Original paper

Non-invasive characterization of coronary artery atherosclerotic plaque using dual energy CT: Explanation in ex-vivo samples

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ABSTRACT

Purpose: In this study non-calcified plaque composition is evaluated by Dual Energy CT (DECT). Energy Dispersive X-ray Spectroscopy (EDS) has been used to study the Plaque composition. An attempt has been made to explain the DECT results with EDS analysis.

Methods: Thirty-two ex-vivo human cadaver coronary artery samples were scanned by DECT and data was evaluated to calculate their effective atomic number and electron density (Z_{eff} & ρ_e) by inversion method. Result of DECT was compared with pathology to assess their differentiating capability. The EDS study was used to explain DECT outcome.

Results: DECT study was able to differentiate vulnerable plaque from stable with 87% accuracy (area under the curve (AUC):0.85 [95% confidence interval {CI}:0.73–0.98}] and Kappa Coefficient (KC):0.75 with respect to pathology. EDS revealed significant compositional difference in vulnerable and stable plaque at $p < .05$. The weight percentage of higher atomic number elements like F, Na, Mg, S, Si, P, Cl, K and Ca was found to be slightly more in vulnerable plaques as compared to a stable plaque. EDS also revealed a significantly increased weight percentage of nitrogen in stable plaques.

Conclusions: The EDS results were able to explain the outcomes of DECT study. This study conclusively explains the physics of DECT as a tool to assess the nature of non-calcified plaques as vulnerable and stable. The method proposed in this study allows for differentiation between vulnerable and stable plaque using DECT.

1. Introduction

Atherosclerosis is characterized by intracellular and extracellular deposition of lipid and its derivatives in the subintimal layer of the arteries [1]. One of the common complications of atherosclerotic plaque is embolization which depends on the vulnerability of the plaque. A calcified plaque is vulnerable by nature [2,3] while a non-calcified plaque can be vulnerable when it shows high extracellular lipid, thin fibrous cap, surface ulceration and hemorrhage [2]. A non-calcified plaque may be vulnerable or stable depending upon the composition of plaque.

Various non-invasive imaging like ultrasound, MRI and CT angiography though may differentiate calcified and non-calcified plaque [4] but have proved to be inadequate to determine the nature of non-calcified plaque. A non-calcified plaque may be vulnerable or stable depending upon its composition. A vulnerable non-calcified plaque has a lipid rich core overlying with a thin fibrous cap ($< 65\,\mu m$) whereas a stable non-calcified plaque may either be fibrous or of intermediate fibro-lipid composition (with $> 65\,\mu m$ thickness of fibrous cap) [2,3,5]. It is to be noted that spatial resolution of modern CT system is limited (range of mm) and does not allow detecting objects of about $65\,\mu m$. Although, CT angiography identifies low-attenuation areas of plaque, more precise identification requires better discrimination of lipid core and fibrous cap which is compromised due to

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their similar X-ray attenuation and thus overlapping Hounsfield Unit (HU) or CT numbers [6–13]. Even an advanced imaging method like Dual Energy CT (DECT) gives overlapping HU values for similar tissues [13–15]. Phantom study have shown that coronary artery with stenosis is more susceptible to variation in HU values due to factors like CT scanner speed, scanning method and scan time after contrast medium injection [16]. Moreover, HU values are machine dependent parameter which means they vary with source spectrum, detector efficiency, filter configuration of CT machine leading to difficulty in characterizing vulnerable and stable plaques.

X-ray attenuation and hence HU values of scanned material depends upon the energy of incoming photons and also on Z_{eff} & ρ_e of the material. Thus from HU values Z_{eff} & ρ_e of the material may be calculated. DECT records two HU values at a point, simultaneously, at two different voltages. These two HU values have been used to get material specific information by Inversion method [17,18] established by us. These material specific informations were electron density (ρ_e) and effective atomic number (Z_{eff}) of non-calcified atherosclerotic plaque [17]. The attenuation coefficients (HU values) obtained in DECT is sensitive to variation in composition of scanned tissues [19]. The present study has attempted to compare vulnerable and stable plaques based upon their Z_{eff} and ρ_e values obtained from DECT inversion. These results were compared to reference standard histopathology to assess its differentiation capability. However, pathological studies do not give chemical specific information which is needed to explain the difference in Z_{eff} values of plaques obtained by DECT inversion. For this, Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray spectroscopy (EDS) chemical analysis were carried out which validated and explained the DECT outcomes.

2. Materials and methods

2.1. DECT study

2.1.1. Sample acquisition

Fifty-five excised human left coronary artery samples were collected from autopsy hearts of all age groups after the approval from Medical Ethics Committee of AIIMS. Proper consent from a relative or legal representative of the deceased was obtained.

Left Anterior Descending (LAD) coronary artery along with adjacent cardiac muscles (to keep the vessel in normal anatomical position) was dissected from its origin till the end (up to the apex of the heart with an average length of 10 cm). The excised LAD samples were immediately placed in 0.9% normal saline and kept in a refrigerator at 4 °C. The autopsy samples of LAD were collected from people who died due to Coronary Artery Diseases (CAD) and also from people (with no known CAD issues) who died due to road traffic accident, fall from height, alcohol intoxication, and suicide. The details of deceased were collected from the medical records.

2.1.2. DECT scanning

Samples were removed from saline just before the DECT scan and were injected with a viscous form of iodinated contrast material [18,20] into the LAD lumen. DECT scans were performed by placing the coronary artery ostium in the cranial position and the rest of the full-length of the samples was aligned along with the z-axis of the couch (Fig. 1a). All scans were performed on Dual Source CT SOMATOM Definition (Siemens AG, Germany) by using Perfusion Blood Volume (PBV) protocol. This protocol used 100 and 140 kVp, electrocardiographic gating (which gives a demo ECG of 60 beats/min), 64×0.6 mm collimation, 83 ms temporal resolution, pitch of 0.25 and rotation time 330 ms. Reconstructed images were obtained from 0.6 mm thick slice, B26f convolution kernel, and 512×512 matrix size. Maximum intensity projection mode was used to evaluate the presence of non-calcified plaque in the LAD and the distance between coronary ostium to the plaque was measured (Fig. 1b). Also, any landmarks such
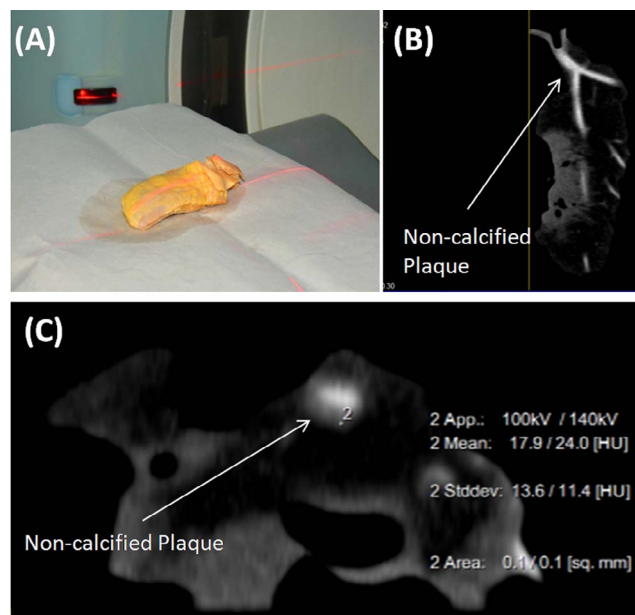

Fig. 1. (a) Section of heart containing LAD, positioned on the scanning table. (b) Typical MIP image of LAD containing soft plaque in proximal part. (c) Corresponding true axial image to read HU values.

as the origin of side branches and their distances from the target plaque were noted down. This measured distance was used as a marker for macroscopic evaluation for the presence of plaque and multiple sections of about 3 mm along the length of the plaque were dissected. Representative sections were submitted to cardiac-pathologist for analysis. From these sections very thin superficial sections were cut for SEM-EDS analysis. Scanned CT data were transferred to the multi-modality workstation for post-scan data processing.

2.1.3. Post scan processing

Images were oriented to get the true axial image of plaque (Fig. 1c). To read the HU values, circular region of interest (ROI) were selected in the axial slices along the length of the plaque starting from the first till the last axial slice of plaque.

These ROI (0.1–0.3 mm²) were placed at the centre of plaque area in axial slices in such a ways that at least each ROI must contain three pixels (3 pixel per ROI) so that HU values can be statistically accepted. Also, ROI dimension must not exceed 0.3 mm² so that contamination due to neighbouring structures (wall, soft tissue, and contrast in lumen) can be avoided. Data was recorded three times (i.e. 3 ROI/axial slice) in an axial slice along the length of the plaque for the same plaque. This process was repeated for all the plaque samples.

2.1.4. DECT inversion

We have used MATLAB; R2015b software (Mathworks, Natick, MA) for all numerical calculation. The HU values of plaques were subjected to a method called inversion algorithm developed by our group [18]. In present paper we further improvised our algorithm which established the relation of Z_{eff} and ρ_e with the HU of the object scanned at 100 and 140 kVp also called HU(100) and HU(140).

$$Z_{eff} = \left[\frac{(\chi(100,140) - a_1)}{b_1} \right]^{\frac{1}{X}} \text{ or } b_1 Z_{eff}^x + a_1 = \chi(100,140) \tag{1}$$

where,

$$\chi(100,140) = \frac{HU(100) - HU(140)}{HU(100) + HU(140)} \tag{2}$$

Here, the functional form of $\chi(100,140)$ maximizes the difference in attenuation at 100 & 140kVp compared to ratio HU(100)/HU(140)