Neoatherosclerosis:
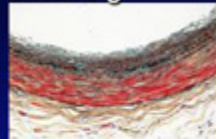## Correlates OCT/IVUS with Histology

Renu Virmani, MD

CVPath Institute

Gaithersburg, Maryland, USA

Progression of Atherosclerosis in Native Coronary Arteries
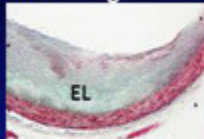
Virmani R, et al. ATVB 2000;20:1262
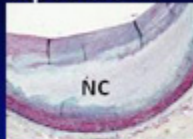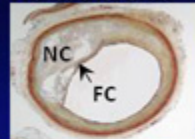

Intimal thickening
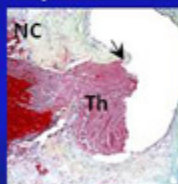
Intimal xanthoma

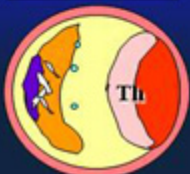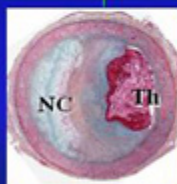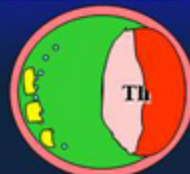Pathologic intimal thickening

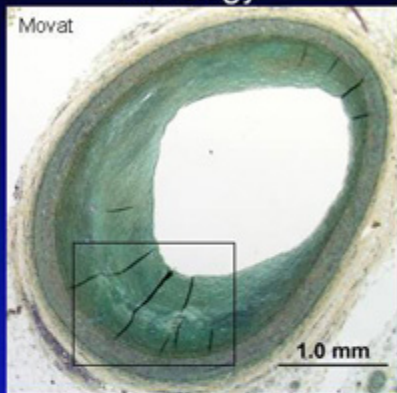Fibrous cap atheroma

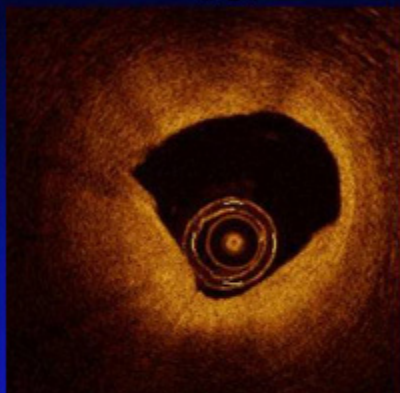Thin-cap Fibroatheroma

Rupture

Erosion

Calcified nodule

Healed Rupture
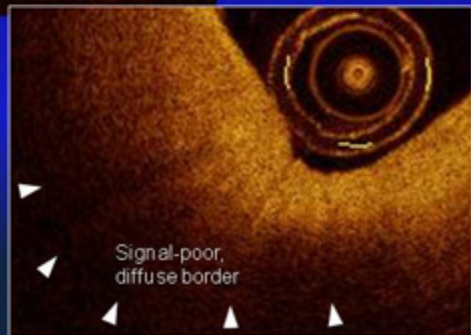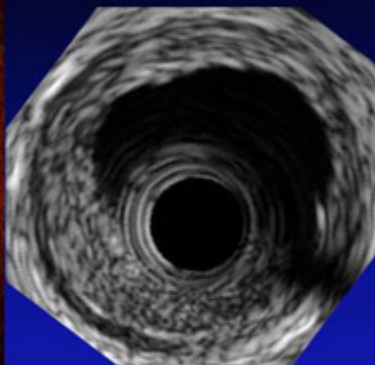
Pathologic Intimal Thickening (PIT) without Macrophages

Histology   OCT   IVUS
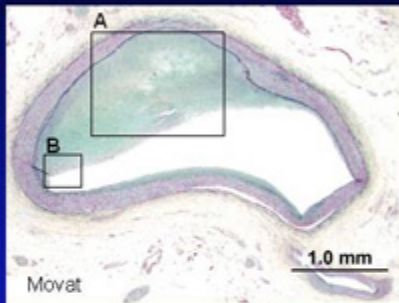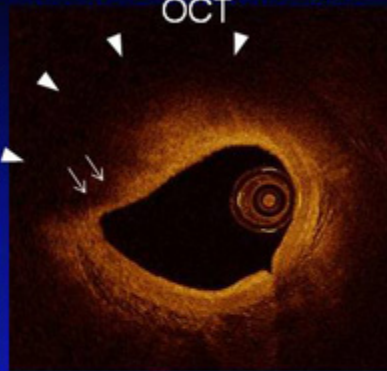
Movat

1.0 mm

Lipid pool

Signal-poor, diffuse border

Not feasible to differentiate between PIT and Fibroatheroma (thick or thin) by OCT or IVUS

Pathologic Intimal Thickening (PIT) with Macrophages

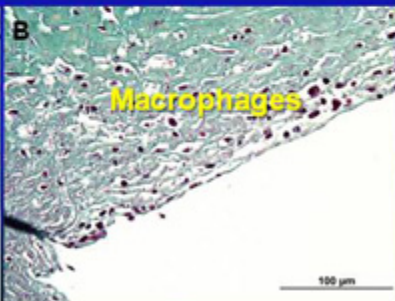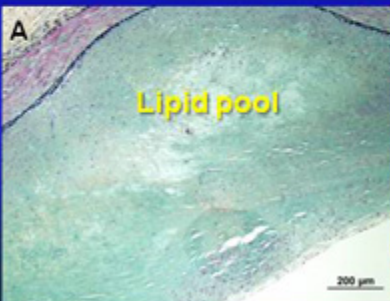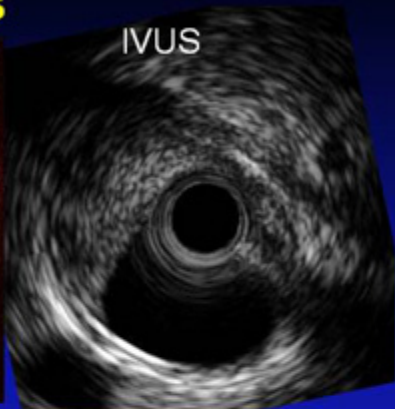Histology

OCT

IVUS

Movat

1.0 mm

A — Lipid pool

200 µm

B — Macrophages

100 µm

Signal-poor, diffuse border
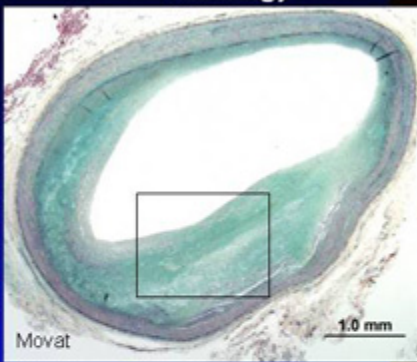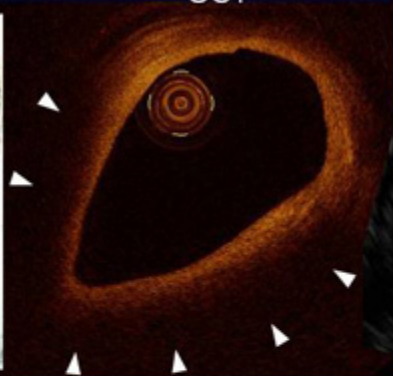
Virtually impossible to make the diagnosis of PIT with macrophages and/or to differentiate from Fibroatheroma on OCT and IVUS

Early Fibroatheroma
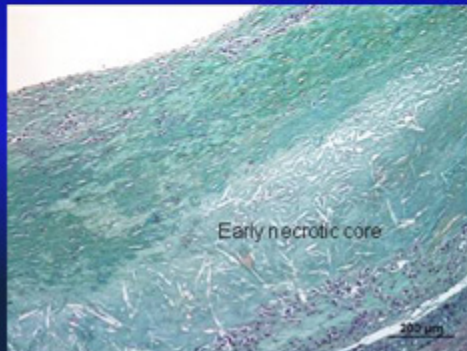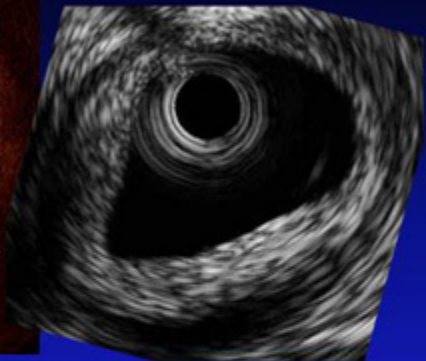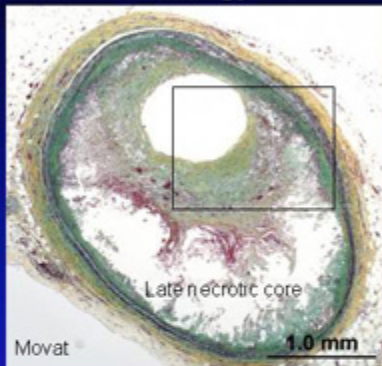

Histology

OCT

IVUS

Movat

1.0 mm

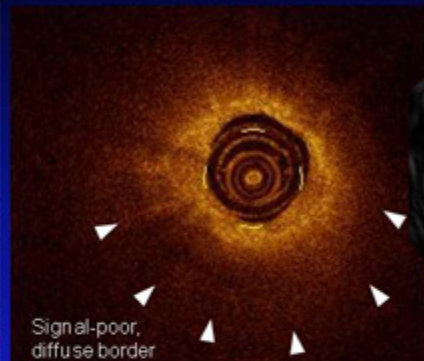Early necrotic core

200 μm

Signal-poor, diffuse border

Fibroatheroma (FA) with macrophage infiltration into fibrous cap

Histology

OCT

IVUS

Late necrotic core

Movat

1.0 mm

Signal-poor, diffuse border

Echo attenuation

Macrophages

Macrophages

CD68 (macrophages)

Signal-rich lesion

NC

NC

NC
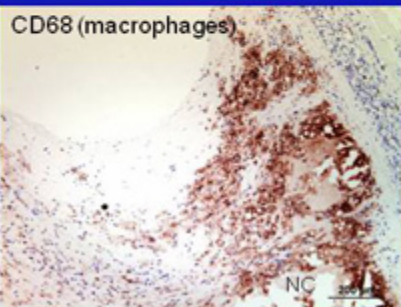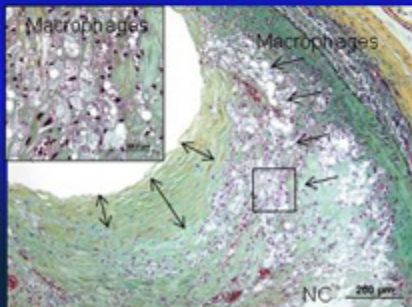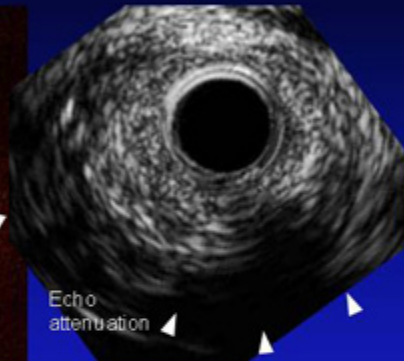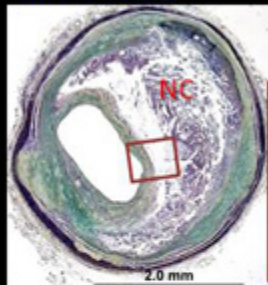
Because lumen is severely narrow this type of lesion on OCT is likely a FA
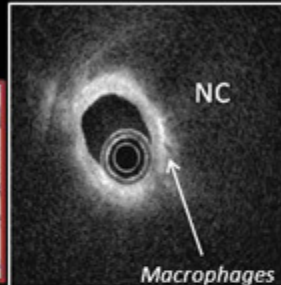
NC=necrotic core

TCFA with Cholesterol Crystals
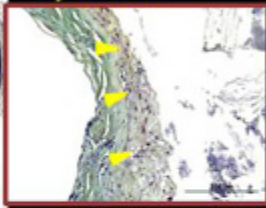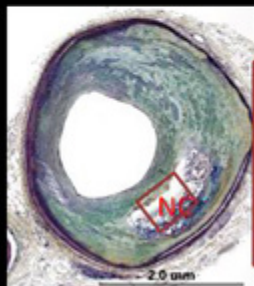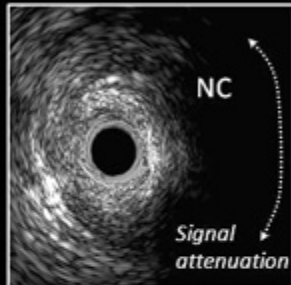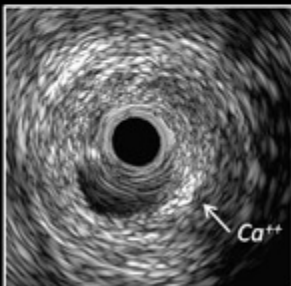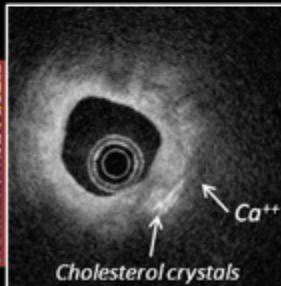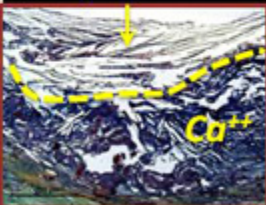
Diffuse hyperintense areas may represent cholesterol crystals by OCT but nor with IVUS

TCFA with Intraplaque Hemorrhage

Plaque Rupture

Histology — OCT — IVUS

Histology (Movat): Plaque rupture, Necrotic core (NC), Thrombus, 1.0 mm; NC, 1.0 mm; NC, 1.0 mm

OCT: Fibrous cap thickness = 60 μm; Signal-poor, diffuse border; Signal-rich lesion with attenuation

IVUS: Echo attenuation
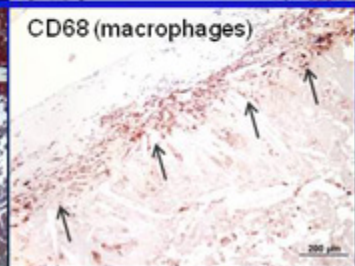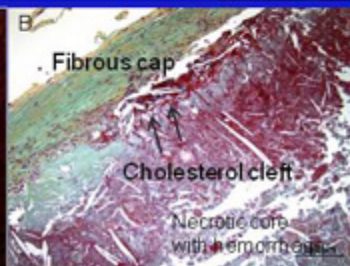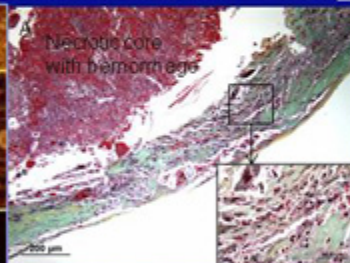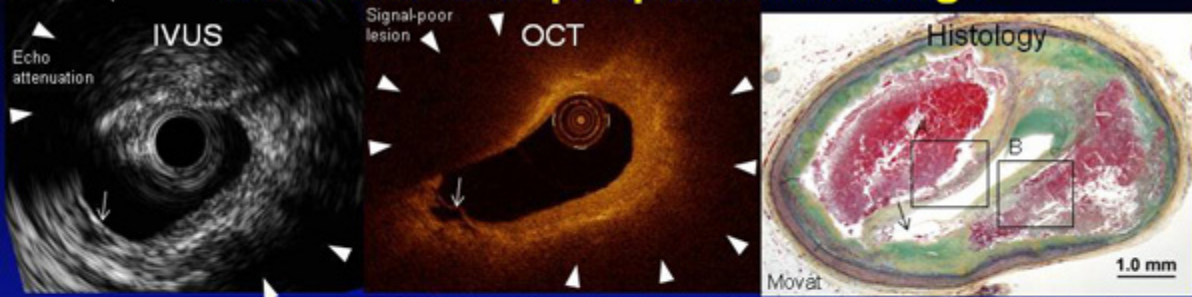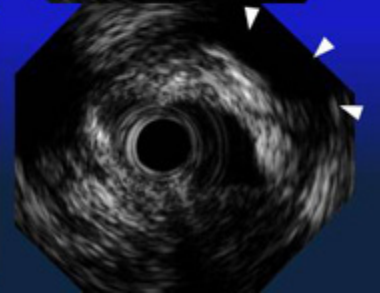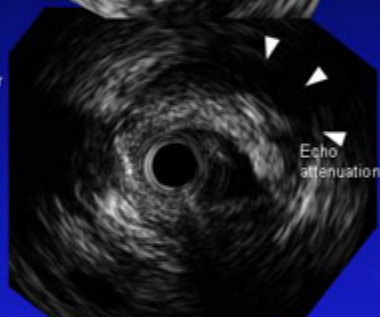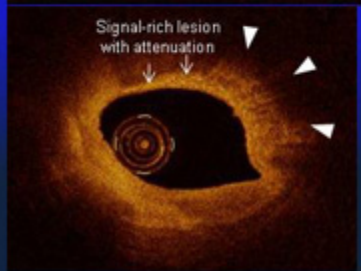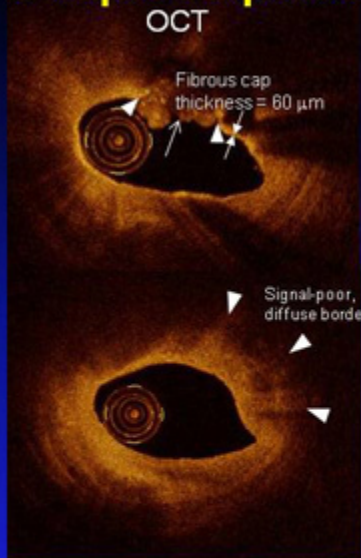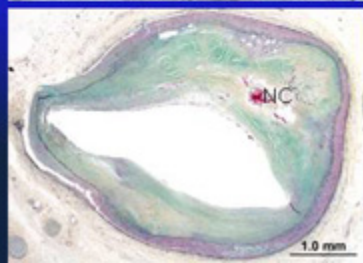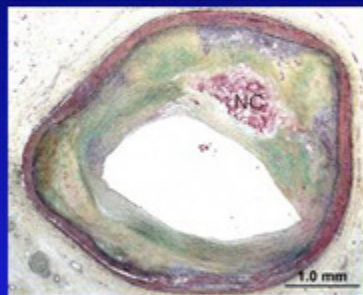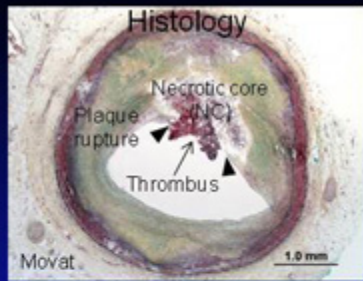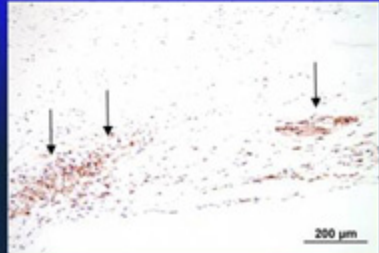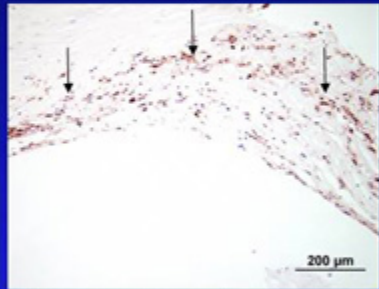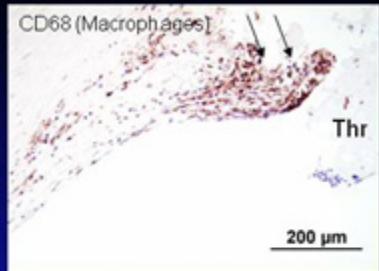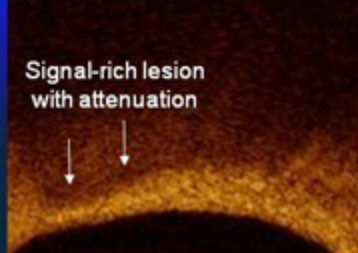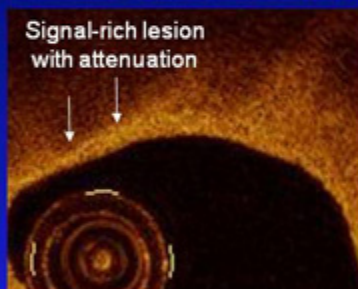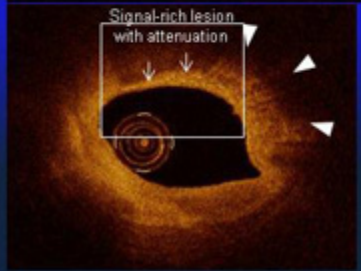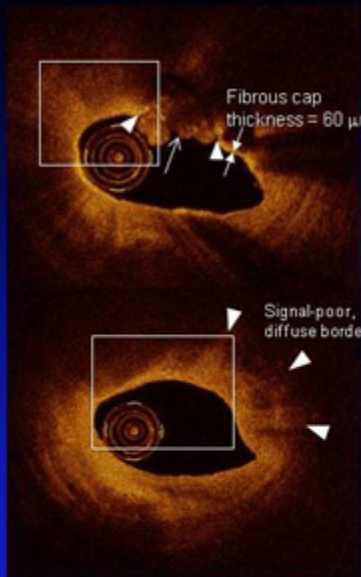
Plaque Rupture

Healed Plaque Rupture and New Fibrous Cap

Histology

1.0 mm

Movat

OCT

IVUS

New Fibrous Layer

Underlying Disease

200 µm

Sirius red

1.0 mm

Signal-rich and-poor layered appearance
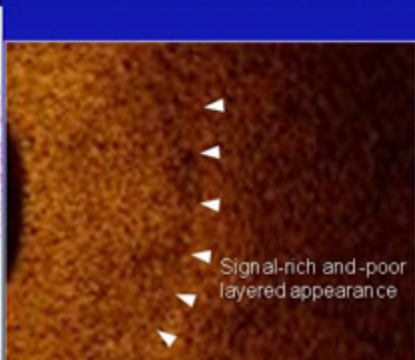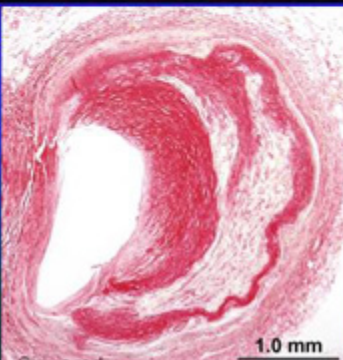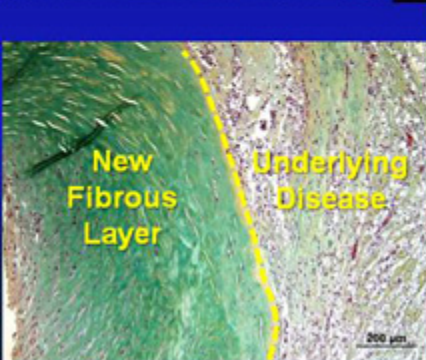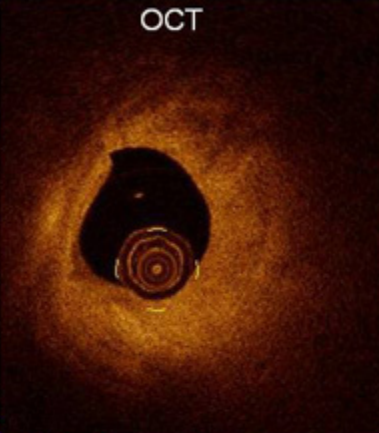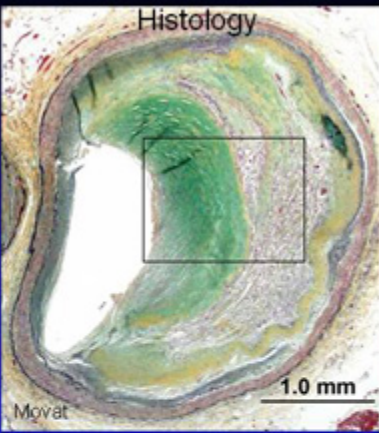
NC = necrotic core

Fibrocalcific Plaque

Histology

OCT

IVUS

Movat — 1.0 mm

Sheet Ca** — H/E — 500 µm

Signal-poor, sharp border area

Bright signal and shadowing
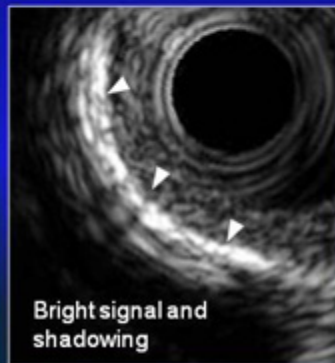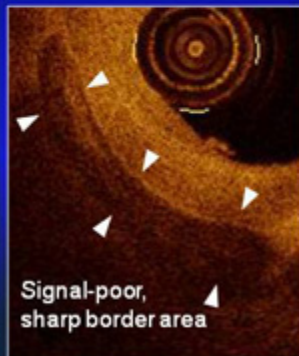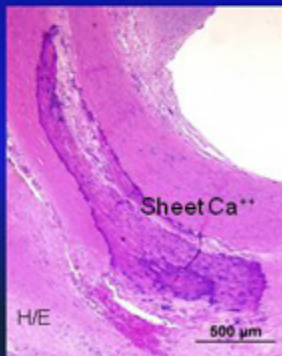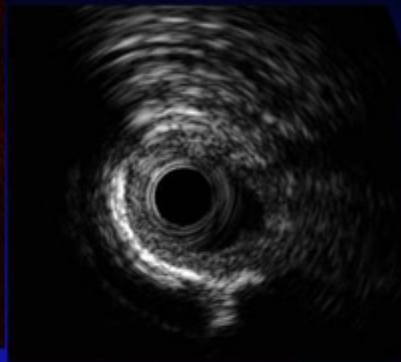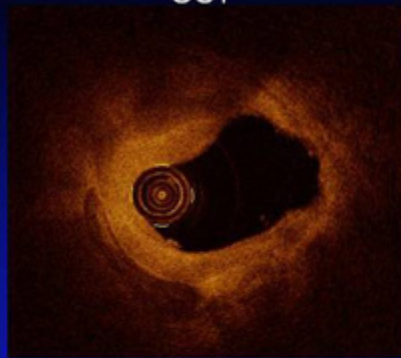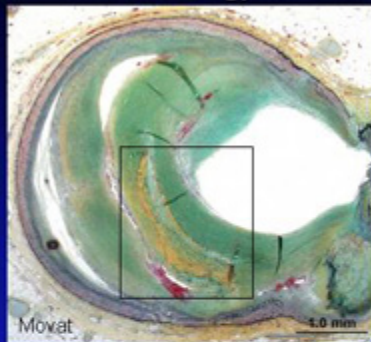
Calcification can be identified by both OCT and IVUS

Components of Atherosclerosis and Imaging by OCT/IVUS

Histologic Tissues		OCT		IVUS
Macrophage (foamy)	◎	Bright signal and trailing shadow	×	Cannot identify
Lipid Pool (PIT)	○	Dark area without clear border; Cholesterol crystals appear to be bright	○	Dark area; Large necrotic core causes signal attenuation
Necrotic Core (Fibroatheroma)	○		○	
Calcification	○	Dark area with clear border	◎	Bright signal with shadowing
Disruption of fibrous cap	◎	Discontinuation of luminal surface with cavity formation	○	Discontinuation of luminal surface with cavity formation
Thrombus	◎	Protrusion with irregular surface	△	Sometimes difficult to identify
Organized thrombus (new layer of fibrous cap)	○	Slightly darker appearance than underlying fibrous tissue	×	Cannot identify

Best Tool to Determine Neoatherosclerosis OCT or IVUS ?

Incidence and Timing of In-stent Neoatherosclerosis

Nakazawa G et al. *J Am Coll Cardiol.* 2011;57:1314
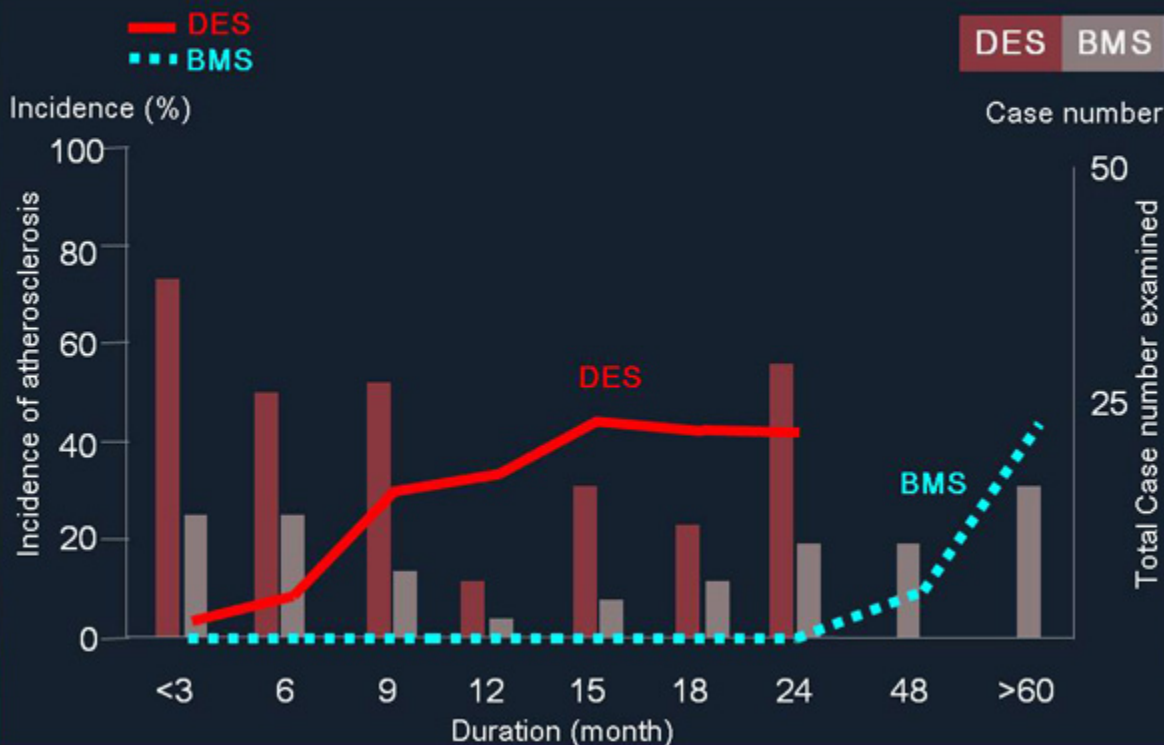
Another Pathway of LST: Neoatherosclerosis

Accumulation of Foamy Macrophages

Early Fibroatheroma (SES, 13 months)

Late FA (SES, 17 months)

Late FA and Ca++ (SES, 10 months)

TCFA (BMS, 61 months)

Plaque Rupture (BMS, 61 months)

Th
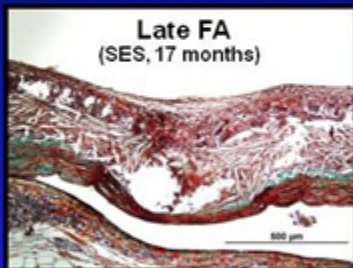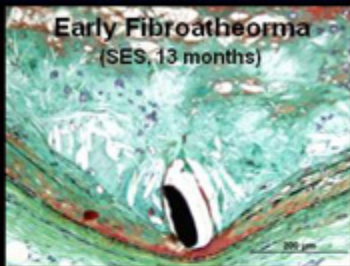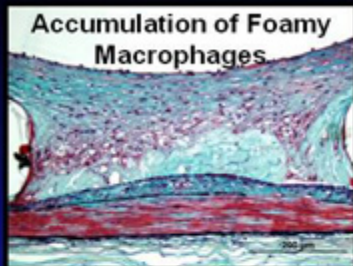
Unlike native coronary arteries, 'lipid pool' does not seem to be the precursor of neoatherosclerosis in the in-stent area.

Neoatherosclerosis begin with the accumulation of foamy macrophages within neointima. Apoptosis of macrophages leads to the formation of a necrotic core.

Modified from Nakazawa G, et al. JACC 2011
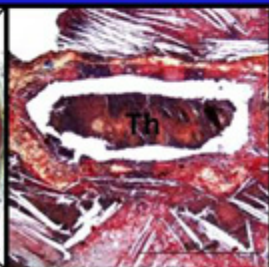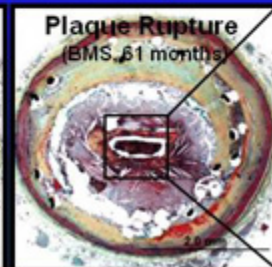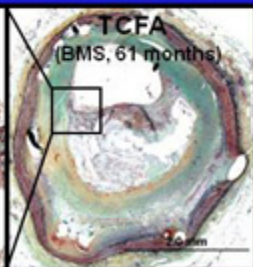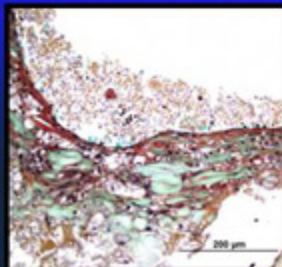
Foamy Macrophage Accumulation on Luminal Surface

72-year-old female, BMS (Palmaz-Schatz stent) implanted in proximal RCA ~10 years antemortem

X-ray

IVUS

OCT

Signal-poor lesion (attenuation)

Histology

H/E

1.0 mm

Signal-rich pattern with attenuation

Foamy macrophages

*

*

*

CD68 (Macrophages)

200 μm

200 μm
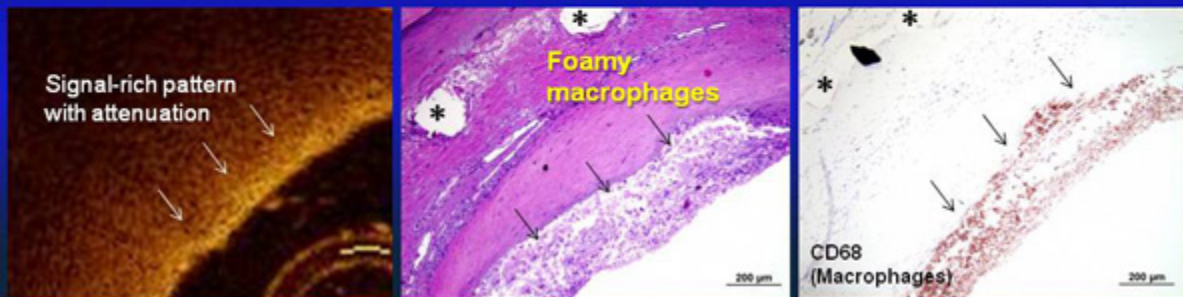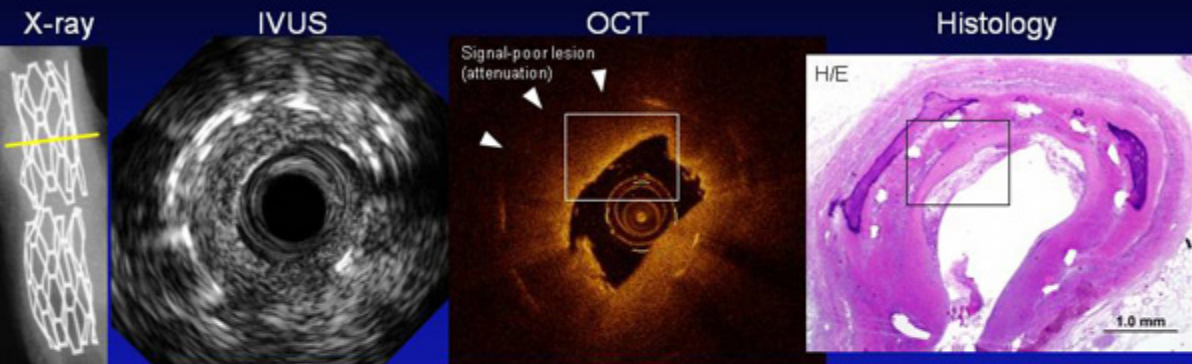
Neoatherosclerosis: Newly formed atherosclerotic change within the neointima.   * Stent strut

Neoatherosclerosis with Necrotic Core

Histology   **OCT/OFDI**   **IVUS**
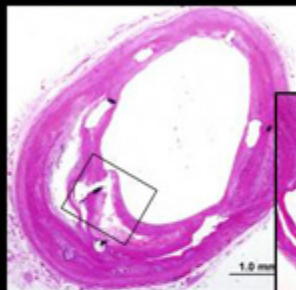
Early NC with macrophage infiltration

NC

Signal-rich
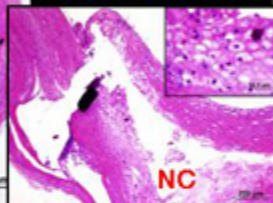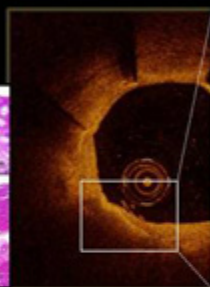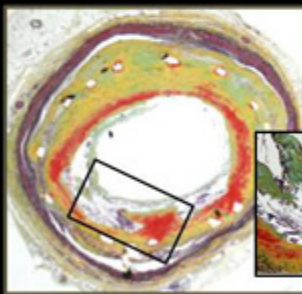
Late NC with cholesterol crystals

NC

Signal-rich
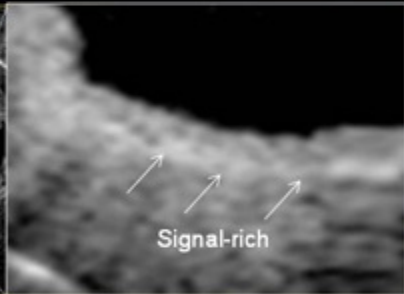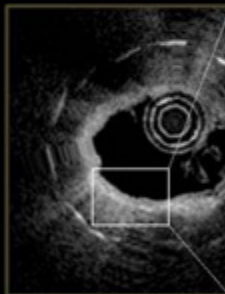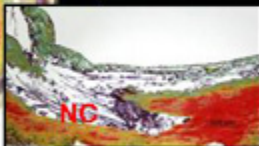
❖ Neoatherosclerosis can be identified by OCT as dark area within neointima, frequently accompanied by bright signals from macrophages or cholesterol crystals, however, it seems difficult for IVUS because of low resolution and artifacts from metal struts.

Calcification within the Neointima
72-year-old female, BMS (Palmaz-Schatz stent) implanted in proximal RCA 10 years antemortem

IVUS

OCT

Histology

Calcification

H/E

1.0 mm

X-ray

Signal-poor, sharp border area

Calcification within the neointima

*

*

200 μm

* Stent strut
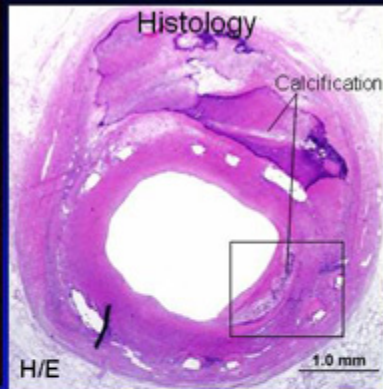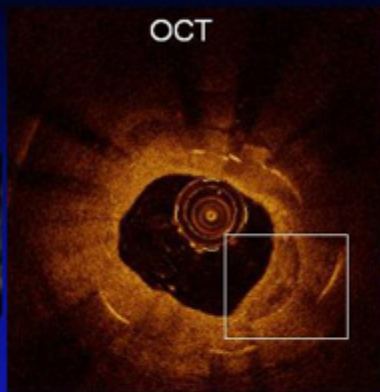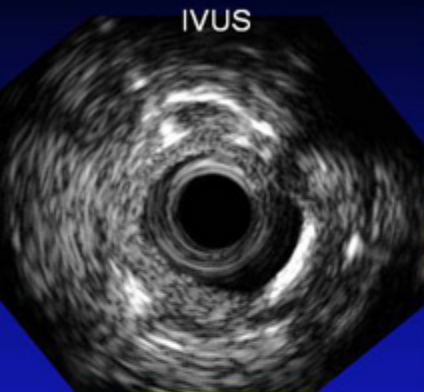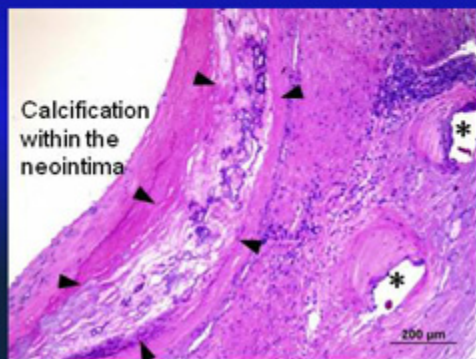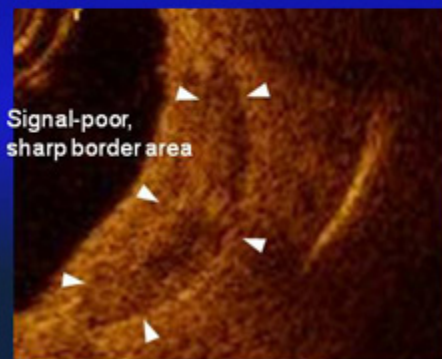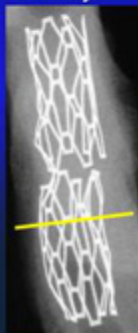
# Speculative Pathway of Neoatherosclerosis
## Different from Atherosclerosis in Native Coronary Artery

Native Atherosclerosis

Normal / Adaptive Intimal Thickening (AIT)

Pathological Intimal Thickening (PIT)

Fatty streak

※Regressive

Characterized by "lipid pool"

Fibroatheroma (FA)

Macrophage infiltration into lipid pool
Necrotic core growth by apoptotic macrophages

Thin cap fibroatheroma (TCFA)

Increase of plaque vulnerability
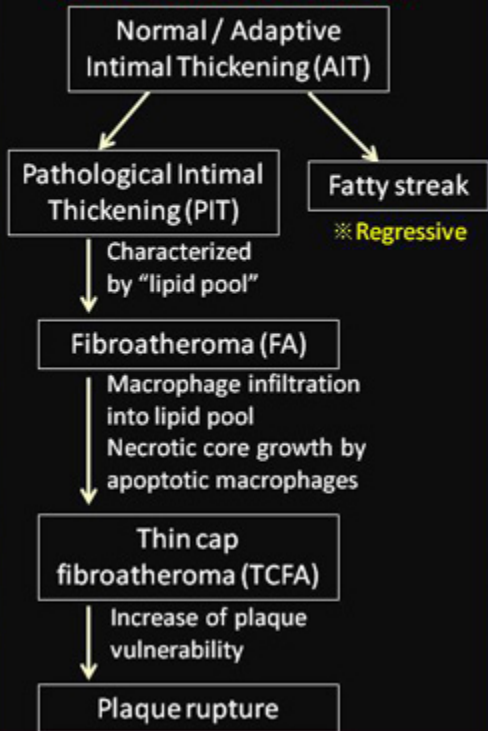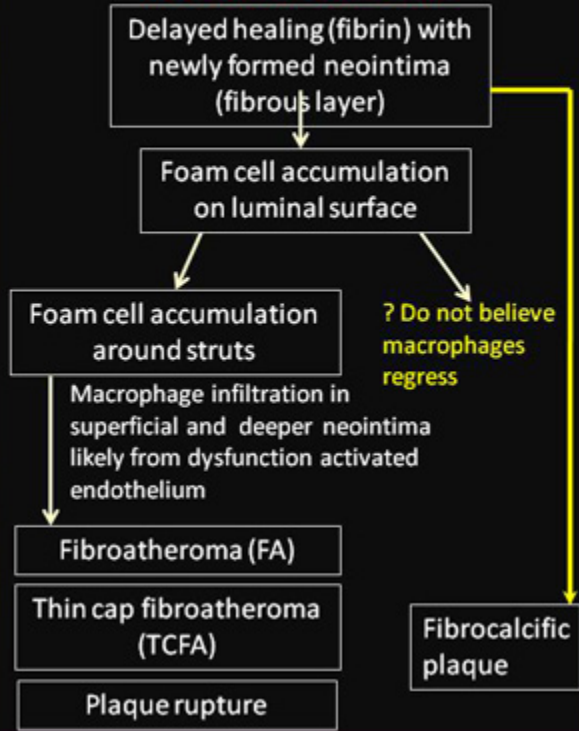
Plaque rupture

Neoatherosclerosis

Delayed healing (fibrin) with newly formed neointima (fibrous layer)

Foam cell accumulation on luminal surface

Foam cell accumulation around struts

? Do not believe macrophages regress

Macrophage infiltration in superficial and deeper neointima likely from dysfunction activated endothelium

Fibroatheroma (FA)

Thin cap fibroatheroma (TCFA)
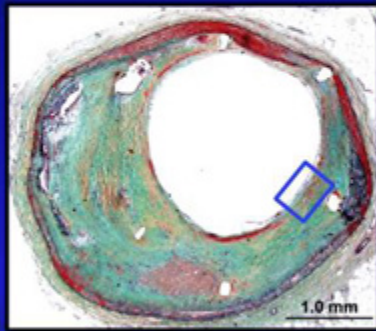
Fibrocalcific plaque

Plaque rupture

Limitations of OCT to Identify Neoatherosclerosis

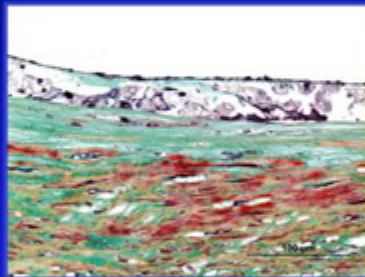# Limitations in Identification of Neoatherosclerosis by OCT

i) Presence of macrophages prevent accurate diagnosis of deep tissues because of signal attenuation.
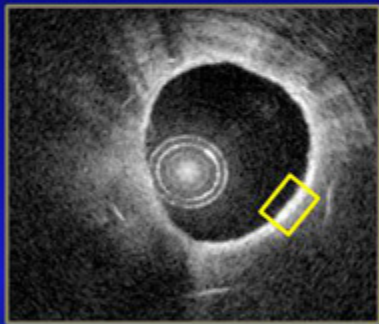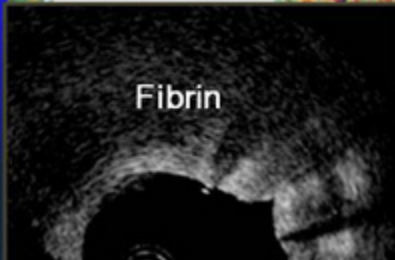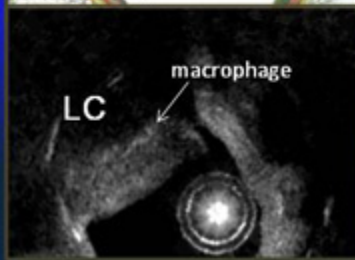

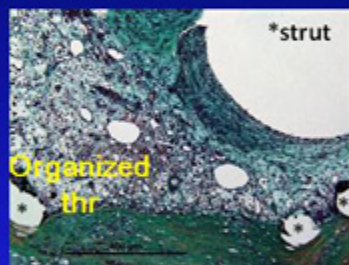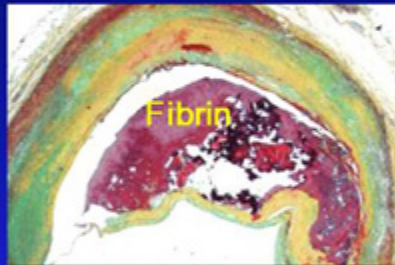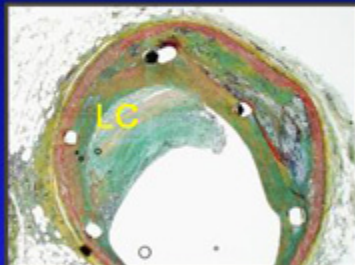OCT-derived TCFA like appearance ??

Macrophage accumulation on fibrous neointimal surface

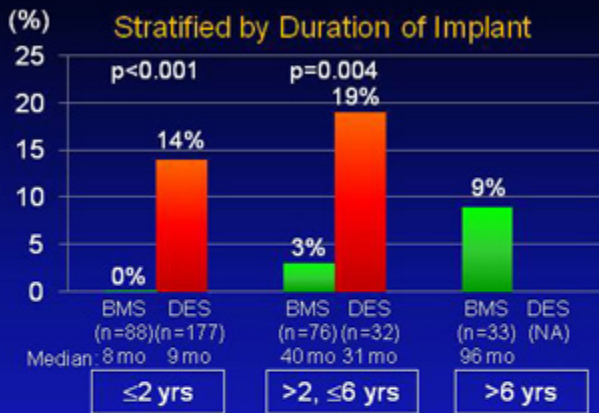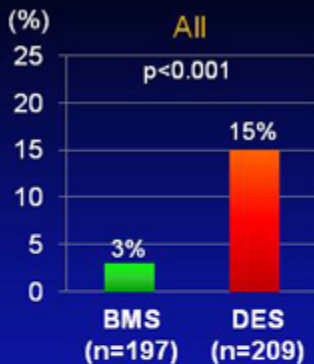# Limitations in Identification of Neoatherosclerosis by OCT

ii) Lipid, fibrin, and organized thrombus exhibit similar dark appearance (layered or heterogeneous) when they exist within neointima (not adjacent to lumen).

Summary and Conclusions

➤ In-stent neoatherosclerosis occur both in BMS and DES; however, for DES implants it is observed more frequently and at an earlier time point as compared to BMS. Foamy macrophages play aa important roles in the progression of neoatherosclerosis than in native coronary artery (likely similar to vein graft).

➤ OCT appears to be a better tool for the detection of neoatherosclerosis than conventional IVUS.

➤ However, the complexity of histology in human coronary arteries does not always allow direct interpretation of neointimal tissues, especially in the presence of fibrin, organized thrombus and foamy macrophages.
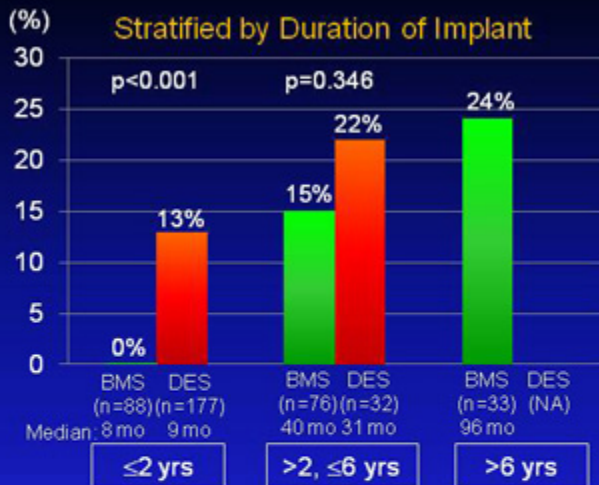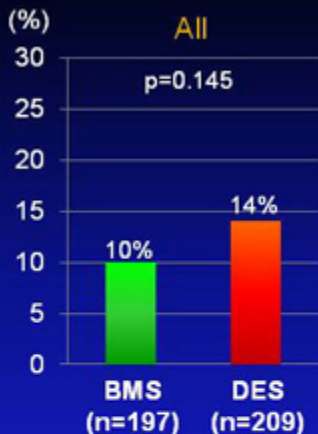
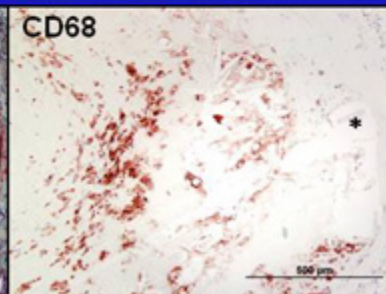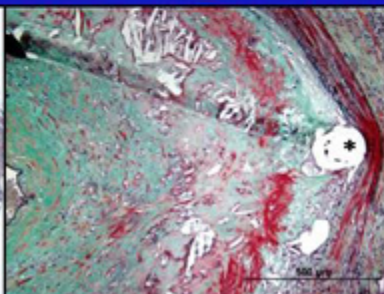Path

Incidence of Foamy Macrophage Clusters
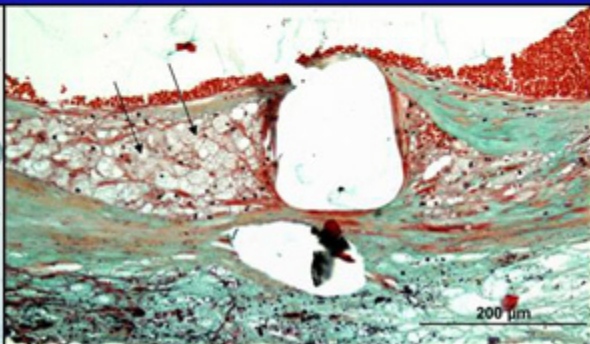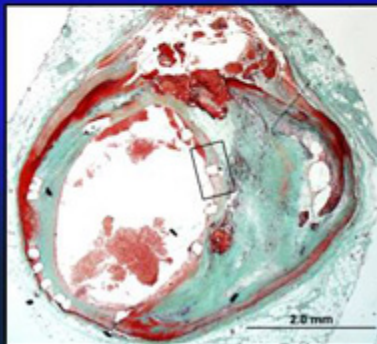
Incidence of Fibroatheroma
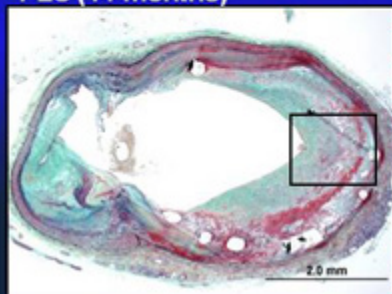
Incidence of Thin-cap Fibroatheroma or Plaque Rupture