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Clinical application of effective atomic number for classifying non-calcified coronary plaques by dual-energy computed tomography

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ABSTRACT

Background and aims: Coronary computed tomography (CT) angiography allows non-invasive classification of non-calcified coronary plaques (NCCPs) based on Hounsfield unit (HU) values. This methodology, however, is somewhat limited for reliable classification of NCCPs. Therefore, we evaluated the effective atomic number (EAN) for classifying NCCPs by single-source dual-energy CT with fast tube voltage switching (SSDECT).

Methods: We prospectively enrolled 18 patients undergoing both SSDECT and intravascular ultrasonography (IVUS). Monochromatic images at 70 keV and EAN images were reconstructed from SSDECT data sets. Regions of interest (ROIs) within NCCPs were placed on IVUS-matched SSDECT images, and mean HU values and EANs for soft and fibrous plaques, classified using IVUS, were compared with an unpaired *t*-test.

Results: We placed 96 ROIs in 29 soft plaques and 37 ROIs in 15 fibrous plaques in 12 coronary arteries of 11 patients. The mean HU value in soft plaques (58.2 ± 32.8 HU) was significantly lower than that in fibrous plaques (103.9 ± 48.3 HU) ($p < 0.001$). The mean EAN in soft plaques (8.7 ± 0.5) was also significantly lower than that in fibrous plaques (9.6 ± 0.5) ($p < 0.0001$). Area under the curve for EAN (0.91) was significantly higher than that for HU value (0.79) in receiver operating characteristic curve analysis ($p = 0.046$). With a cutoff EAN of 9.3, sensitivity was 90% and specificity, 87%; whereas with a cutoff HU value of 55.0 HU, sensitivity was 62% and specificity, 93%.

Conclusions: EAN measurement by SSDECT can be clinically useful for accurately classifying soft and fibrous coronary plaques.

1. Introduction

Coronary computed tomography angiography (CCTA) is widely used for noninvasive and accurate assessment of coronary artery stenosis. CCTA also allows noninvasive classification of non-calcified coronary plaques (NCCPs) and identification of soft plaques, which are at high risk for plaque rupture and subsequent acute coronary syndrome (ACS), based on Hounsfield unit (HU) value measurement [1–3]. The HU value of coronary plaques correlates well with its histological type. Specifically, low-attenuation plaques are often soft plaques [4]. This methodology, however, is somewhat limited because of the susceptibility to the beam-hardening effect with standard computed tomography (CT) systems. The HU value generally depends not only on the material's atomic number but also on its density and X-ray photon energy.

Single-source dual-energy CT with fast tube voltage switching (SSDECT) can simultaneously acquire both high-energy (140 kVp) and low-energy (80 kVp) data sets by fast switching of the tube voltage, thereby greatly reducing beam-hardening effects and generating monochromatic and material density images from the projection data [5,6]. The effective atomic number (EAN), which can be accurately computed from the SSDECT data sets [7], is clinically

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useful for predicting the composition of renal stones [8] and carotid plaques [9]. EAN is an index developed more than a half century ago to determine materials' compositions [10,11]. The present study assessed the clinical usefulness of EAN for classifying NCCPs on CCTA by SSDECT, using intravascular ultrasonography (IVUS) as a reference.

2. Materials and methods

2.1. Subjects

Eighteen patients with stable angina or suspected coronary artery disease underwent CCTA by electrocardiography (ECG)-gated SSDECT (GSI Cardiac; GE Healthcare, Milwaukee, WI) using a dedicated CT scanner with garnet-based detectors (Discovery CT750 HD, GE Healthcare) before IVUS (Opticross; Boston Scientific, Boston, MA) consecutively between December 2013 and April 2015. IVUS was performed in all of the patients before percutaneous coronary intervention (PCI). The patients who did not undergo SSDECT within 4 months of IVUS and in whom NCCP classification through IVUS was not feasible were excluded from the further analysis. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and the institutional review board of Tokyo Women's Medical University approved this prospective study. Written informed consent was obtained from all the patients included in the present study.

2.2. CT imaging technique

Using a prospectively ECG-gated axial or step-and-shoot scan technique, SSDECT was performed with switching the tube voltage from 80 to 140 kVp during a single projection within 0.25 ms, as previously reported [12]. Unless contraindicated, patients with heart rates higher than 60 beats per minute (bpm) were orally administered metoprolol 1 mg/kg body weight (Seloken; Astra Zeneca, Tokyo, Japan) 90 min before each SSDECT examination and were also administered 0.3 mg of nitroglycerin (Nitropen; Nippon Kayaku, Tokyo, Japan) sublingually just before acquisition of the localization images. SSDECT was applied to the patients with a mean heart rate of less than 65 bpm and heart rate variability (defined as the standard deviation of the heart rate) of less than 5 bpm. We performed the cardiac scan during a single breath-hold in the head-to-foot direction using the following scan parameters: tube current, 600 mA; rotation time, 350 ms; temporal resolution, 175 ms; collimation, 64 × 0.625 mm; and padding time, 80–120 ms. Administration of the contrast medium was performed as described previously [12].

The volume CT dose index (CTDIvol) and dose–length product (DLP) were recorded for each CT scan. We calculated the mean CTDIvol and DLP in all of the patients undergoing SSDECT. We approximated the mean effective dose (ED) in the patients using the following equation: $ED = \kappa \times DLP$, where κ is equal to 0.014 $mSv \cdot mGy^{-1} \cdot cm^{-1}$ [13].

2.3. IVUS image acquisition and evaluation

Before each PCI procedure, unfractionated heparin (100 IU/kg body weight) was administered intravenously. Additional heparin boluses were administered intravenously to maintain an activated clotting time of >300 s. IVUS catheter was introduced into the coronary artery distal to the target lesion and retracted at a constant speed of 0.5 mm/s with an automatic tracking device.

NCCPs were analyzed in both the longitudinal and short-axis views in coronary segments 1, 2, 3, 5, 6, 7, 11, and 13 (according to the American Heart Association classification) whose lumen diameter was ≥ 3 mm [14]. Coronary segments 5, 6, 7, 11, and 13 by American Heart Association classification corresponds to coronary segments 11, 12, 13, 18, and 19 by BARI classification [15]. Starting from the fiduciary points, such as landmark side branches and sites of calcified plaques, the coronary vessels were analyzed at 3-mm intervals using an IVUS viewer. Coronary plaques were defined as structures within and/or adjacent to the coronary arterial lumen that could be clearly distinguished from the vessel lumen and the surrounding pericardial tissue, as previously reported [2]. Whereas structures with echogenicity greater than that of the adjacent vessel lumen were defined as calcified plaques, those with echogenicity less than that of the vessel were NCCPs. The NCCPs were further classified as fibrous or soft by comparing the echogenicity with that of the adventitia, according to the previously reported IVUS classification [16]. Tissues with low echogenicity inside an instent restenosis or near extensively calcified plaque, mixed atheroma or those likely to be thrombi were excluded from further analysis.

2.4. CT image post-processing

From the data acquired from the SSDECT scans, we reconstructed axial monochromatic images at 70 keV with the minimum slice thickness of 0.625 mm and field of view of 5 × 5 cm^2 at the best cardiac phase during diastole. We used the standard kernel and adaptive statistical iterative reconstruction algorithm with a blending ratio of 50% with the filtered back-projection algorithm [6]. We performed further image post-processing and SSDECT analysis using the dedicated software (GSI Viewer; GE Healthcare) in an external dedicated workstation (Advantage Workstation version 4.5; GE Healthcare). Curved-multiplanar-reconstruction stretched views of the coronary arteries at 70 keV were matched with longitudinally reconstructed IVUS data sets. Short-axis monochromatic images of the coronary arteries at 70 keV were spatially matched with the corresponding IVUS frames to construct paired data sets of spatially approximated sections between SSDECT and IVUS (Fig. 1).

Using the short-axis monochromatic images at 70 keV, an observer experienced in CCTA placed circular regions of interest (ROIs) with the diameter of 0.5 mm within each NCCP identified by IVUS to determine the mode HU values. We analyzed only NCCPs large enough to place two or more ROIs with no overlap inside to minimize the effect of marginal tissues. Others were excluded from further analysis. ROIs were automatically placed also on the short-axis EAN images at the same locations by referring to the same section of the monochromatic images at 70 keV using a copy-and-paste function with image post-processing software (ImageJ 1.48v, National Institutes of Health, MD, USA) to determine the mode EANs [17]. The mean HU values and EANs for each NCCP were calculated by averaging the mode HU values and the mode EANs in two to five ROIs, respectively. Reproducibility of the DECT measurements was checked using 14 slices from the first consecutive 4 patients by the same observer (i.e., intra-observer reproducibility) and by the other observer (i.e., inter-observer reproducibility).

2.5. Statistical analysis

Statistical analysis was performed using JMP for Macintosh (version 12.0; SAS Institute, NC, USA). For comparison of prediction of plaque types, we used an unpaired *t*-test. Receiver operating characteristic (ROC) curve analysis was performed to estimate the cutoff HU value and the EAN for classifying soft and fibrous plaques. Area under the curve was compared using a χ^2 test. Intraclass correlation coefficients were calculated to assess intra- and inter-observer reproducibility of those measurements. A p value < 0.05

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