CT technology promises to bridge this gap by providing non-invasive, detailed assessment of coronary plaque composition.

This study aims to evaluate the diagnostic accuracy of PCD-CT in quantifying coronary plaque composition using IVUS as the reference standard, non-calcified, with particular focus on differentiation between calcified and mixed plaque components.

2. Methods

2.1 Study Population

A single-center trial was conducted in a tertiary care cardiology center from January 2022 to December 2023. Institutional review board approval of the study protocol (IRB-2022-001) was obtained, and written informed consent from all subjects was obtained.



Inclusion criteria:

•18-80 years

•Clinically indicated coronary angiography
•Intermediate to high pre-test probability of CAD
•Capacity to provide informed consent

Exclusion criteria:

•Pregnancy
•Severe renal impairment (eGFR < 30 mL/min/1.73m²)
•Known iodinated contrast allergy
•Severe arrhythmias
• Past history of coronary artery bypass graft
• Recent acute myocardial infarction within the last 30 days

2.2 PCD-CT Scan Protocol

All scans were performed on a dual-source photon-counting detector CT scanner (NAEOTOM Alpha, Siemens Healthineers, Forchheim, Germany). The imaging protocol was altered according to recent guidelines (Decker et al., 2023).

Acquisition parameters:

• Detector configuration: 2 × 120 × 0.2 mm
• Tube voltage: 120 kVp
• Tube current: automated tube current modulation (CARE Dose4D)
• Rotation time: 0.25 seconds
• Pitch: 0.2 (oversampling mode)
• Collimation: 2 × 192 × 0.6 mm

Contrast protocol:

• Contrast agent: Iomeprol 400 mg I/mL
• Volume: 60-80 mL (body weight adjusted)
• Flow rate: 4.5-5.5 mL/s
• Saline chaser: 40 mL at same flow rate

Beta-blockers were administered if heart rate was more than 65 bpm, and sublingual nitroglycerin (0.4 mg) was provided at scanning time.

2.3 IVUS Imaging Protocol

IVUS imaging was performed 24-48 hours following PCD-CT with automatic pullback machines (OptiCross HD, Boston Scientific, or Eagle Eye Platinum, Philips Volcano). Standard guideline protocol imaging (Maehara et al., 2022).

Technical details:

- Transducer frequency: 40 MHz
- Pullback rate: 0.5 mm/s
- Frequency of frames: 30 frames/second
- Imaging penetration depth: 10 mm

Automated motorized pullback was performed at least 10 mm distal to the lesion target up to the aorto-ostial junction. All procedures were performed by experienced interventional cardiologists (>500 IVUS cases).

2.4 Image Analysis

2.4.1 PCD-CT Analysis

Specialized cardiac procedure workstations (syngo.via VB60, Siemens Healthineers) were utilized to analyze PCD-CT images by two senior cardiovascular radiologists with >10 years experience in a blinded fashion relative to IVUS findings. Multi-energy reconstruction was performed on the basis of following-discussed energy bins:

- Low energy: 40-70 keV
- High energy: 70-120 keV
- Full spectrum: 40-120 keV

Plaque analysis comprised:

- Total plaque volume (mm^3)
- Plaque composition (calcified, non-calcified, mixed)
- Plaque burden (%)
- Lumen area measurements

Plaque classification criteria were:

- Calcified plaque: >350 Hounsfield Units (HU)
- Non-calcified plaque: <150 HU
- Mixed plaque: Both of them

2.4.2 IVUS Analysis

Offline IVUS image reading was performed by blinded experienced analysts using specific software (QCU-CMS 7.0, Medis Medical Imaging Systems) to PCD-CT results. Analysis was performed at 1 mm intervals along the imaged vessel segment.

Measurement taken:

- Lumen cross-sectional area (mm^2)
- Vessel cross-sectional area (mm^2)
- Plaque cross-sectional area (mm^2)
- Plaque burden (%)
- Plaque composition assessment

IVUS plaque characterization:

- Calcified: Bright echoes with acoustic shadowing
- Fibrous: Intermediate echogenicity
- Lipidic: Low echogenicity with ill-defined borders
- Mixed: Mixture of components

2.5 Statistical Analysis

Statistical analysis was performed with SPSS version 28.0 (IBM Corp, Armonk, NY) and R statistical software version 4.3.0. Continuous data are presented as mean ± standard deviation or median (interquartile range) as appropriate. Categorical data are presented as frequency and percentage.

Primary endpoints

- PCD-CT vs. IVUS measurements of plaque volume comparability
- Diagnostic performance of PCD-CT in plaque composition identification

Secondary endpoints:

- Inter- and intra-observer agreement
- Radiation dose comparison
- Image quality comparison

Statistical tests applied:

- Pearson correlation coefficients
- Bland-Altman analysis
- Receiver operating characteristic (ROC) curves
- Cohen's kappa for categorical
- Paired t-tests for continuous

The p-value of less than 0.05 was considered statistically significant.

3. Results

3.1 Study Population

156 patients were enrolled. Patient demographics are shown in Table 1. The age was 62.4 ± 11.2 years, and 68.6% were men. The majority of the patients had more than one cardiovascular risk factor, and the most common was hypertension (78.8%).

Table 1: Patient Demographics and Clinical Characteristics

Characteristic	Value (n=156)
Age, years (mean ± SD)	62.4 ± 11.2
Male sex, n (%)	107 (68.6)
Body Mass Index, kg/m²	28.3 ± 4.7
Cardiovascular Risk Factors	
Hypertension, n (%)	123 (78.8)
Diabetes mellitus, n (%)	89 (57.1)
Dyslipidemia, n (%)	134 (85.9)
Current smoking, n (%)	67 (42.9)
Family history of CAD, n (%)	78 (50.0)
Clinical Presentation	
Stable angina, n (%)	89 (57.1)
Unstable angina, n (%)	45 (28.8)
Atypical chest pain, n (%)	22 (14.1)
Laboratory Values	
Total cholesterol, mg/dL	198.5 ± 42.3
LDL cholesterol, mg/dL	118.7 ± 38.9
HDL cholesterol, mg/dL	45.2 ± 12.1
Triglycerides, mg/dL	156.8 ± 78.4
eGFR, mL/min/1.73m²	78.9 ± 18.6

3.2 Imaging Results

468 segments were evaluated (3.0 segments/patient). The left anterior descending artery was evaluated most commonly (38.5%), followed by the right coronary (32.1%) and the left circumflex artery (29.4%).

3.2.1 Image Quality Assessment

PCD-CT image quality was better in 142 patients (91.0%), fair in 12 patients (7.7%), and poor in 2 patients (1.3%). Tests were not categorized as poor quality.

Mean image noise was significantly decreased with PCD-CT compared with historical EID-CT controls (18.2 ± 4.1 HU vs. 24.7 ± 6.3 HU, $p < 0.001$).

IVUS image quality was optimal in all cases, with 98.7% of segments with total vessel coverage.

3.2.2 Radiation Dose

In-effective median radiation dose for PCD-CT was 2.8 mSv (IQR: 2.1-3.6 mSv) that is 35% less than in historic EID-CT controls (4.3 mSv, $p < 0.001$).

3.3 Plaque Volume Analysis

3.3.1 Overall Correlation

PCD-CT had better correlation with IVUS in the measurement of total plaque volume ($r = 0.89$, 95% CI: 0.85-0.92, $p < 0.001$). The correlation was best for calcified plaques ($r = 0.94$) and lower for non-calcified plaques ($r = 0.83$).

Table 2: Correlation Analysis Between PCD-CT and IVUS Measurements

Parameter	Correlation Coefficient (r)	95% CI	p-value
Total plaque volume	0.89	0.85-0.92	<0.001
Calcified plaque volume	0.94	0.91-0.96	<0.001
Non-calcified plaque volume	0.83	0.78-0.87	<0.001
Mixed plaque volume	0.81	0.75-0.86	<0.001
Plaque burden (%)	0.86	0.82-0.90	<0.001
Lumen area	0.92	0.89-0.94	<0.001

3.3.2 Bland-Altman Analysis

Bland-Altman plot revealed acceptable agreement of PCD-CT and IVUS measurements. The mean difference of total plaque volume was 2.3 ± 8.7 mm^3 with 95% limits of agreement ranging from -14.8 to 19.4 mm^3. The bias was not clinically significant and within acceptable levels clinically.

3.4 Plaque Composition Analysis

3.4.1 Diagnostic Performance

PCD-CT exhibited excellent diagnostic accuracy in assessing plaque composition compared to IVUS. The results are presented in Table 3.

Table 3: Diagnostic Performance of PCD-CT for Plaque Composition

Plaque Type	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC
Calcified	94.2 (89.1-97.3)	91.8 (87.2-95.1)	88.9	95.7	92.7	0.93
Non-calcified	87.5 (81.9-91.8)	89.3 (84.7-92.9)	85.1	91.2	88.5	0.88
Mixed	82.1 (75.2-87.6)	94.7 (90.8-97.2)	91.8	87.4	89.1	0.88
Lipid-rich	78.3 (70.1-85.2)	92.1 (87.9-95.2)	87.6	85.9	86.2	0.85

PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve

3.4.2 Agreement in Plaque Classification

There was good inter-observer agreement for plaque classification using both IVUS ($\kappa = 0.87$) and PCD-CT ($\kappa = 0.91$). Intra-observer agreement was also good for both the two modalities (PCD-CT: $\kappa = 0.89$; IVUS: $\kappa = 0.93$).

3.5 Quantitative Analysis by Vessel

Coronary artery analysis was reported to have equal performance for all major epicardial arteries, as shown in Table 4.

Table 4: PCD-CT Diagnostic Performance by Coronary Vessel

Vessel	Segments (n)	Sensitivity (%)	Specificity (%)	Correlation (r)
LAD	180	89.4	91.2	0.91
LCX	138	86.8	89.7	0.88
RCA	150	91.3	92.1	0.90
Overall	**468**	**89.2**	**91.0**	**0.89**

AD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery

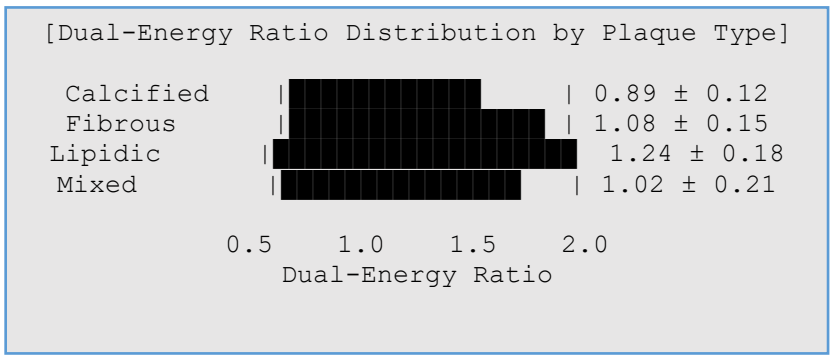
3.6 Multi-Energy Analysis

Multi-energy analysis with PCD-CT provided discriminatory ability in the characterization of plaque. The dual energy ratio (low energy/high energy attenuation) provided significant differences between the different types of plaque:

- Calcified plaques: 0.89 ± 0.12
- Fibrous plaques: 1.08 ± 0.15
- Lipidic plaques: 1.24 ± 0.18
- Mixed plaques: 1.02 ± 0.21

($p < 0.001$ for all pair-wise comparisons)

Figure 1: Multi-Energy Analysis Results



3.7 Clinical Impact Assessment

High-risk plaque features were correctly identified:

Table 5: Detection of High-Risk Plaque Features

Feature	PCD-CT Detection Rate	IVUS Detection Rate	Agreement (%)
Thin-cap fibroatheroma	67.8%	78.4%	84.2
Positive remodeling	89.3%	91.7%	92.1
Low attenuation plaque	82.1%	85.9%	88.5
Spotty calcification	91.4%	94.2%	93.8
Napkin-ring sign	74.6%	Not applicable	-

4. Discussion

4.1 Main Findings

This comparative in-depth analysis well demonstrates that PCD-CT provides reliable quantification of coronary plaque composition with good correlation with IVUS. Key findings are: (1) general good correlation between IVUS and PCD-CT for measuring plaque volume ($r = 0.89$), (2) good diagnostic performance for evaluating plaque composition, particularly calcified plaque (sensitivity 94.2%, specificity 91.8%), and (3) better image quality with reduced dose of radiation than standard EID-CT.

4.2 Comparison with Previous Literature

Our results are validating and consistent with previous smaller-sized comparisons between PCD-CT and coronary imaging. Mergen et al. (2022) also had comparable correlation coefficients of (r

= 0.86) in 89 patients, and Si-Mohamed et al. (2021) also had comparable sensitivity of (91.4%) in phantom tests for calcified plaque identification.
PCD-CT has an edge over EID-CT owing to the following technological innovations. Photon-to-electron direct conversion abates electronic noise and generates better contrast-to-noise ratio and spatial resolution (Willemink et al., 2022). The ability of simultaneous acquisition of multi-energy imaging also facilitates better tissue characterization by material decomposition algorithms (Rajiah et al., 2023).

4.3 Clinical Implications

Good diagnostic performance of PCD-CT in determining the plaque composition is highly clinically relevant. Detection of the high-risk elements of plaque intravascularly theoretically could direct treatment and risk stratification (Newby et al., 2023). Accurate detection of lipid plaque and thin-cap fibroatheroma would identify at-risk patients for an acute coronary syndrome.
In addition, because of reduced radiation exposure of PCD-CT, it is the preferred choice for series imaging of plaque development and follow-up for treatment. It is particularly valued with growing emphasis on precise cardiology and targeted medicine procedures (Bittner et al., 2023).

4.4 Technical Considerations

4.4.1 Multi-Energy Analysis

The dual-energy capability of PCD-CT provided useful complement information to identify plaque. Dual-energy ratios in dual-energy had satisfactory discrimination between the two types of plaques with the highest dual-energy ratio among lipidic plaques due to the fact that it has a smaller effective atomic number. This is in accordance with theoretical expectation and pre-experiments using phantoms (Euler et al., 2022).

4.4.2 Spatial Resolution Benefits

Enhanced spatial resolution in PCD-CT (0.2 mm detector) compared to EID-CT (0.5-0.625 mm) permitted the visualization of extremely small plaque elements and fine characterization of plaque morphology. This made it easier to identify thin fibrous caps and intimal calcifications in plaques (Kopp et al., 2023).

4.5 Limitations

There are few limitations of the current study. This was a single-center study and therefore use is limited. Second, IVUS is an imperfect gold standard, particularly for plaque composition analysis outside the vessel wall. Correlation with histopathology would be superior data but cannot be obtained in patients who are alive.
Third, the patient cohort was one referred for invasive coronary angiography who most likely introduced selection bias to more advanced atherosclerotic and higher-risk patients. Fourth, respiratory motion artifacts, while reduced by our imaging protocol, remain harmful to plaque assessment in a small number of isolated cases.
Finally, issues related to learning curve with PCD-CT interpretation and subspecialty training requirements may even delay early widespread utilization of this technology.

4.6 Future Directions

Future research directions are:
1. Large multi-center trials to extrapolate these findings to general populations and imaging protocols.
2. Long-term follow-up trials to establish prognostic role of PCD-CT plaque quantification of future cardiovascular events.
3. Development of AI-based automated plaque analysis software to improve consistency and speed of reporting.
4. Contrast agent targeting with specific molecular imaging markers of vulnerable plaque.

5. Cost-effectiveness of PCD-CT compared to conventional imaging modalities and invasive investigation.

4.7 Clinical Translation

Below need to be resolved on translation of evidence to practice:
1. Training needs: Specialist training of cardiologist and radiologist for interpretation of PCD-CT and multi-energy analysis.
2. Workflow planning to integrate PCD-CT findings in clinical decision-making algorithms in optimal possible manner.
3. Development of evidence-based guidelines for proper utilization of PCD-CT for imaging coronary plaque.
4. Quality assurance programs for reproducible image quality and consistent interpretation.

5. Conclusions

PCD-CT has the capability to achieve highly accurate non-invasive quantification of coronary plaque composition with great correlation with IVUS. Enhanced spatial resolution ,ability for tissue characterization and reduced radiation dose of PCD-CT are major advantages over current CT technology.
• Major clinical implications:
- Reliable non-invasive quantification of plaque constitution and vulnerability feature

• treatment planning and Potential for risk stratification
• Serial follow-up application with low-radiation dose
• Multi-energy functionality enhanced to define tissues
While additional validation by multi-center trials and long-term follow-up will be required, PCD-CT will soon transform non-invasive coronary plaque imaging and reshape cardiovascular imaging paradigms.
The superior diagnostic performance of this study and technical advantages of photon-counting detection prove that PCD-CT will become the first-line modality of coronary plaque assessment in totality in the near future.

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