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Comparative Diagnostic Accuracy of Dual-Energy CT Myocardial Perfusion Imaging by Monochromatic Energy Versus Material Decomposition Methods

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Abstract

Purpose—To compare the diagnostic value of monochromatic and material decomposition (MD) dual-energy computed tomography (DECT) imaging for the evaluation of ischemia.

Methods—Patients with suspected coronary artery disease underwent rest-stress DECT and SPECT perfusion imaging. DECT images were reconstructed between 40–140keV and through MD of iodine/muscle.

Results—MD and monochromatic imaging had a sensitivity, specificity, negative predictive, positive predictive value, and accuracy of 89%, 40%, 67%, 73% and 71%; and 91%, 67%, 67%, 91% and 86%, respectively ($p = 0.05$).

Conclusion—DECT using monochromatic energy displayed a non-significantly higher diagnostic accuracy for myocardial ischemia as compared with DECT MD.

Keywords

Dual-energy computed tomography (DECT); Coronary Artery Disease (CAD); Myocardial segments; Monochromatic energy; Perfusion defects; Ischemia

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Disclosure of Interest

All authors have no conflicts of interest to disclose.

1.1 INTRODUCTION

Novel innovations in CT technology have enabled the clinical applicability of dual-energy CT (DECT) for cardiac purposes (1,2). Foremost, prior studies have documented enhanced tissue differentiation, along with high image quality and improved accuracy for detection of coronary artery disease (CAD) using DECT imaging (3–6). Its ability to improve tissue characterization is based on exploiting the difference in energy-related attenuation of tissues (7), providing additional information regarding tissue composition, which is often disguised by conventional single-energy CT (SECT). To this end, DECT permits the acquisition of two fundamentally distinct types of CT images, namely, material density and monochromatic images.

As tissue attenuation profiles obtained at two different energy levels are exclusive for a given material, the disparity in energy-related absorption properties between the two X-ray spectra utilized in DECT allows for one to distinguish materials of sufficiently diverse attenuation profiles. In addition to material-specific images, virtual monochromatic images can be generated, which are analogous to conventional SECT images. Albeit, monochromatic images depict a scanned object at a single X-ray energy level, rendering these images less susceptible to beam-hardening artifacts (4,8,9). Hence, the implementation of these DECT imaging techniques enables the evaluation of myocardial perfusion by iodine-based material decomposition and the enhancement of iodine-containing tissues at low keV monochromatic imaging, respectively (4).

Some studies have demonstrated the feasibility of DECT for assessment of myocardial perfusion, reporting excellent diagnostic values (1,2). Nevertheless, studies determining the diagnostic role of DECT myocardial perfusion imaging (MPI) using material basis decomposition methods compared with monochromatic imaging are sparse at present. The purpose of this study, therefore, was to assess the feasibility and diagnostic utility of detecting myocardial ischemia via iodine-based material decomposition and monochromatic DECT imaging, while employing single photon emission computed tomography (SPECT) as a reference standard.

1.2 METHODS

1.2.1 Study population

The present study was a cross-sectional, observational, diagnostic study. Data were obtained from a clinical cohort of patients who were referred for the evaluation of known or suspected coronary artery disease (CAD). A total of 16 patients underwent both stress/rest SPECT and DECT MPI. Patients with valvular disease, left bundle branch block, non-ischemic cardiomyopathy, or prior coronary artery bypass graft surgery were excluded. The appropriate institutional review board (local medical ethics review committee) waived the need for written informed consent as the current study was based purely on clinical data collection.

1.2.2 Dual-energy computed tomography

All patients were scanned on single-source CT system equipped with gemstone detectors with fast primary speed and low afterglow designed for spectral imaging (Discovery CT750 HD, GE Healthcare, Milwaukee, WI, USA). A total of 10 patients underwent first stress imaging followed by rest, whereas 6 patients had rest followed by stress imaging. All patients were instructed to refrain from caffeine and xanthine derivatives 24 hours prior to stress DECT imaging. Stress myocardial perfusion imaging was performed after intravenous administration of dipyridamole (0.56 mg/kg) and iodinated contrast (iobitridol, Xenetix 350TM, Guerbet, France) using prospective ECG gating including 150–200 msec of temporal padding aimed to comprise approximately 40–75 % of the R-R interval, since systolic as well as diastolic phases were required for the analysis. A stress acquisition commenced three minutes after dipyridamole administration using a dual phase protocol with 50–70 mL of iodinated contrast followed by a 30–40-mL saline chaser. A bolus tracking technique was used to synchronize the arrival of contrast at the level of the coronary arteries with the start of the scan. For rest DECT acquisition, intravenous propranolol 5 mg was administered before the rest scan to achieve heart rates < 60 bpm. Image acquisition at rest was performed using the same protocol as for stress-DECT, after sublingual administration of 2.5–5 mg of nitroglycerine. As only a mid-diastolic window was required for rest acquisitions, the scan was performed using a 100 msec padding centered at 75 % of the cardiac cycle. Delayed enhanced DECT imaging was not performed. All CT examinations were performed in dual-energy mode in which kVp switched rapidly (0.3–0.5 milliseconds) between low (80 kV) and high (140 kV) tube potential at full inspiration, thereby allowing the reconstruction of low and high-energy projections and generation of monochromatic image reconstructions.

1.2.3 Single-photon emission computed tomography

At the time of the stress DECT perfusion scans, two minutes after dipyridamole administration and immediately before the CT scan, 10 to 15 mCi of technetium-99m-methoxy isobutyl isonitrile (99mTc-MIBI) was administered. Stress-SPECT image acquisition commenced 60 minutes following the administration of the radiotracer using a dual head gamma camera over a 90° circular orbit (GE Medical Systems. Millennium MG, Milwaukee, USA). Data were acquired in a 128 × 128 matrix for 32 projections in a step and shoot format. Rest-SPECT image acquisition was completed within 24 to 48 hours after stress-SPECT, after administration of 10 to 15 mCi of 99mTc-MIBI.

1.2.4 Image interpretation

The DECT images were evaluated and reconstructed using a 3D workstation (Advantage Workstation version 4.6, GE Healthcare). The DECT MPI data sets were reconstructed using a monochromatic energy level of 40 keV. On the basis of two-material decomposition of muscle and iodine content, iodine distribution maps of myocardium were generated. Thus the iodine content of each voxel within the myocardium was determined, and the corresponding pixels were color-coded. The myocardium was divided into a 17-segment model according to the definition of the American Heart Association (10). Myocardial perfusion was initially graded in a qualitative manner, whereby a defect was defined as an area of distinct hypoenhancement compared to normal surrounding myocardium.

Subsequently, a semiquantitative analysis was performed to classify only the visually graded defects with a signal density < 2 standard deviation (SD) of the average signal density of surrounding myocardium as true perfusion defects (11). Two experienced readers blinded to patient's clinical history graded all the scans. A third reader was used to adjudicate any discrepancies between the first two readers. All SPECT images were reconstructed and analysed using a commercially available software package (Cedars QPS/QGS, Cedars-Sinai Medical Center, Los Angeles, California, USA). The myocardium was divided into a 17-segment model, and for each segment, myocardial perfusion was visually analysed using a standard 5-point scoring system (0 = normal, 1 = equivocal, 2 = moderate, 3 = severe reduction of radioisotope uptake, and 4 = absence of detectable tracer uptake). A SPECT study was judged abnormal if there were 2 adjacent segments with a stress score 2. A defect was considered reversible if any stress perfusion defect was associated with a rest score 1 or a stress defect score of 4 with a rest score of 2. The DECT (CI and DI) and SPECT (DI and CP) studies were evaluated by two independent readers. Upon discordance a third reader was asked to adjudicate any discrepancies.

1.2.5 Statistical methods

Continuous variables are presented as means $\pm$ SD, and categorical variables are expressed as counts. Differences between continuous variables were compared using an unpaired Student's t-test. The performance of monochromatic DECT MPI and the basis-pair material decomposition methods were determined using sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy on a per-patient and per-vessel basis, respectively. A McNemar non-parametric test was employed to compare the diagnostic accuracy of monochromatic imaging at 40 keV and iodine-muscle basis decomposition. A two-sided p-value with a 0.05% significance level was considered for all tests. The Statistical Package for Social Sciences (SPSS) version 20 (IBM SPSS Statistics, IBM Corporation, Armonk, New York) was used to perform all statistical analyses.

1.3 RESULTS

Of 16 patients, 1 underwent only rest-DECT imaging while there was 1 scan with severe beam hardening artefacts due to extensive calcifications of the mitral valve annulus. Subsequently, these patients were omitted from analyses; hence the analytic sample comprised a total of 14 patients. Baseline characteristics of the study population are reported in Table 1.

1.3.1 SPECT MPI findings

Based on SPECT MPI, reversible perfusion defects were observed in 11 of the 14 (79%) patients, 11 of the 42 vascular territories (26%), and 32 of the 238 segments (13%), respectively.

1.3.2 Dual-energy CT MPI findings

Overall, 229 myocardial segments (96%) and 39 vascular territories (93%) of the 14 patients were analyzed using DECT. Monochromatic DECT identified 27 segments (12%) and 10 vessel territories (26%) as ischemic. By use of the material decomposition method, iodine-

muscle basis pair identified abnormal myocardial perfusion within 37 (16%) segments as well as 12 (31%) vascular territories.

1.3.3 Diagnostic performance of monochromatic DECT and material density imaging

The diagnostic performance of monochromatic 40 keV energy and iodine-muscle basis material decomposition method, sensitivity, specificity, NPV, PPV, and accuracy of DECT MPI were 91%, 67%, 67%, 91% and 86%; and 89%, 40%, 67%, 73% and 71%, respectively (Figure 1). Monochromatic imaging was more accurate, although not statistically significant ($p = 0.05$), compared with material density imaging using iodine-muscle basis pairs (Figure 1).

1.4 DISCUSSION

In this study, we found that detection of myocardial ischemia by DECT MPI demonstrated good agreement with SPECT. Monochromatic DECT imaging at 40 keV exhibited a non-significantly higher diagnostic performance as compared with material density imaging using iodine-muscle basis pairs.

Evaluation of myocardial ischemia is considered the cornerstone in the diagnosis of patients with suspected CAD (12,13). Clinical-decision making based on anatomical information alone is potentially misleading, as the anatomical appearance of coronary stenosis is only a modest predictor of its hemodynamic significance (14). Notably, angiographic-guided revascularization is shown to confer no symptomatic or prognostic benefit (15). Therefore, assessment of myocardial perfusion is an important aspect in the evaluation of CAD for permitting a more judicious referral for coronary revascularization. CT technology has undergone rapid advancements in recent years, enabling the application of DECT imaging for the assessment of myocardial blood flow (2). Mapping of iodine-based contrast agents by CT provide a surrogate for myocardial perfusion and several studies have reported on the validity and feasibility of this approach (16–18). Further still, DECT possess favorable characteristics compared to conventional CT such as the generation of monochromatic images, mitigating artifacts that result from beam hardening (9,19). Monochromatic images are synthesized using two approaches, depending on the utilized DECT device. In principle, the basis material decomposition is performed in an image-domain for images acquired with a dual-source CT, whereas material decomposition is typically performed in projection-domain for those images obtained with a single source DECT device with rapid voltage switching (19). The latter approach provides a more comprehensive beam-hardening correction (9,19,20). However, a direct comparison between monochromatic DECT imaging at 40 keV and material density imaging using iodine-muscle basis pairs for the detection of myocardial perfusion defects has, to the best of our knowledge, never been performed.

In the present study, we explored the diagnostic performance of monochromatic imaging at 40 keV, obtained with a single source CT with rapid voltage switching, exploiting the low K-edge of iodine (33.2 keV) to gain more contrast attenuation. Previous studies observed increased conspicuity of iodine-based contrast agents achieved with low tube voltage, while facilitating reduction of iodine load and radiation dose (8,21,22). In a recent study, Scheske et al reported improved signal-to-noise and contrast-to-noise ratios in both the myocardium

and coronary arteries with low energy monochromatic imaging as compared with polychromatic CT (4). Therefore, an optimal difference in contrast attenuation between normally perfused myocardium (high attenuation) and ischemic myocardium is anticipated at low monochromatic imaging. In the present study, monochromatic energy levels at 40 keV outperform iodine/muscle basis pairs for the detection of perfusion deficits. Higher energy levels (data not shown) come at a loss of contrast conspicuity, which is attributable to the low K-edge of iodine. Consequently, monochromatic DECT imaging exhibited high diagnostic accuracy (93%), which is fitting with previous studies (3,16–18,23) – albeit in a small sample of patients with prevalent CAD referred for detection of myocardial ischemia as indicated by SPECT MPI. In spite of this, however, its high sensitivity and NPV were offset by a moderate specificity and PPV.

Considering CCTA already enables the rule out of obstructive CAD with near to absolute certainty (24), DECT MPI as an adjunct to CCTA should possess high specificity in order to diminish the number of false-positive CCTA scans. However, DECT may have detected perfusion defects that were not observed with SPECT imaging owing to its low spatial resolution, which may have caused a real perfusion defect on CT to be classified as a false-positive finding. Although earlier studies have determined the diagnostic performance of DECT MPI, studies comparing monochromatic to material decomposition imaging for detection of myocardial ischemia are lacking. Notably, monochromatic imaging was as accurate as material decomposition for detection of myocardial ischemia. The two-material decomposition using iodine and muscle pairs resulted in a less accurate assessment of perfusion. One plausible explanation for this finding is the influence of infarcted tissue and/or microvascular disease on the enhancement of left ventricle iodine content based on iodine/muscle decomposition. Furthermore, accuracy of material decomposition imaging has mainly been negatively impacted by the relatively high rate of false-positive findings as compared with monochromatic imaging. It is, however, not unthinkable that the perfusion deficits seen utilizing iodine/muscle basis pairs are indeed true defects that may have gone undetected with SPECT MPI as a results of its lower spatial resolution. Thus, material decomposition imaging would have been unfairly considered inferior to monochromatic imaging. In light of this, forthcoming high quality studies are clearly needed in order to mitigate bias related to reference standards and patient selection to establish the diagnostic performance of DECT MPI for detection of myocardial ischemia in patients undergoing screening for CAD.

1.5 Study limitations

Some limitations of our study should be acknowledged. The study was limited in sample size, given the early evaluation of DECT MPI at our site. Further, delayed enhancement was not performed in this study because of radiation exposure concerns. However, Meinel et al reported no incremental diagnostic value of delayed acquisitions (25). In addition, the high prevalence of perfusion defects on SPECT indicates selection of patients at high risk. The results should be interpreted with caution, and may not be applicable to populations with a lower risk for CAD. Furthermore, the accuracy of DECT MPI was compared against a background of SPECT, while other non-invasive imaging modalities such as MRI and PET are demonstrated to be more sensitive for the detection of myocardial ischemia (26).

Nevertheless, this is the first study to compare the diagnostic performance of monochromatic and material decomposition imaging for the detection of myocardial ischemia.

1.6 Conclusion

Monochromatic DECT imaging at 40 keV exhibited a non-significantly higher diagnostic performance as compared with material density imaging using iodine-muscle basis pairs for the detection of myocardial ischemia as defined by perfusion defects detected with SPECT. The current findings suggest that monochromatic CT imaging may be a useful adjunct for CCTA for the assessment of myocardial perfusion in the clinical setting.

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Figure 1. Diagnostic performance of monochromatic and material decomposition using an iodine/muscle basis pairs

NPV, negative predictive value; PPV, positive predictive value.

Table 1

Demographic characteristics of the study population (n = 14).

Variable	Mean $\pm$ SD or N (%)
Age (years)	63 $\pm$ 9
Body mass index (kg/m ²)	28 $\pm$ 3
Male gender	8 (57%)
Diabetes Mellitus	4 (29%)
Hypertension	12 (86%)
Smoking history	3 (21%)
Dyslipidemia	11 (79%)
Myocardial infarction	6 (43%)