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Multimodality Imaging Atlas of Coronary Atherosclerosis

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NEW HIGH-RESOLUTION IMAGING TECHNOLOGIES HAVE ENHANCED OUR UNDERSTANDING OF THE CORONARY atherosclerotic disease process, and this atlas provides a multimodality pictorial review of the development of histologically verified coronary atherosclerosis. A modified American Heart Association classification scheme system based on morphological plaque features and the propensity of plaque for thrombosis or cause of sudden cardiac death has recently been proposed. This classification scheme incorporates 5 categories of coronary atherosclerotic lesions (Table 1) (1,2). These categories include nonatherosclerotic lesions (intimal thickening and intimal xanthoma) and progressive atherosclerotic lesions (pathological intimal thickening, fibroatheroma, thin fibrous cap atheroma, rupture, erosion, calcified nodule, and fibrocalcific plaque). The description of these categories is based on the accretion of lipid in relationship to fibrous cap formation, lipid pool transition into necrotic core, the thinning or thickening of fibrous cap, and presence of thrombosis. Furthermore, plaque characteristics such as angiogenesis, intraplaque hemorrhage, inflammation, calcification, cell death, and proteolysis are presented as descriptive terms along with features like culprit lesion associated with thrombus. This multimodality imaging atlas of ex vivo human hearts illustrates this morphological classification through computed tomography (CT), intravascular ultrasound (IVUS), optical frequency domain imaging (OFDI) and corresponding histological characteristics (Figs. 1 to 7) (3–8).

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Table 1. Correlation of AHA Plaque Nomenclature With Descriptive Scheme

AHA Classification (2)	Descriptive Scheme (1)
Type III	Pathologic intimal thickening
Type IV	Fibrous cap atheroma
Type Va, Vb, Vc	Healed plaque rupture with or without calcification
Type VI	Thin cap fibroatheroma
Type VI	Plaque hemorrhage/plaque rupture

AHA = American Heart Association.

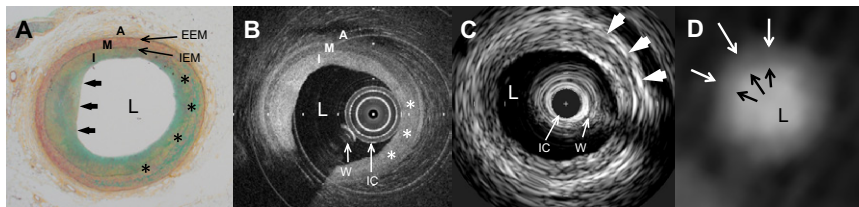


Figure 1. Adaptive Intimal Thickening With Focal Loss of Media

The earliest change in the arterial wall that can be detected by current imaging technologies is intimal thickening. These lesions can be detected soon after birth, consisting mainly of proteoglycan-rich matrix and smooth muscle cells. Histopathology (A) demonstrates three distinct layers: intima (I), media (M), and adventitia (A). The intima is asymmetrically thickened (black arrowheads), the normal media is seen between the external elastic membrane (EEM) and internal elastic membrane (IEM) while a focal loss of media is indicated with black *. Optical frequency domain imaging (OFDI) (B) provides the best correlation with the histopathology findings and demonstrates asymmetric intimal thickening and a focal loss of media (white *). Intravascular ultrasound (IVUS) (C) depicts the collagen rich adventitia as bright echos (white arrowheads), however, the distinction between the intima and media can not be easily appreciated. Coronary CT angiography (CTA) (D) demonstrates a thickened coronary wall. The black arrows indicate the inner border of the vessel wall, while the white arrows indicate the outer border of the vessel wall. Further characterization of the coronary wall layers is not possible. IC = imaging catheter; L = coronary lumen; W = guide wire.

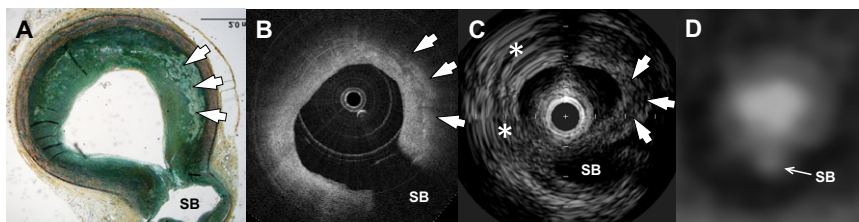


Figure 2. Pathologic Intimal Thickening

Pathologic Intimal Thickening is thought to represent the building block for atherosclerotic plaque development and it is sometimes referred to as an “intermediate lesion.” The thickened intima often contains deposits of lipid in a proteoglycan rich matrix called lipid pools that are devoid of smooth muscle cells and macrophages close to the media, but without evidence of a necrotic core. Histopathology (A) demonstrates minimal luminal obstruction, a thickened intima with lipid accumulation close to the media (light green areas, white arrowheads). The lipid pool is visualized by both OFDI (signal loss) and IVUS (echolucent area) although the differentiation is difficult (B and C, white arrowheads). The outer boundary of the plaque is not visualized by OFDI, whereas the side branch is partially shadowed by the guide wire. In IVUS artifacts (nonuniform rotational distortion) limit the boundary recognition between intima and media and allow only partial plaque characterization. CTA clearly demonstrates a thicker noncalcified plaque (plaque depth is approximately 1.5 mm) but further differentiation of plaque composition is not possible. SB = coronary artery side branch.

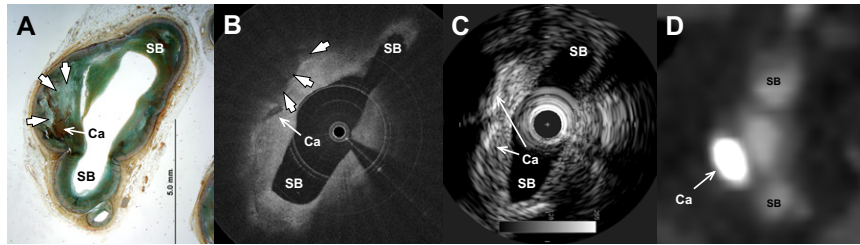


Figure 3. Pathologic Intimal Thickening With Calcification

Histopathology (A) demonstrates a thickened intima which contains lipid pools close to the media (white arrowheads) and spotty calcification (Ca). OFDI (B) demonstrates the intimal thickening, the lipid pool and the spotty calcification (low density area with sharp boundary indicated by "Ca"). In IVUS (C), acoustic shadowing limits assessment of plaque properties, the lipid pool is not visualized. CTA (D) demonstrates the calcification with significant blooming artifact (about 4 times overestimation of calcified area) (3) as well as the noncalcified plaque component but without further characterization. SB = coronary artery side branch.

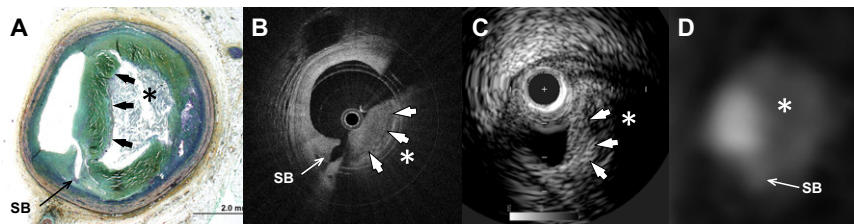


Figure 4. Late Fibroatheroma

The American Heart Association differentiates between Type IV and V fibrous cap atheroma lesions on the basis of the thickness of the fibrous cap and the presence of a lipid or necrotic core, whereas Virmani et al. (1) defined these lesions as fibrous cap atheroma (Table 1) (4). The fibrous cap is composed of smooth muscle cells in a proteoglycan rich matrix. As the plaque matures the lipid core consolidates and accrues necrotic debris and cholesterol crystals. Histopathology (A) demonstrates a fibroatheroma with a thick fibrous cap (black arrows) and a large necrotic core (*). It is known that the size of the necrotic core is significantly associated with its likelihood to rupture (5,6). OFDI (B) also depicts a thick fibrous cap (white arrows) and the large necrotic core with typical low intensity appearance (*). IVUS (C) demonstrates a narrowed coronary lumen with an eccentric plaque. The plaque is heterogeneous with an echolucent core and an overlying echodense fibrous layer (white arrows). There is signal drop out due to the plaque thickness (*). CTA (D) reveals a large noncalcified plaque segment. In this case, however, the plaque can be further characterized based on differences in CT attenuation. Specifically, there is a difference in attenuation between a central low attenuation area (corresponding to the lipid-rich necrotic core, *) and rim of high CT attenuation (corresponding to fibrous plaque tissue). This CT attenuation pattern has been described as the napkin-ring sign, the CT signature of high-risk coronary atherosclerotic plaque (7).

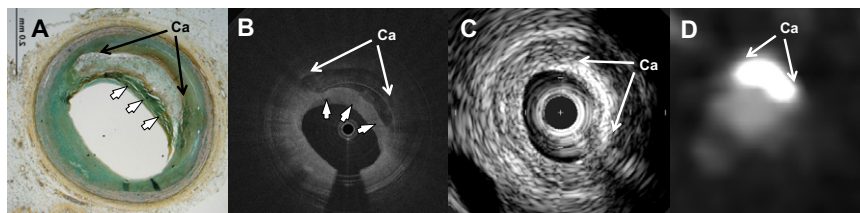


Figure 5. Fibrocalcific Plaque With Sheet Calcification

If the calcium area exceeds 10% in the absence of a necrotic core it constitutes a fibrocalcific plaque. In contrast to the fibroatheroma, the dominant component of a fibrocalcific plaque is calcification and not necrotic core. Both histology and OFDI (A and B) demonstrate extensive sheet calcification (Ca) with a shallow intimal layer between the calcification and the lumen (white arrowheads). The sharp delineation of the calcification against the intima can be appreciated in OFDI. IVUS (C) permits visualization of the calcification (Ca) as an echo bright area with acoustic shadowing. CTA (D) demonstrates a calcified plaque that appears much larger than in OFDI or histology as a result of extensive blooming artifact. As a result, the thickened intima cannot be distinguished as an underlying noncalcified plaque. This is an example that plaque that appears as calcified in CTA images, usually also has significant noncalcified portion. Thus, current differentiation between mixed and calcified plaques based on CTA images may be artificial.

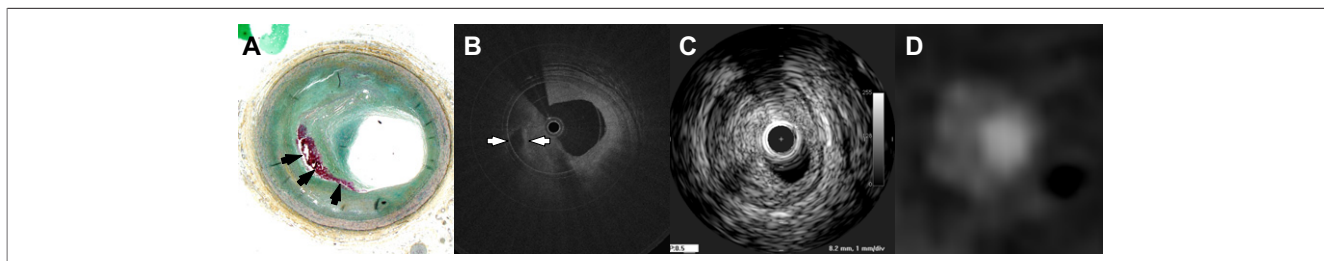


Figure 6. Late Fibroatheroma With Intraplaque Hemorrhage

Histopathology (A) demonstrates intraplaque hemorrhage (black arrowheads). OFDI (B) demonstrates inhomogeneous plaque with both low- and high-intensity areas (white arrowheads). IVUS (C) confirms the gross plaque morphology (asymmetric fibrotic thickening) but is unable to depict the area of intraplaque hemorrhage. CTA (D) also demonstrates the gross noncalcified plaque morphology with an inhomogeneous intraplaque attenuation pattern. This could be an expression of advanced/complex plaque morphology. However, intraplaque hemorrhage or neointima cannot be differentiated.

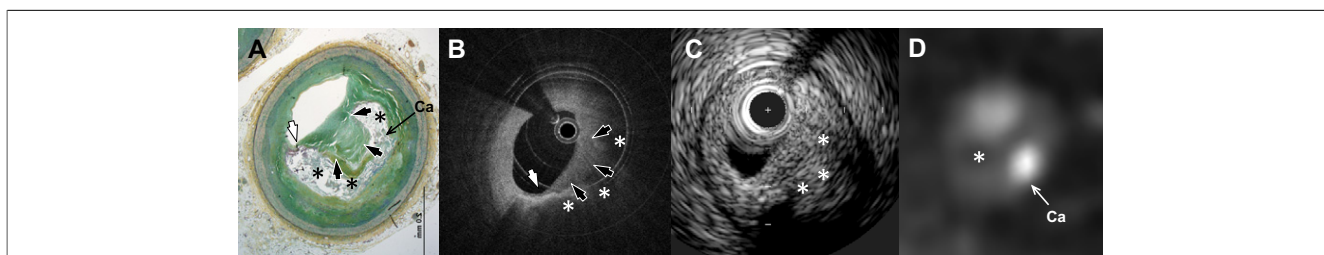


Figure 7. Thin Cap Fibroatheroma With Spotty Calcification

Thin cap fibrous atheroma describes a plaque with a necrotic core and a fibrous cap of $< 65 \mu\text{m}$. This number corresponds to the upper 95% confidence limit of the fibrous cap in a series of ruptured plaques in which the minimal cap thickness was $23 \pm 19 \mu\text{m}$ (8). The majority of sudden cardiac deaths are attributable to rupture of this type of plaque with subsequent formation of a luminal thrombus. The exact mechanism for fibrous cap thinning is unclear. However, prevailing perspectives include extensive apoptosis of the smooth muscle layer with a breakdown of the collagen/proteoglycan structure by matrix metalloproteinases (MMPs) released from macrophages. However, the trigger for this event has yet to be defined. Histopathology (A) demonstrates a thin cap fibroatheroma. The cap is thin at the shoulders (white arrow) and thicker in the center (black arrows). Under the fibrous cap a necrotic core (*) and spotty calcification (Ca) is present. OFDI (B) accurately identifies the thin cap shoulder (white arrow) of the large fibrotic cap (black arrows) and the underlying necrotic core (*). However, the calcification and large parts of the fibrous tissue cannot be visualized due to the limited penetration depth of the light. This remains a significant limitation of this technique particularly in larger vessels. IVUS (C) demonstrates large noncalcified plaque with a slightly lower central echogenicity, potentially indicating lipid accumulation (*). The large plaque burden in this lesion reduces signal penetration and may limit the ability of IVUS to detect spotty calcification in this example. CTA demonstrates napkin-ring like attenuation pattern (7). More work is required to determine *in vivo* if this sign can be used as a marker of a culprit lesion in subjects that present with an acute coronary syndrome or as a marker of plaques that are prone to rupture.

Conclusions

We demonstrate that the core *in vivo* imaging strategies are promising but remain limited by their invasive nature (IVUS, OCT), poor penetration (OCT), limited spatial resolution (IVUS, CT), and ionizing radiation (CT). Advanced reconstruction and post-processing techniques and the development of hybrid technologies (near infrared spectroscopy, IVUS-OCT, PET-CT) may usher in a new era in plaque imaging.

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