Imaging of Microcalcifications and Ruptured Caps in Human Atherosclerotic Plaques using Contrast Enhanced High Resolution Micro Computed Tomography

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Introduction: The rupture of a thin cap Fibroatheroma (FA) is recognized as a key determinant of asymptomatic myocardial infarctions. Also, it is now well stablished the existence of numerous microcalcifications (μCalcs) in at least one third of fibrous caps in non-ruptured human fibroatheromas [1-7]. Using Finite Element analysis it was shown that μCalcs do intensify 200-500% the background circumferential stress in the cap tissue, and thus, they can transform a stable plaque into a vulnerable one [5,7-9]. However, the presence of μCalcs at the rupture site of FAs has not been yet well stablished since the thrombus often hampers the imaging of μCalcs at the rupture site. In this study, a contrast enhanced high-resolution μCT (CE-HRμCT) approach was developed to allow the imaging of μCalcs and ruptured caps under a thrombus.

Materials and Methods: Ninety-six human coronary arteries were harvested from 32 atherosclerotic whole human hearts obtained from the National Disease Research Interchange. Both left and right coronary arteries were dissected preserving their ostium and segments from the right coronary artery (RCA), the left anterior descending artery (LAD) and the circumflex artery (LCX). In total, 72 non-ruptured FAs and 18 fibroatheromas occluded with a thrombus were identified. In all but three of these atheromas, calcification was detected at 2.1-μm resolution CE-HRμCT.

Results and Discussion: The newly developed contrast-enhanced HRμCT (CE-HRμCT) approach provides superior imaging of tissue composition and atheroma morphology. Fig. 1A & 1E show a coronary artery in which the soft plaque cannot be distinguished, only inferred due to the thickening of the artery wall. However, the same sample incubated with contrast agent in Fig. 1B unequivocally shows important details of the atheroma, such as the necrotic core (dark spot in Figure 1B & 1F), intima, media, adventitia, internal and external elastic lamina. Fig. 1C & 1G display a blood vessel occluded by a thrombus imaged using μCT without contrast agent and the same sample with contrast agent in Fig. 1D & 1H. The thrombus and tissue composition of the atheroma cannot be distinguished in the sample without contrast agent, but they are readily visible when the sample is scanned with the contrast agent.

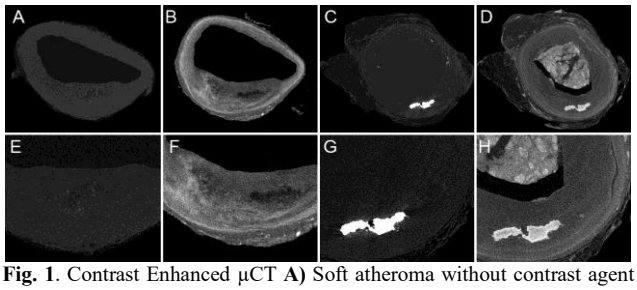

Fig. 1. Contrast Enhanced μCT **A)** Soft atheroma without contrast agent (CA), **B)** same atheroma with CA, **C)** Occluded vessel without CA, **D)** same vessel with CA, **E-H)** Magnified views of **A-D**. CEμCT allows distinguishing with clarity the morphology (including internal and external elastic lamina) and tissue composition in soft atheromas, fibroatheromas and ruptured atheromas with occluding thrombus.

Conclusions: CE-HRμCT improves the distinction of hard and soft tissues in blood vessels. It reveals a detailed tissue composition map of the intima, media, adventitia, internal elastic lamina, lipid pool, thrombi, ruptured caps and μCalcs. It enables the imaging of ruptured caps containing a thrombus, which was not possible before, providing unprecedented 3D information on the tissue composition and morphology. This methodology also significantly advanced our 3D fluid-solid interaction models of atheromas rupture using tissue-specific voxel data.

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