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Dual-energy computed tomography imaging to determine atherosclerotic plaque composition: A prospective study with tissue validation

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ABSTRACT

Background: Identifying vulnerable coronary plaque with coronary CT angiography is limited by overlap between attenuation of necrotic core and fibrous plaque. Using x-rays with differing energies alters attenuation values of these components, depending on their material composition.

Objectives: We sought to determine whether dual-energy CT (DECT) improves plaque component discrimination compared with single-energy CT (SECT).

Methods: Twenty patients underwent DECT and virtual histology intravascular ultrasound (VH-IVUS). Attenuation changes at 100 and 140 kV for each plaque component were defined, using 1088 plaque areas co-registered with VH-IVUS. Hounsfield unit thresholds that best detected necrotic core were derived for SECT (conventional attenuation values) and for DECT (using dual-energy indices, defined as difference in Hounsfield unit values at the 2 voltages/their sum). Sensitivity of SECT and DECT to detect plaque components was determined in 77 segments from 7 postmortem coronary arteries. Finally, we examined 60 plaques in vivo to determine feasibility and sensitivity of clinical DECT to detect VH-IVUS –defined necrotic core.

Results: In contrast to conventional SECT, mean dual-energy indices of necrotic core and fibrous tissue were significantly different with minimal overlap of ranges (necrotic core, 0.007 [95% CI, −0.001 to 0.016]; fibrous tissue, 0.028 [95% CI, 0.016–0.050]; $P < .0001$). DECT increased diagnostic accuracy to detect necrotic core in postmortem arteries (sensitivity, 64%; specificity, 98%) compared with SECT (sensitivity, 50%; specificity, 94%). DECT

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sensitivity to detect necrotic core was lower when analyzed in vivo, although still better than SECT (45% vs 39%).

Conclusions: DECT improves the differentiation of necrotic core and fibrous plaque in ex vivo postmortem arteries. However, much of this improvement is lost when translated to in vivo imaging because of a reduction in image quality.

1. Introduction

Rupture-prone coronary atherosclerotic plaques typically have a large necrotic core and thin fibrous cap[1]; differentiation of these features is therefore critical for imaging modalities to identify potentially high-risk plaques. Although coronary CT angiography (CTA) can identify some plaque features that predict acute coronary syndrome, such as positive arterial remodeling and low-attenuation areas of plaque,[2] more precise identification requires better discrimination of these components from each other. Plaque elements can be characterized by their CT attenuation profiles; however, studies that used conventional single-energy CT (SECT) found limiting overlap of the attenuation ranges of necrotic core and fibrous plaque.[3,4]

Tissue attenuation profiles are determined both by physical properties of constituent elements (atomic number and density) and by delivered x-ray energy. For example, dual-energy CT (DECT) provides differing attenuation of materials at 2 different energies and can differentiate fatty liver from tumor or can determine the composition of renal stones.[5,6] In theory, DECT should further separate attenuation values of coronary plaque components, allowing easier differentiation. Indeed, 2 separate sequential scans with different energies on ex vivo coronaries showed that calcified plaques had the largest and lipid-rich plaques the least difference in attenuation on DECT.[7] However, the ability of DECT to differentiate necrotic core from fibrous tissue has never been tested. Furthermore, sequential scanning cannot be used for rapidly moving coronary arteries, and the ability of DECT to identify plaque composition in vivo is unknown. The 2-tube, 2-detector configuration of dual-source scanners allows acquisition of 2 temporally registered data sets of different energies. We therefore determined whether DECT could differentiate plaque components better than SECT and to identify these components ex vivo against postmortem histology and in vivo against virtual histology intravascular ultrasound (VH-IVUS).

2. Methods

2.1. Study protocol

The local institutional review board approved the entire study, and participants gave fully informed consent. Subjects with stable angina or acute coronary syndrome scheduled for percutaneous coronary intervention underwent both VH-IVUS and coronary CTA with data sets used initially for derivation and then validation of DECT plaque analysis. VH-IVUS was acquired with Eagle-Eye Gold catheters (Volcano Corporation, San Diego, CA) as described previously.[8] CT data were acquired with a Somatom Definition 64-slice dual-source machine (Siemens, Germany). Intravenous metoprolol was administered if heart rate was >65 beats/min. Images were acquired simultaneously at 140 kV, 82 mAs (tube A) and 100 kV, 164 mAs (tube B) with 64 × 0.6-mm collimation. A triphasic injection protocol with intravenous contrast (iopamidol [Niopam 370]; Bracco, UK) was used after a 20-mL timing bolus.

2.2. Co-registration of DECT and VH-IVUS plaque components

CT image analysis was performed with Circulation III software (Siemens). Curved multiplanar coronary artery reconstructions were compared with longitudinal reconstructed IVUS data sets. To facilitate plaque component sampling VH-IVUS was used to identify plaque cross-sectional images that were either predominantly fibrous plaque or contained a large confluent necrotic core or dense calcification as previously described.[9] These plaque locations were co-registered from IVUS to coronary CTA by triangulation with the use of reference measurements from coronary ostia and side branches (Fig. 1). Areas of hypoattenuating or hyperattenuating plaque on cross-sectional coronary CTA images were classified as necrotic core, fibrous plaque, or calcified plaque, depending on matched corresponding VH-IVUS frames. Attenuation was sampled at 8 points distributed throughout these areas and lumen, to give mean CT attenuation values (Hounsfield units) (Fig. 2). DECT acquisition yielded 2 data sets with matching attenuation values at different energies for each plaque component.

2.3. Validation of necrotic core detection with DECT

2.3.1. Postmortem validation

The left anterior descending artery was dissected in 10 autopsy hearts within 24 hours of death with 40 to 50 mm of surrounding tissue to maintain structural integrity. Vessels were wax-embedded for mechanical support, and the left main stem ostium and distal left anterior descending artery were cannulated. Seven of 10 arteries were suitable for imaging (occluded arteries were not used). Vessels were submerged and pressure-perfused with phosphate-buffered saline at 37°C at 100 mm Hg. DECT acquisition was performed with the same peak tube voltages as in vivo, using contrast diluted to achieve luminal attenuation comparable with in vivo scans.

After imaging, arteries were fixed with formalin, and the external surface was marked at 1-cm intervals to aid co-registration. Each 1-cm coronary artery block was cut into segments 400 μm in length, processed for histology, sectioned