



# Monochromatic image reconstruction by dual energy imaging allows half iodine load computed tomography coronary angiography



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## ABSTRACT

**Purpose:** To compare image interpretability and diagnostic performance of dual-energy CT coronary angiography (DE-CTCA) performed with 50% iodine load reduction versus single energy acquisitions (SE-CTCA) with full iodine load.

**Materials and methods:** The present prospective study involved patients with suspected coronary artery disease (CAD) clinically referred for CTCA. DE-CTCA with 50% iodine volume load was performed first, and after heart rate returned to baseline SE-CTCA was performed using full iodine volume load. The primary endpoint was to compare image interpretability between groups. DE-CTCA was performed by rapid switching between low and high tube potentials (80–140 kV) from a single source, allowing the generation of monochromatic image reconstructions ranging from 40 to 140 keV. Image quality assessment was performed using a 5-point Likert scale.

**Results:** Thirty-six patients constituted the study population. The mean heart rate before the CT scan (DE-CTCA  $57.3 \pm 10.7$  bpm vs. SE-CTCA  $58.5 \pm 11.2$  bpm,  $p=0.29$ ) and the mean effective radiation dose ( $3.5 \pm 1.9$  mSv vs.  $3.8 \pm 0.9$  mSv,  $p=0.48$ ) did not differ between groups. Likert image quality scores were similar between groups (DE-CTCA  $4.42 \pm 0.98$  vs. SE-CTCA  $4.43 \pm 0.84$ ,  $p=0.67$ ). Signal-to-noise and contrast-to-noise ratios were significantly lower with DE-CTCA, driven by lower signal density levels at 60 keV compared to SE-CTCA. The sensitivity and specificity for the detection of stenosis >50% was indistinguishable between groups (DE-CTCA 84.4% (69.9–93.0%), 87.1% (81.6–91.2%); SE-CTCA 84.4% (69.9–93.0%), 87.1% (81.6–91.2%).

**Conclusions:** In this pilot, prospective study, dual energy CTCA imaging with half iodine load achieved comparable interpretability than full iodine load with single energy CTCA.

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## 1. Introduction

Based on robust evidence collected during the past two decades, computed tomography coronary angiography (CTCA) has gained a role in the evaluation of symptomatic patients with low to intermediate likelihood of coronary artery disease (CAD) [1–3]. Since the incidence of contrast-induced acute kidney injury is closely related to iodine volume load and concentration, there is an essential need

for technical developments that can achieve a significant reduction in the iodinated contrast load [4,5].

Previous investigators have achieved a 20% contrast volume reduction using a lower tube voltage, although at the expense of higher tube current thus leading to persistently elevated effective dose radiation levels [6]. Dual-energy CT (DECT) allows the reconstruction of low and high energy projections and generation of monochromatic image reconstructions [7]. Consequently, higher intravascular attenuation levels can be attained through low energy monochromatic imaging, since with the administration of iodine vessels portray higher attenuation levels at lower energies than at higher energies due to the fact that lower energies are closer to 33.2 keV, the K edge of iodine [8]. We previously demonstrated that aortic CT angiography using DECT imaging allows up to 60% iodine volume reduction with similar image quality and interpretability

**Abbreviations:** DECT, dual energy computed tomography; SECT, single energy computed tomography; CTCA, computed tomography coronary angiography; CAD, coronary artery disease.

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than full iodine load with conventional single energy CTA imaging [9]. Accordingly, we attempted to explore whether we could extrapolate those findings to the evaluation of the coronary tree using CTCA.

## 2. Methods

### 2.1. Study population

The present was a single-center, investigator driven, prospective study, that involved patients with suspected CAD clinically referred for CTCA due to chest pain, anginal equivalents, or inconclusive stress tests. All patients underwent dual energy (DE) CTCA with 50% iodine volume load and, subsequently, single energy (SE) CTCA with full iodine volume load. All patients included were more than 40 years old, in sinus rhythm, able to maintain a breath-hold for 15 s; without a history of contrast related allergy, renal failure, or hemodynamic instability. Additional exclusion criteria comprised a body mass index  $>32 \text{ kg/m}^2$ , a history of previous myocardial infarction within the previous 30 days, previous percutaneous coronary revascularization or coronary bypass graft surgery, or chronic heart failure. Patients with pacemakers or implantable devices were excluded.

The primary endpoint of the study was to evaluate image interpretability of DE-CTCA with half iodine load compared to SE-CTCA with full iodine load. The secondary endpoint was to compare the diagnostic performance between groups in a subset of patients who underwent invasive coronary angiography. The institution's Ethics Committee approved the study protocol, which complied with the Declaration of Helsinki, and written informed consent was obtained from all patients.

### 2.2. Image acquisition

Patients were scanned using a 64-slice high definition scanner (Discovery HD 750, GE Healthcare, Milwaukee, USA), after intravenous administration of iodinated contrast (iobitridol, Xenetix 350TM, Guerbet, France) through an antecubital vein. Patients with a heart rate of  $>65$  beats per minute received 50 mg oral metoprolol one hour prior to the scan or 5 mg intravenous propranolol if needed in order to achieve a target heart rate of less than 60 bpm. In order to avoid any potential presence of residual intravascular contrast material, DE-CTCA with 50% iodine volume load was performed first and, 15–20 min later and after heart rate returned to baseline. SE-CTCA was performed using full iodine volume load.

All studies were acquired using prospective ECG-gating applying a 100 ms padding centered at 75% of the cardiac cycle for patients with a heart rate lower than 60 bpm, a 200 ms padding centered at 60% of the cardiac cycle for patients with a heart rate between 60 and 74 bpm, and a 100 ms padding centered at 40% of the cardiac cycle for patients with a heart rate higher than 74 bpm. DE-CTCA was performed by rapid switching (0.3–0.5 milliseconds) between low and high tube potentials (80–140 kV) from a single source, thereby allowing the reconstruction of low and high energy projections and generation of monochromatic image reconstructions ranging from 40 to 140 keV. Other scanner-related parameters were a gantry rotation speed of 350 ms, collimation width of 0.625 mm, 600–640 mA, a slice interval of 0.625 mm, and a temporal resolution of 175 ms. Maximum tube voltage and current for SE-CTCA were adjusted according to the body habitus (100 kV or 120 kV for patients with body mass index  $<30 \text{ kg/m}^2$  or larger, respectively). All SE-CTCA acquisitions were obtained using the high-definition mode.

For SE-CTCA with full iodine volume load acquisitions (body mass index  $\times 0.9$ ), iodinated contrast volume was injected using

a three-phase injection protocol, as follows. Phase 1: 50% of the total iodinated contrast volume being injected undiluted at a rate of 4.5–5.0 ml/sec; phase 2: the other 50% of the contrast medium mixed at a 60:40 saline dilution, injected at a rate of 4.5–5.0 ml/sec; and phase 3: a 40 ml saline chasing bolus at a rate of 4.5–5.0 ml/sec. DE-CTCA angiograms with half iodine volume load were obtained using a three-phase protocol, as follows. Phase 1: 50% of the total iodinated contrast volume mixed at a 50:50 saline dilution being injected at a rate of 4.0–5.0 ml/sec; phase 2: the other 50% of the contrast medium mixed at a 30:70 saline dilution, injected at a rate of 4.0–5.0 ml/sec; and phase 3: a 40 ml saline chasing bolus at a rate of 4.0 to 5.0 ml/sec. All patients received a 40 ml timing bolus to synchronize the data acquisition with the arrival of contrast material in the aorta, consisting of a combination of 20 ml contrast medium and 20 ml of saline at a rate of 5.5 ml/sec. Image acquisition was performed after sublingual administration of 2.5–5 mg of isosorbide dinitrate.

All reconstructions were performed using a standard kernel. SE-CTCA studies were reconstructed using a standard iterative reconstruction algorithm, at 40% ASIR (Adaptive Statistical Iterative Reconstruction). DE-CTCA studies were reconstructed at independent monochromatic energy levels ranging from 40 keV to 80 keV with incremental levels of 10 keV, in order to establish the lowest energy level (hence with higher signal density) with the highest contrast-to-noise-ratio (CNR) and signal-to-noise ratio (SNR) and consequently use it for comparison against SE-CTCA. Based on an interim analysis (data not shown), 60 keV with iterative reconstruction algorithm (ASIR) was the lowest energy level with the highest CNR and SNR, therefore it was used for further comparisons against SE-CTCA.

### 2.3. Image analysis

DE-CTCA image analyses were performed off-line on a dedicated workstation, using a commercially available dedicated software tool (AW 4.6, GE Healthcare) by consensus of two experienced level 3–certified coronary CTCA observers (PC, AD), blinded to the clinical data [10]. SE-CTCA were analyzed two weeks later by the same observers blinded to the clinical data. Axial planes, curved multiplanar reconstructions, and maximum intensity projections at 1–5 mm slice thickness were used according to 18-segment Society of Cardiovascular Computed Tomography Classification [11]. Images were evaluated on a per segment basis and per territory basis. Segments with a reference diameter lower than 1.5 mm were not included in the analysis. Each segment was graded as follows: normal; non-significant stenosis ( $<50\%$ ); significant stenosis ( $\geq 50\%$ ); or uninterpretable. Uninterpretable segments due to motion artifacts or severe calcification were assumed as positive for the diagnostic performance analysis.

Quantitative image quality assessment was performed using a 5-point Likert scale, as follows: (1) and (2) Non-diagnostic, impaired image quality due to motion artifacts or severe calcification that precluded appropriate assessment; (3) Suboptimal but sufficient, reduced image quality due to motion artifacts, image noise or low contrast attenuation, but sufficient to rule out obstructive disease; (4) Good, presence of mild motion artifacts, image noise, coronary calcifications or low contrast, but preserved ability to evaluate the presence of stenosis as well as to identify the presence mild atherosclerosis; and (5) Excellent, absence of motion artifacts, high intraluminal attenuation and clear delineation of vessel walls, with the ability to evaluate both the presence of obstructive disease and mild atherosclerosis.

The extent of vascular attenuation (in Hounsfield units) was measured using standardized regions of interest of  $20 \text{ mm}^2$  at the aortic root and at the epicardial fat. Signal density (mean Hounsfield units), noise (mean standard deviation of the signal density), and

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