

# *Pathologic and Clinical Evidence of Neoatherosclerosis*

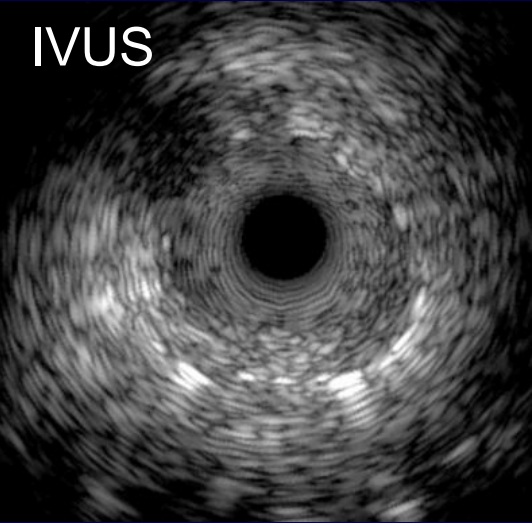
Michael Joner, MD

CVPath Institute Inc., Gaithersburg, MD

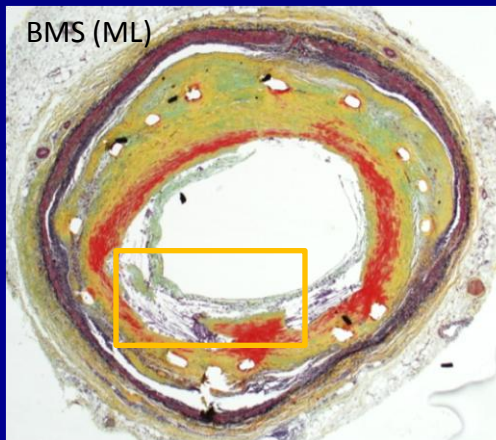
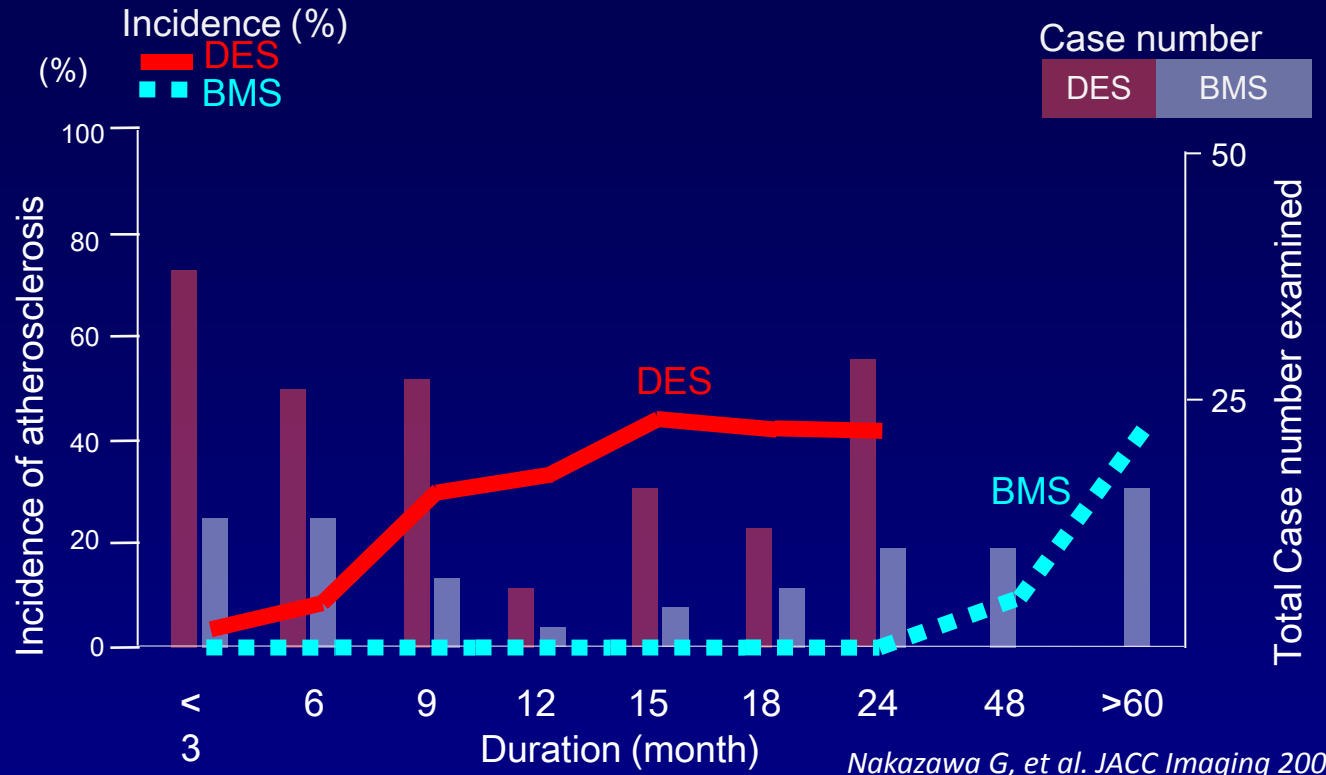
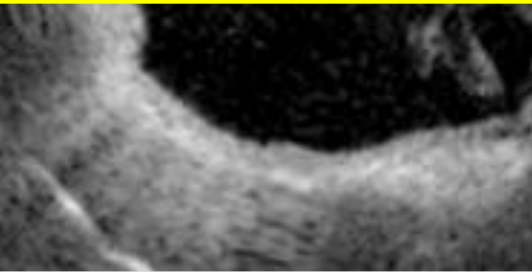
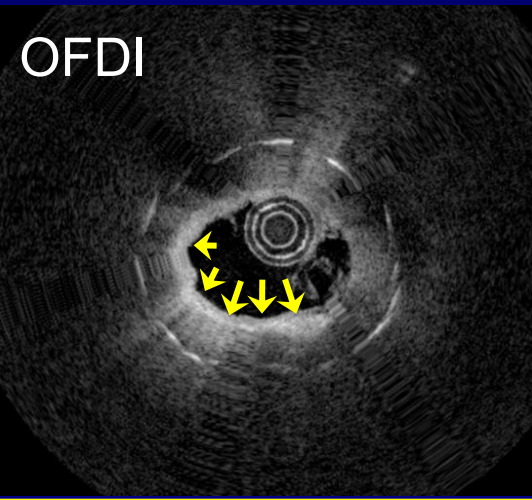
German Heart Center Munich, Germany

# Incidence and Timing of Atherosclerotic Change

IVUS



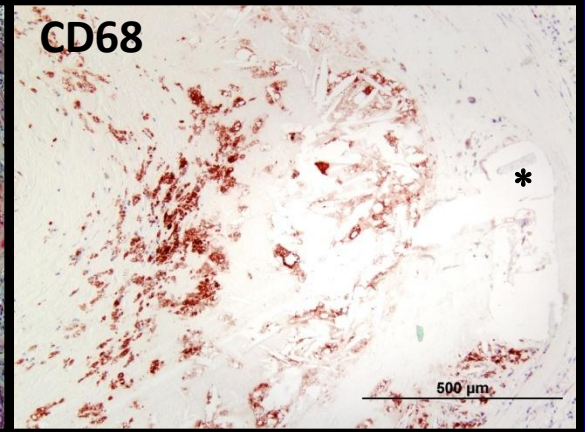
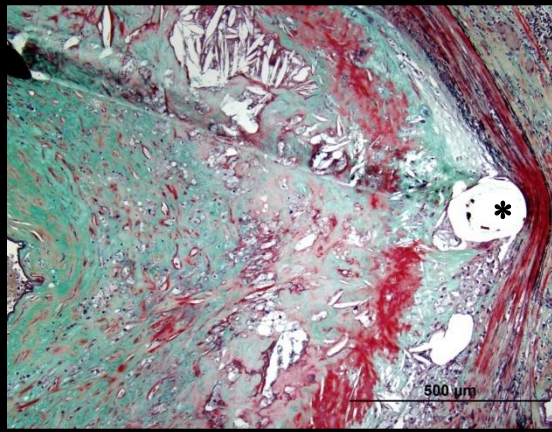
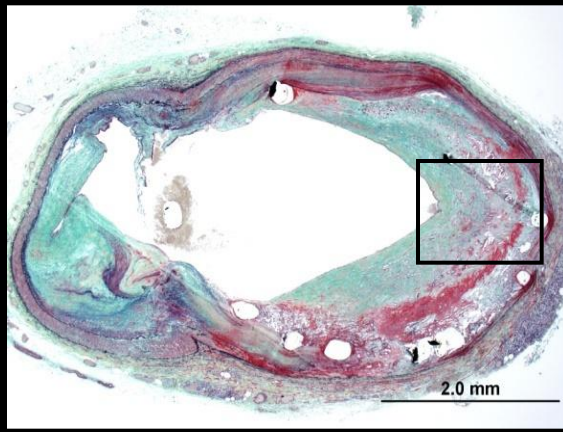
OFDI



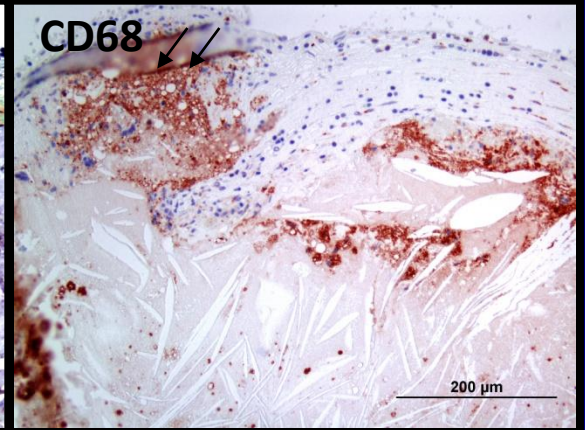
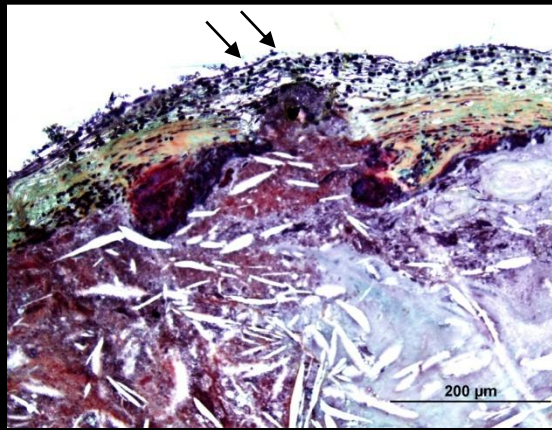
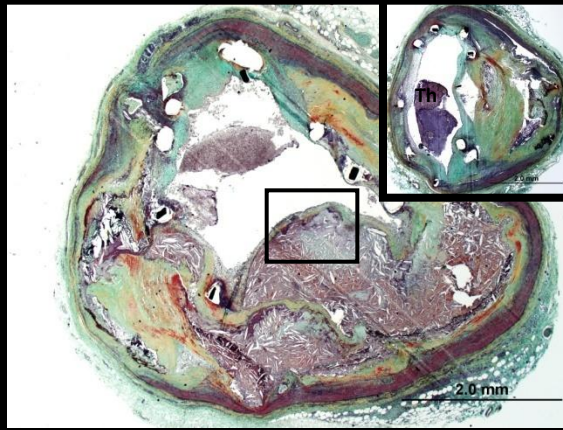


# Neoatherosclerosis Following PES, SES, and BMS Implantation

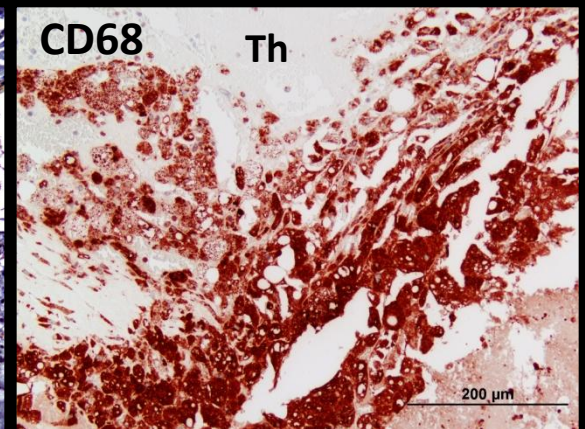
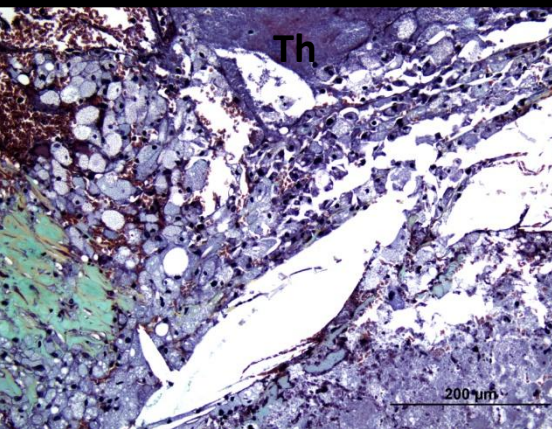
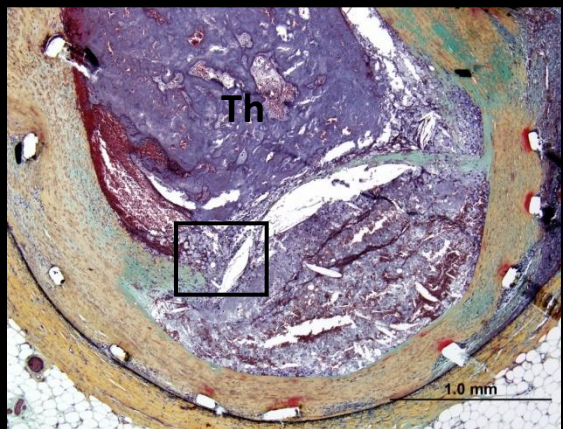
PES  
(14 months)



SES  
(23 months)



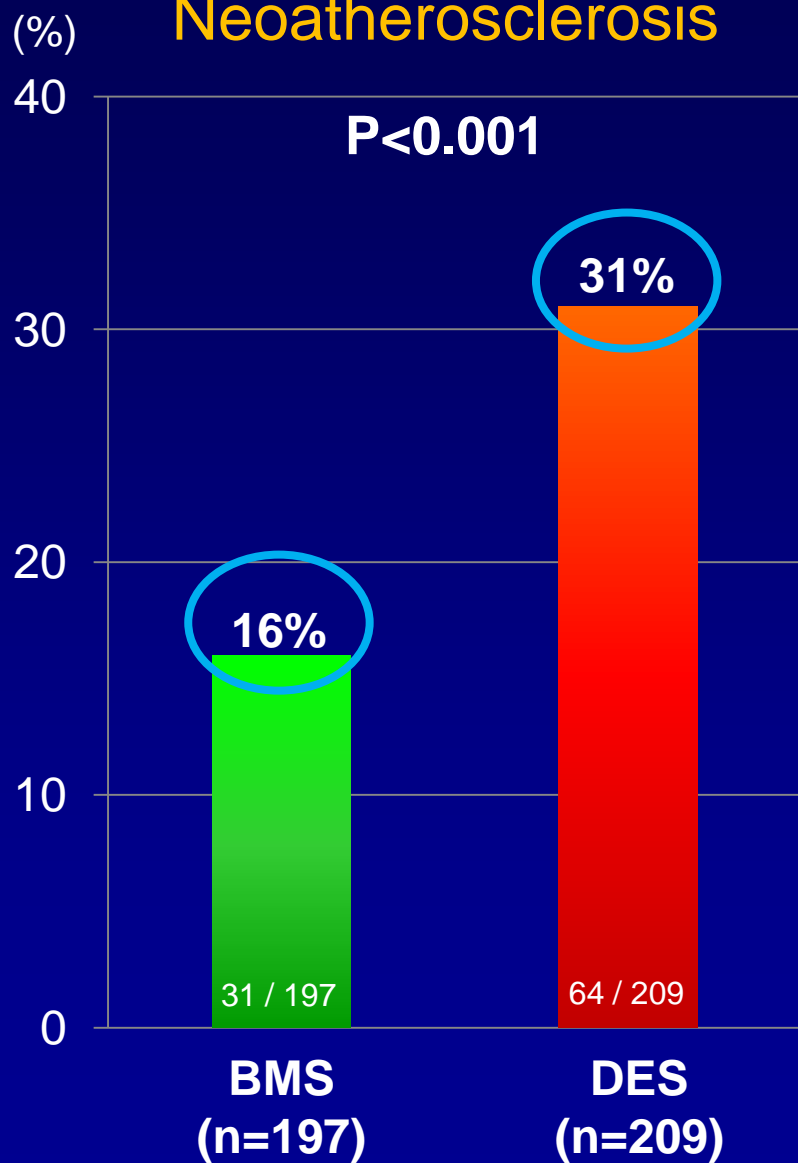
BMS  
(96 months)



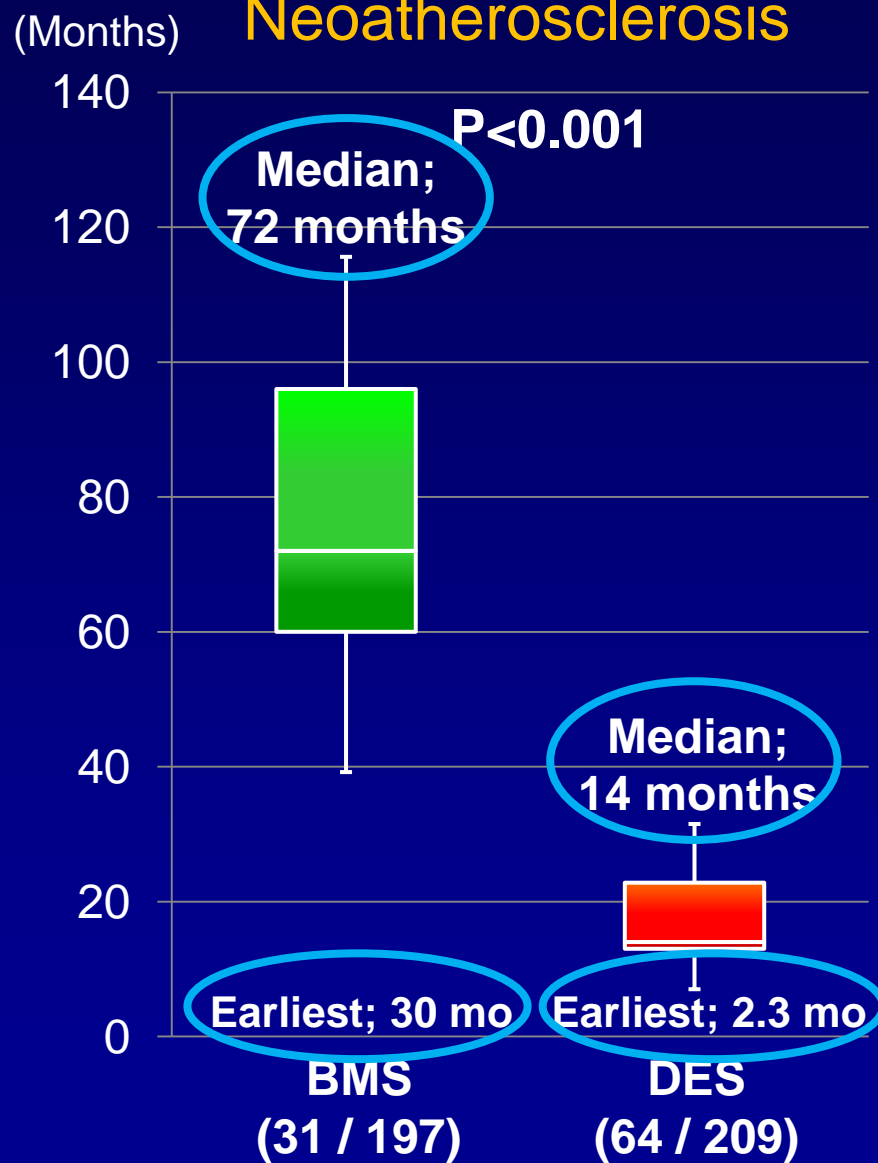


# Incidence and Timing of Neoatherosclerosis

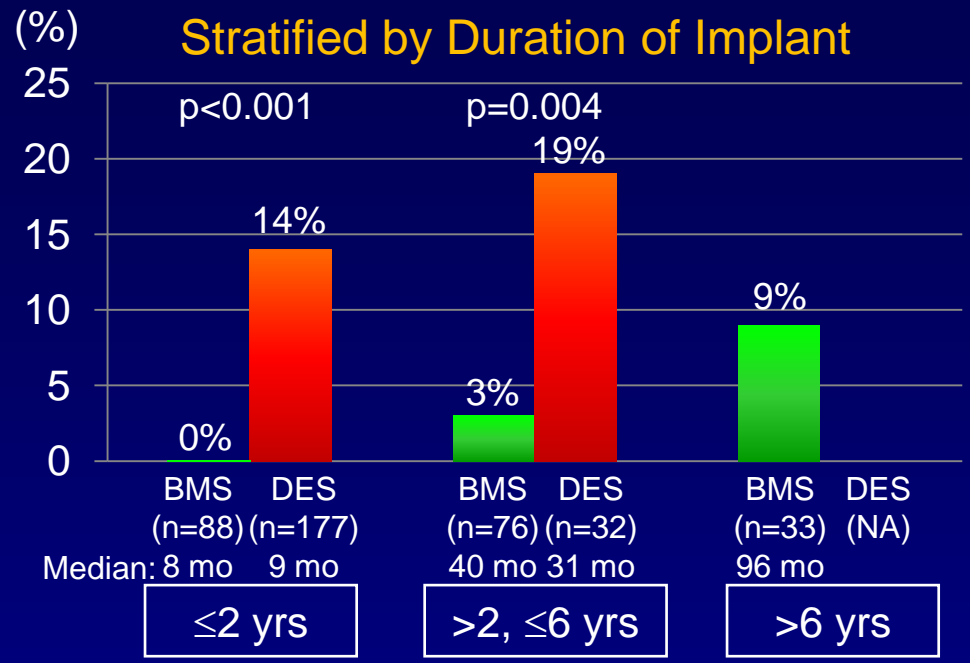
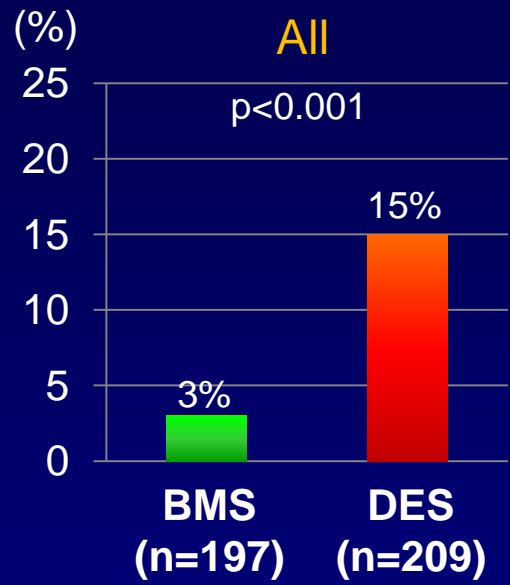
## Incidence of Neoatherosclerosis



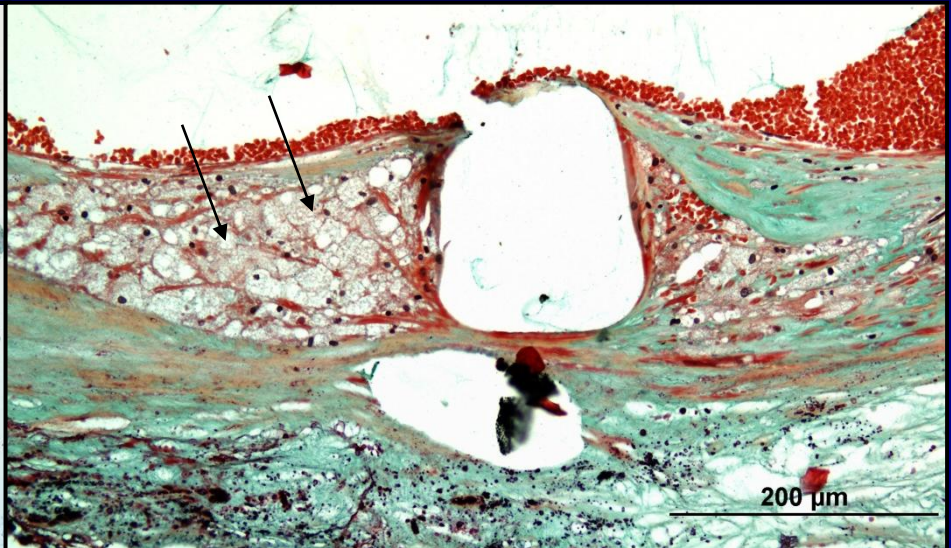
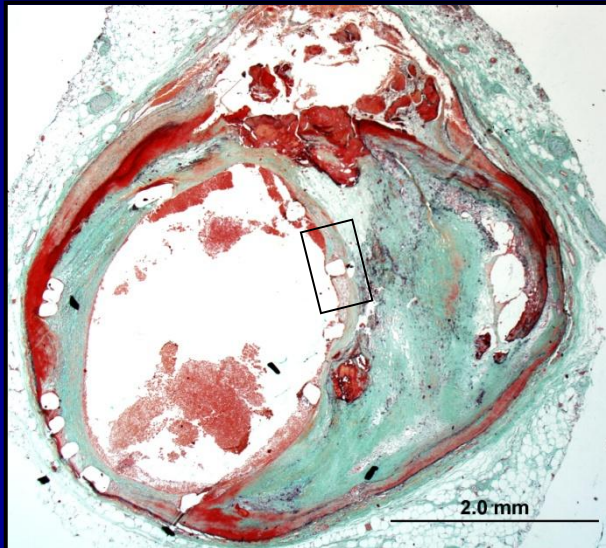
## Duration of Implant with Neoatherosclerosis



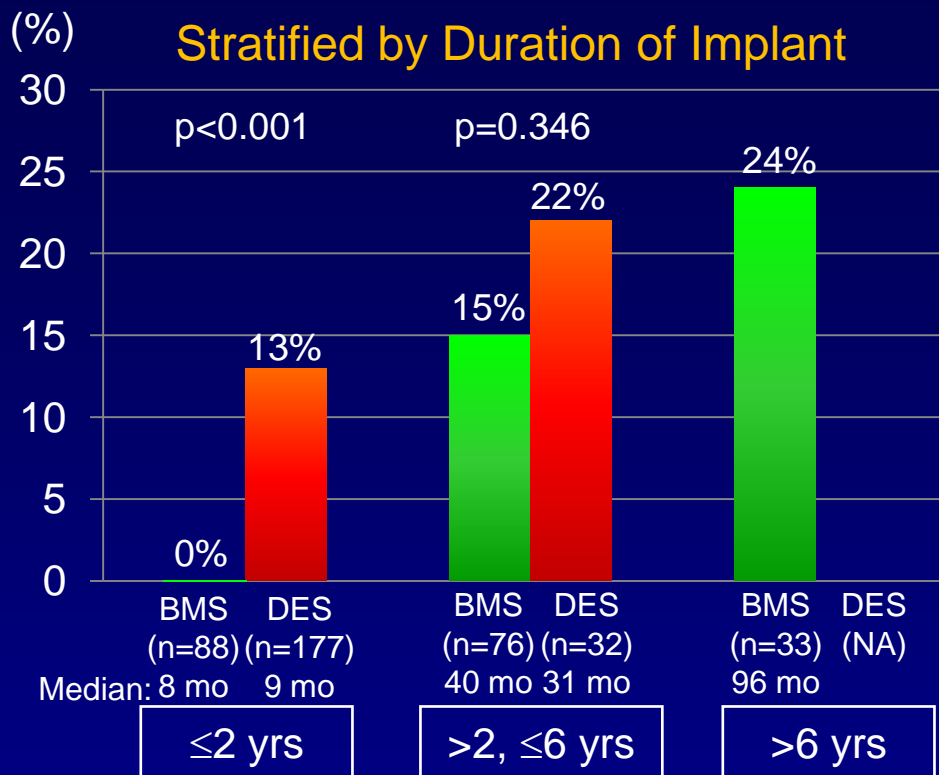
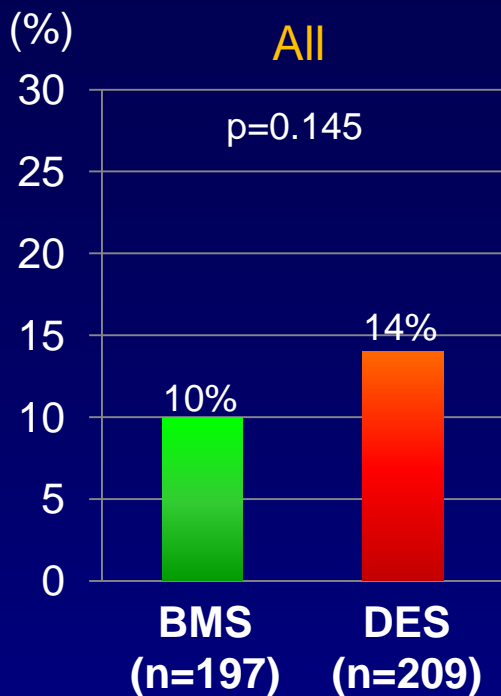
# Incidence of Foamy Macrophage Clusters



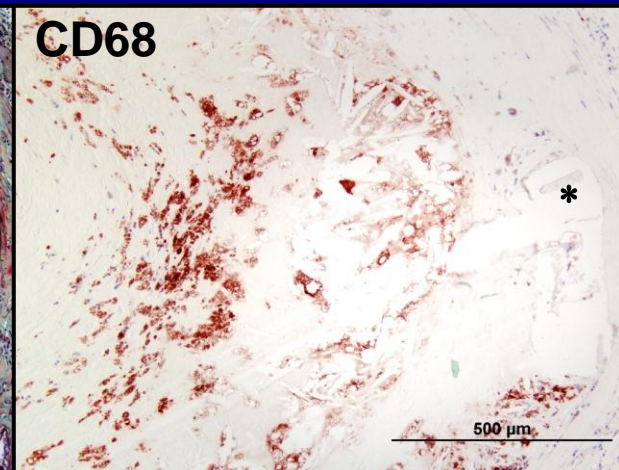
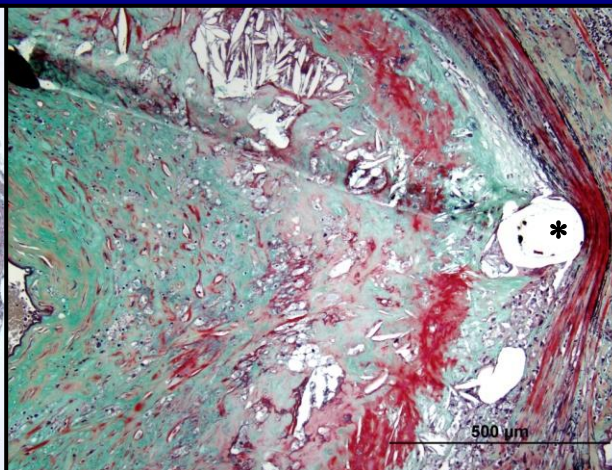
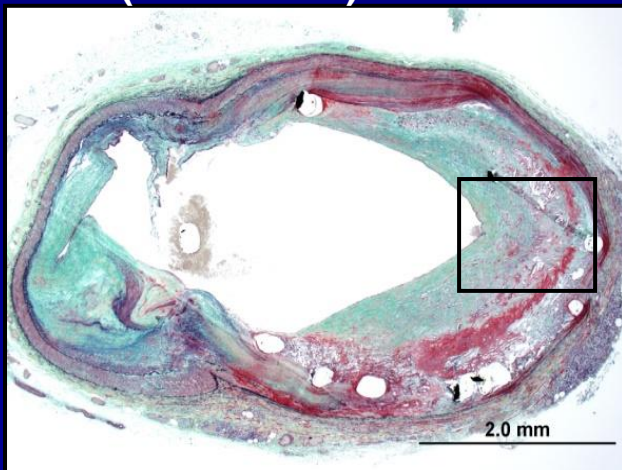
PES (7 months)



# Incidence of Fibroatheroma

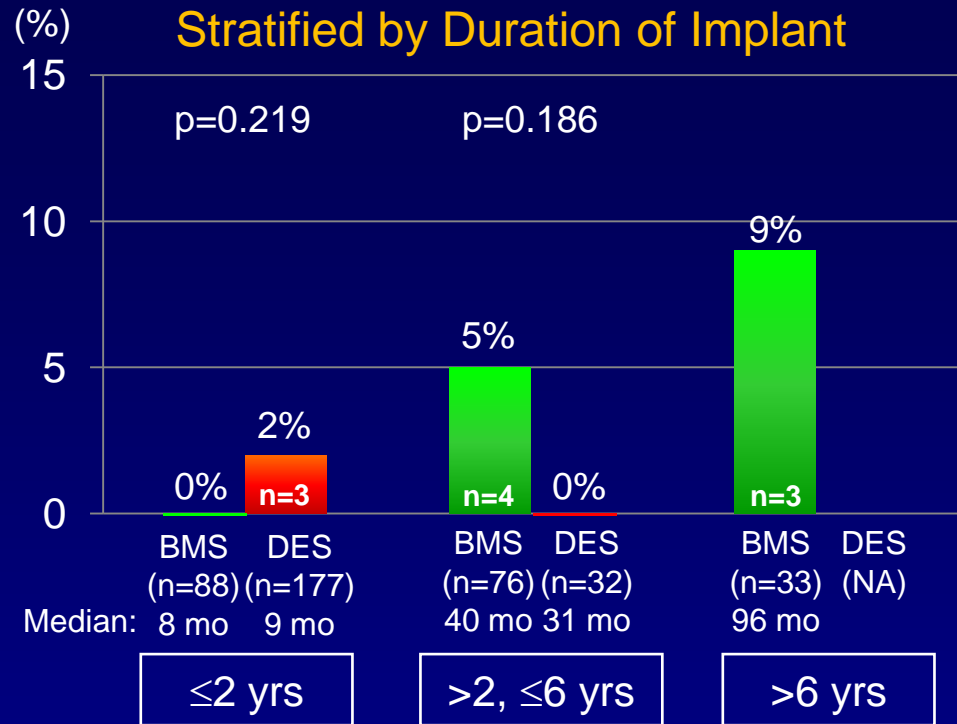
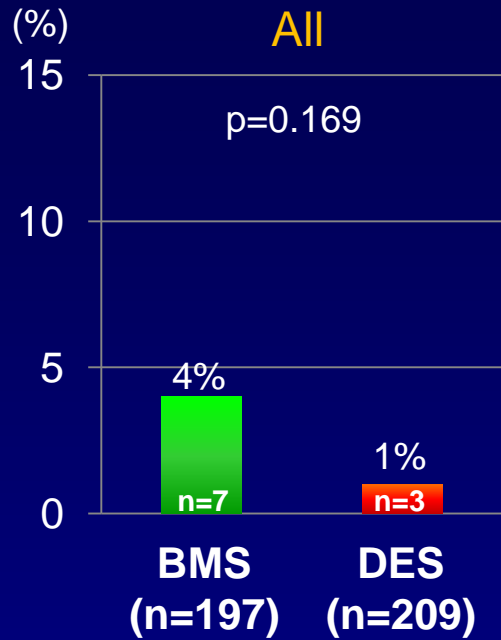


**PES (14 months)**

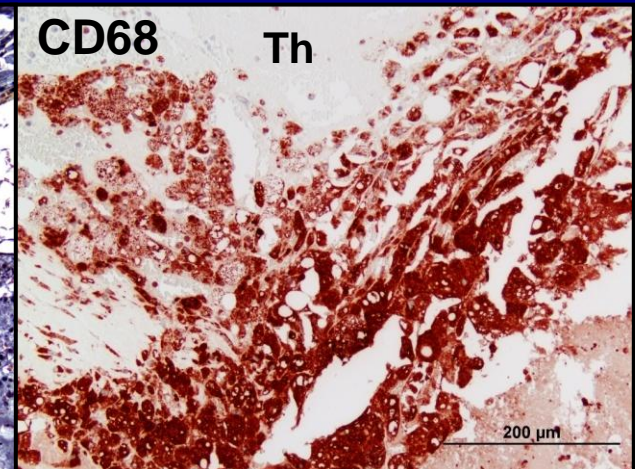
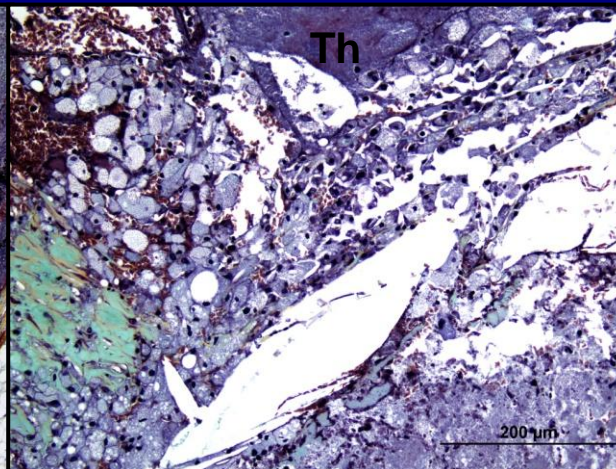
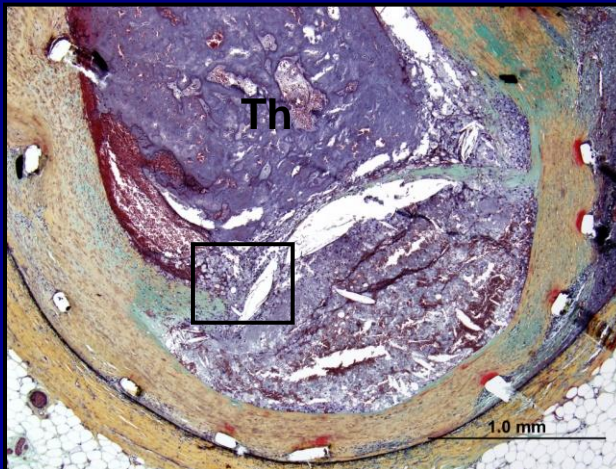




# Incidence of Thin-cap Fibroatheroma or Plaque Rupture



**BMS (96 months)**



# Independent Risk Factors for Neoatherosclerosis (Multiple Logistic Generalized Estimating Equations Modeling)

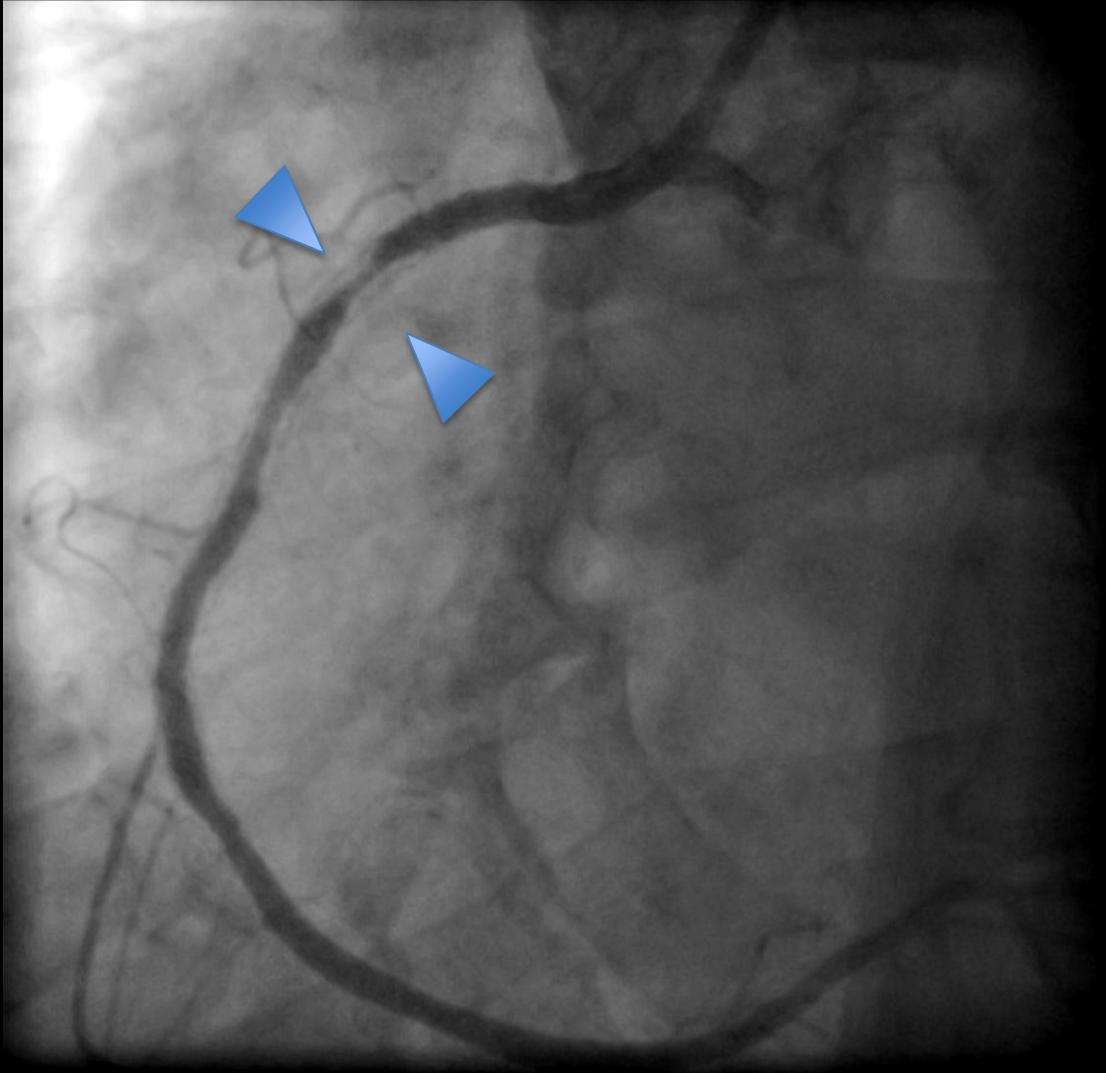
| Variables                       | Odds Ratio | 95% CI         | P value |
|---------------------------------|------------|----------------|---------|
| Age (per year)                  | 0.963      | 0.942 – 0.983  | <0.001  |
| Duration of implant (per month) | 1.028      | 1.017 – 1.041  | <0.001  |
| SES usage                       | 6.534      | 3.387 - 12.591 | <0.001  |
| PES usage                       | 3.200      | 1.584 - 6.469  | 0.001   |
| Underlying unstable lesion*     | 2.387      | 1.326 - 4.302  | 0.004   |

\* “Underlying unstable lesion” includes ruptured plaque and thin-cap fibroatheroma.



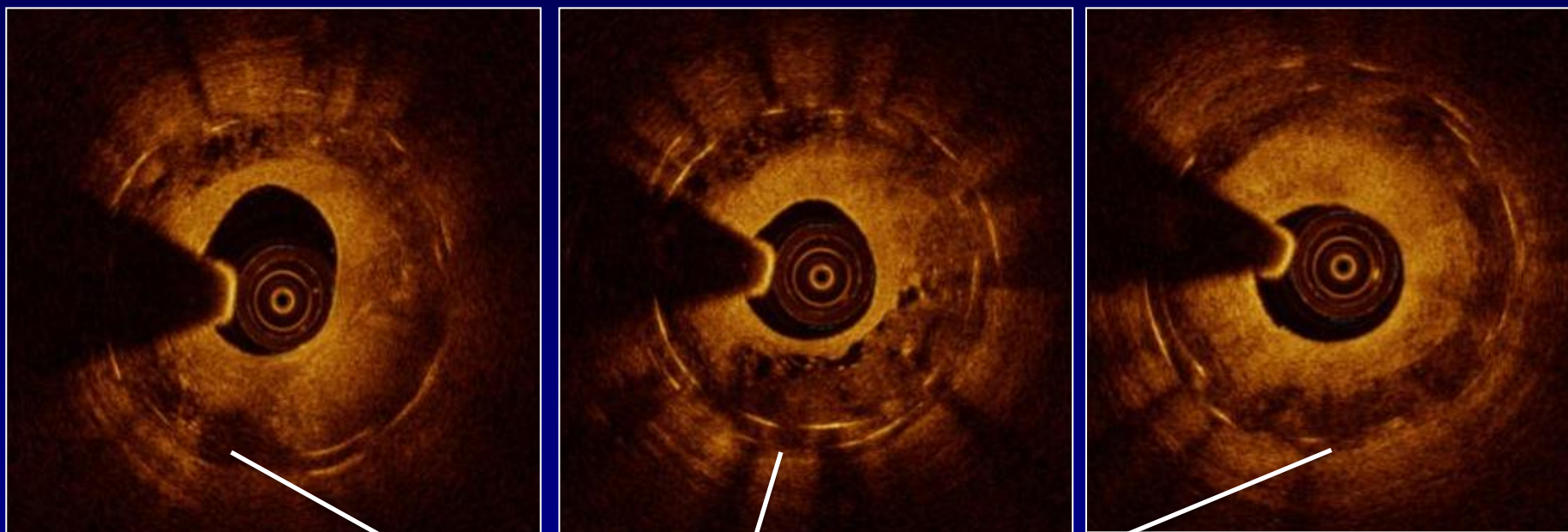
# Case Presentation

- 65-year old male
- Unstable angina pectoris
  
- Single vessel coronary artery disease
- Recanalisation of chronic total occlusion proximal RCA (SES) 2006
- Repeat stenting for in-stent restenosis proximal RCA (SES) 2008



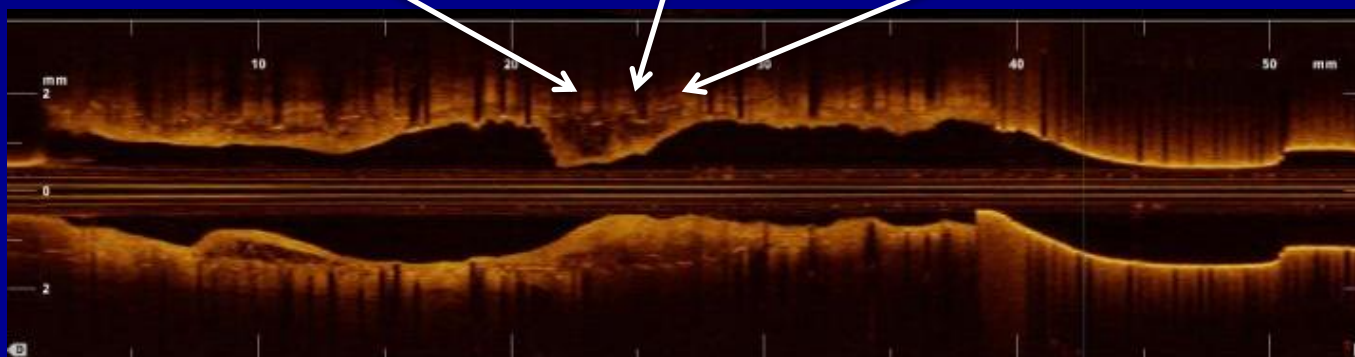


# Optical coherence tomography (OCT) imaging



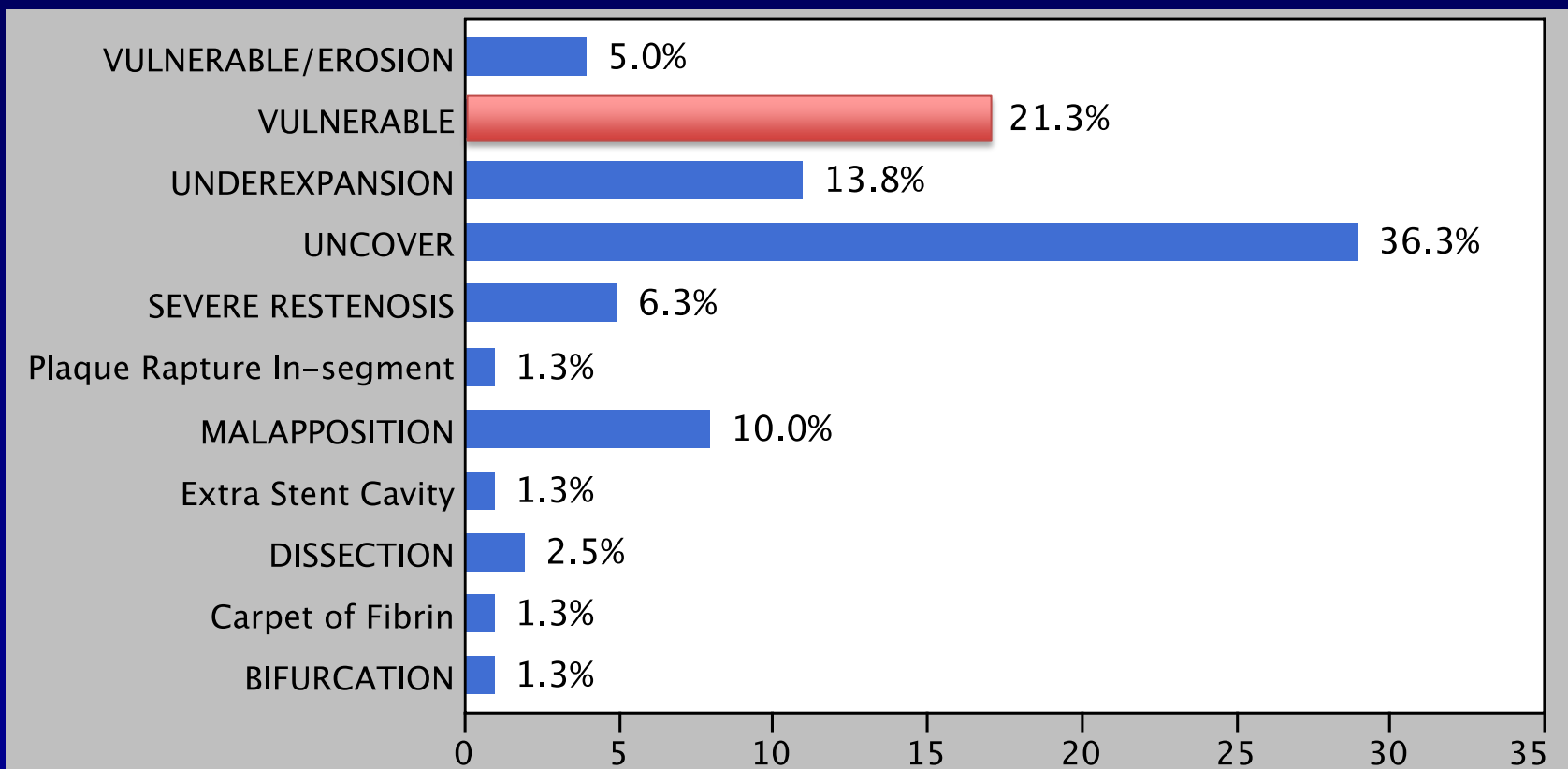
Distal

proximal



# Main Factors of Late Stent Thrombosis in 80 OCT Patients

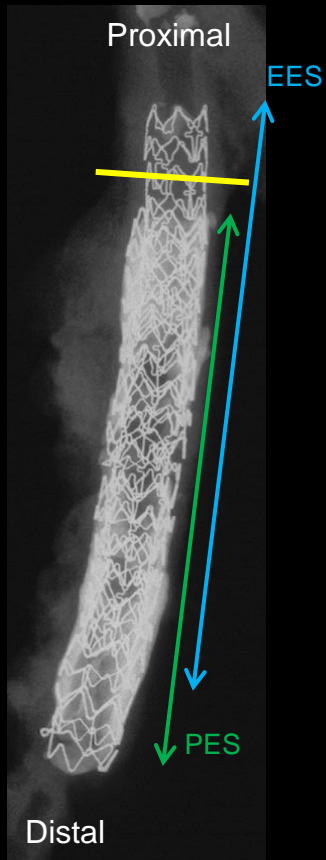
**PRESTIGE Registry with over 500 cases of LST**



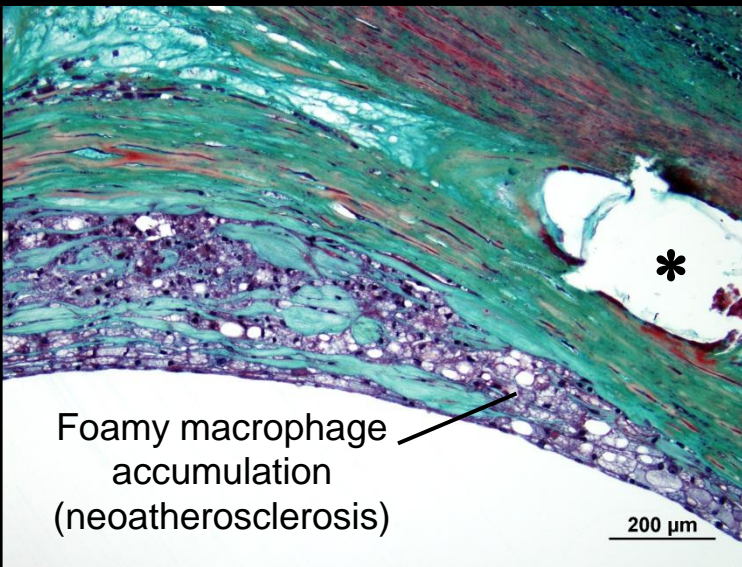
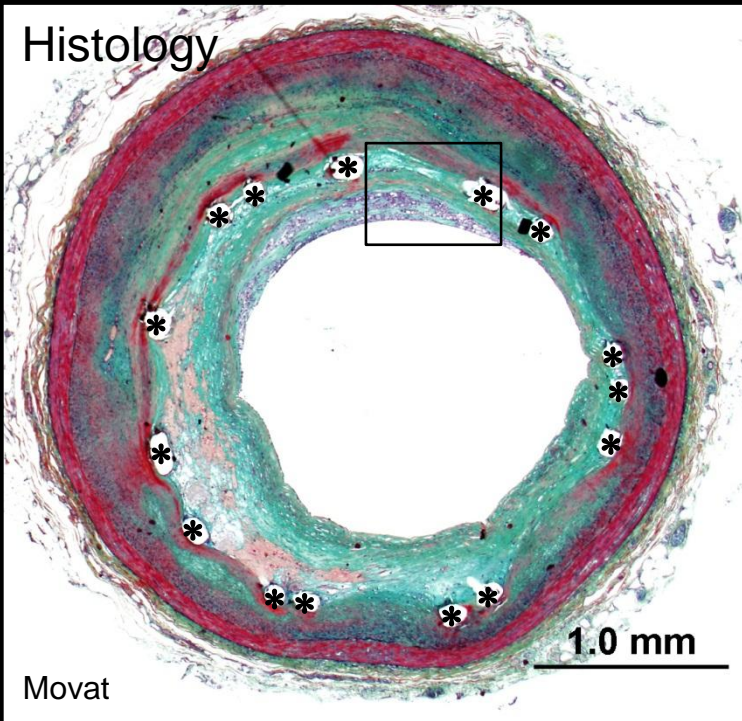


# Neoatherosclerosis within the EES

49M, EES  
within the PES  
in mid LAD

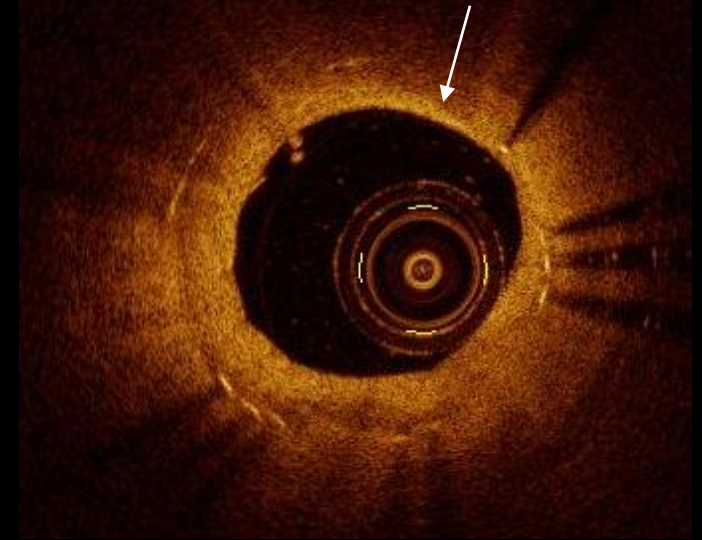


\* Stent strut

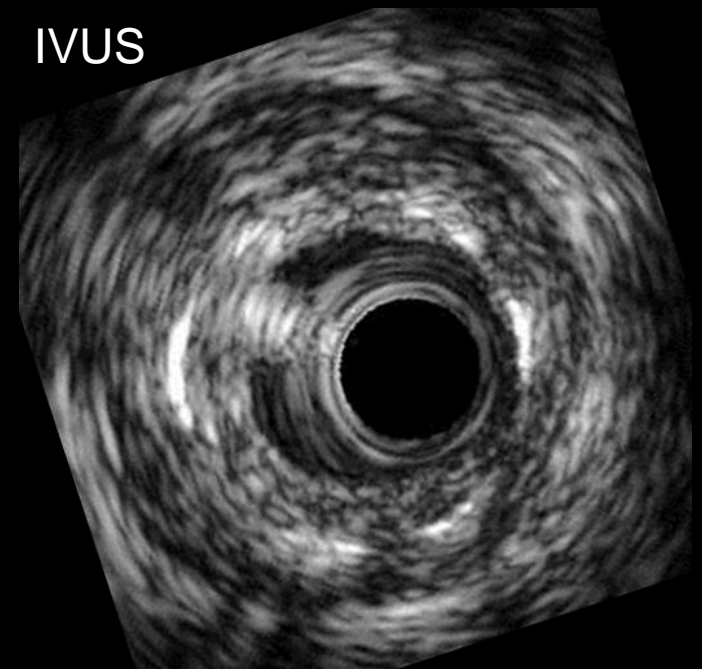


OCT

Signal-rich lesion  
with attenuation

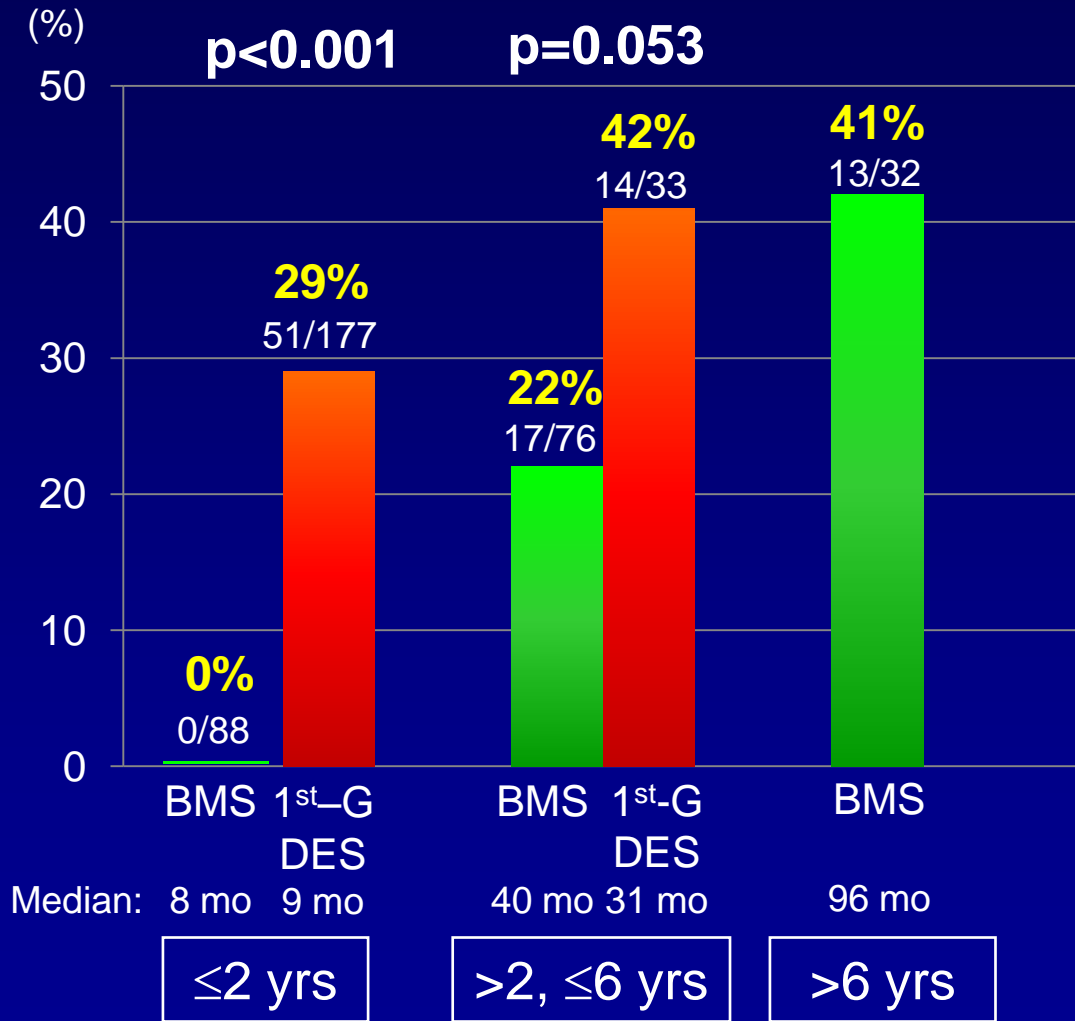


IVUS

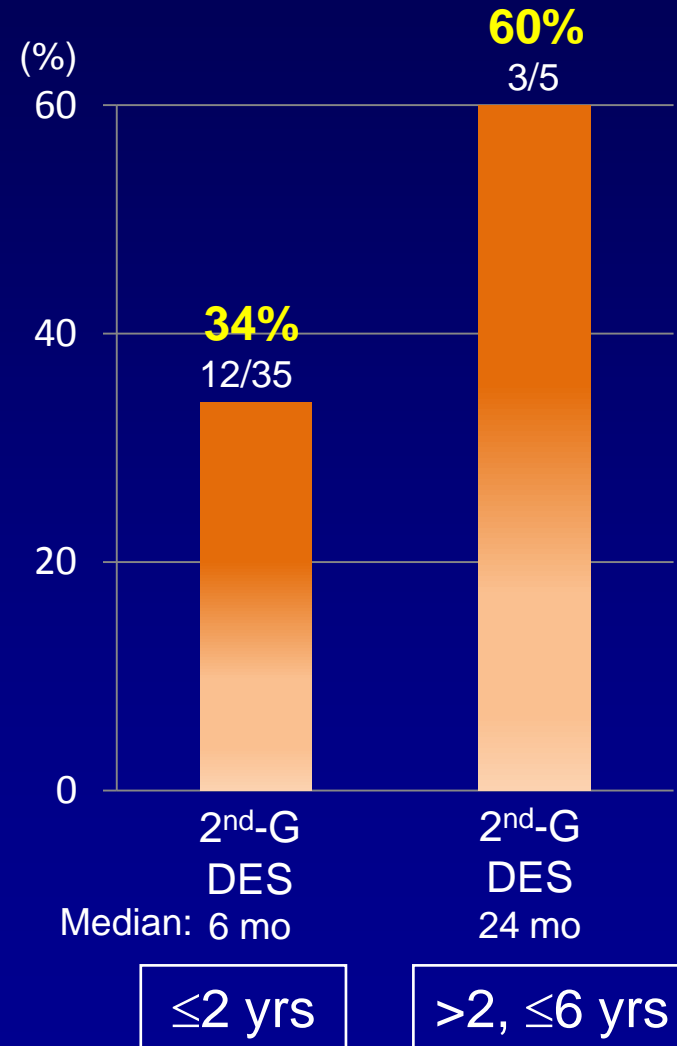


# Incidence of Neoatherosclerosis Stratified by Duration of Implant

## BMS, 1<sup>st</sup> and 2<sup>nd</sup> Generation DES



Nakazawa G, *JACC*. 2011;57:1314-22



(Unpublished data, includes cases of vein graft)

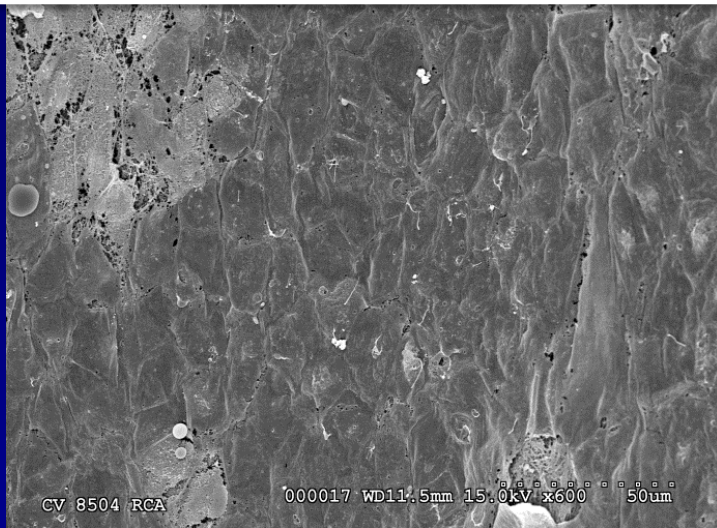


# Poorly Formed Endothelial Cell Junctions Following Stent Placement in Humans: Scanning Electron Microscopy Findings

71-year-old woman who died of stroke

**BMS**

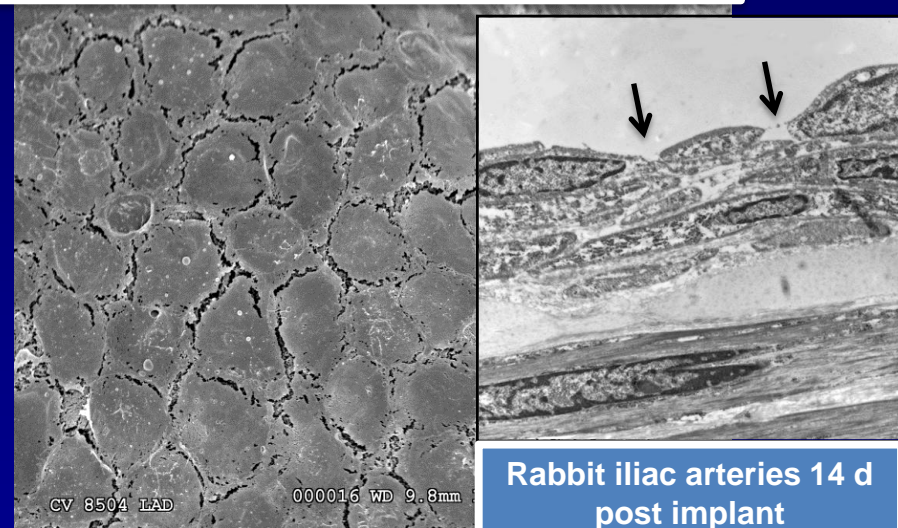
Implanted in RCA 2 y antemortem



Pavement-shaped endothelial cells with endothelial cell-to-cell contact, a small area exhibits poorly formed cell junctions

**SES**

Implanted in LAD 16 m antemortem

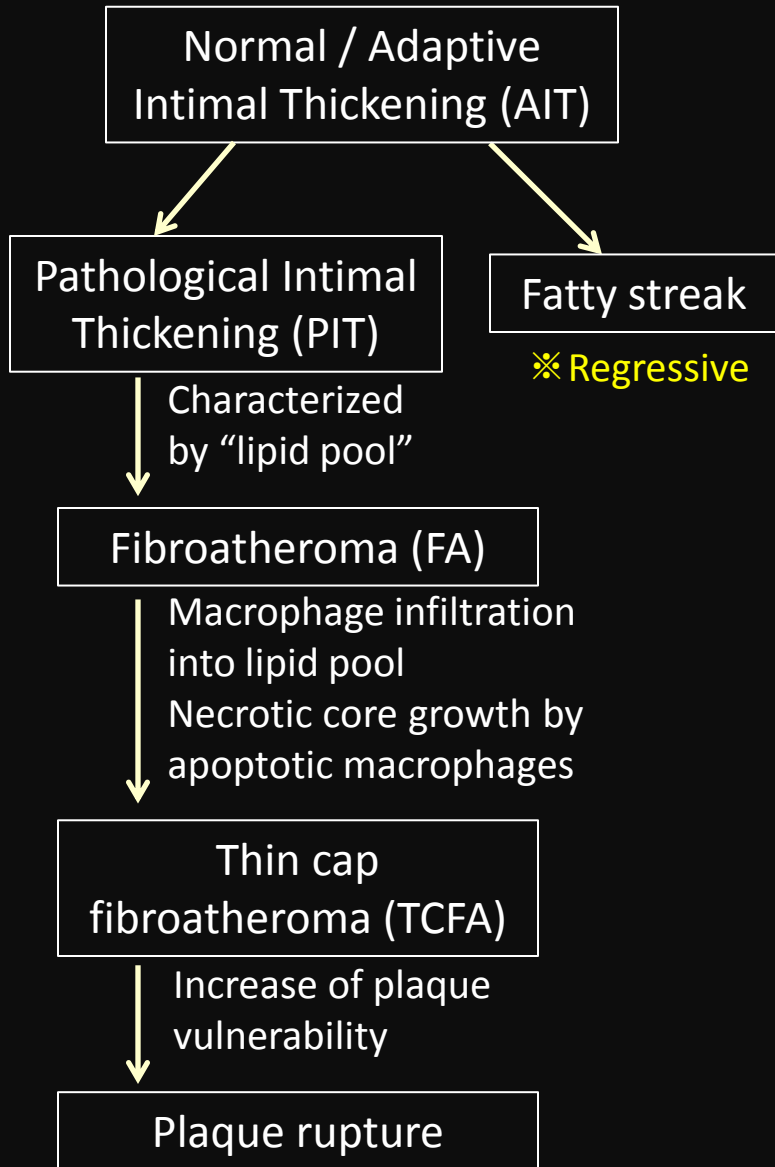


Poorly formed endothelial cell junctions

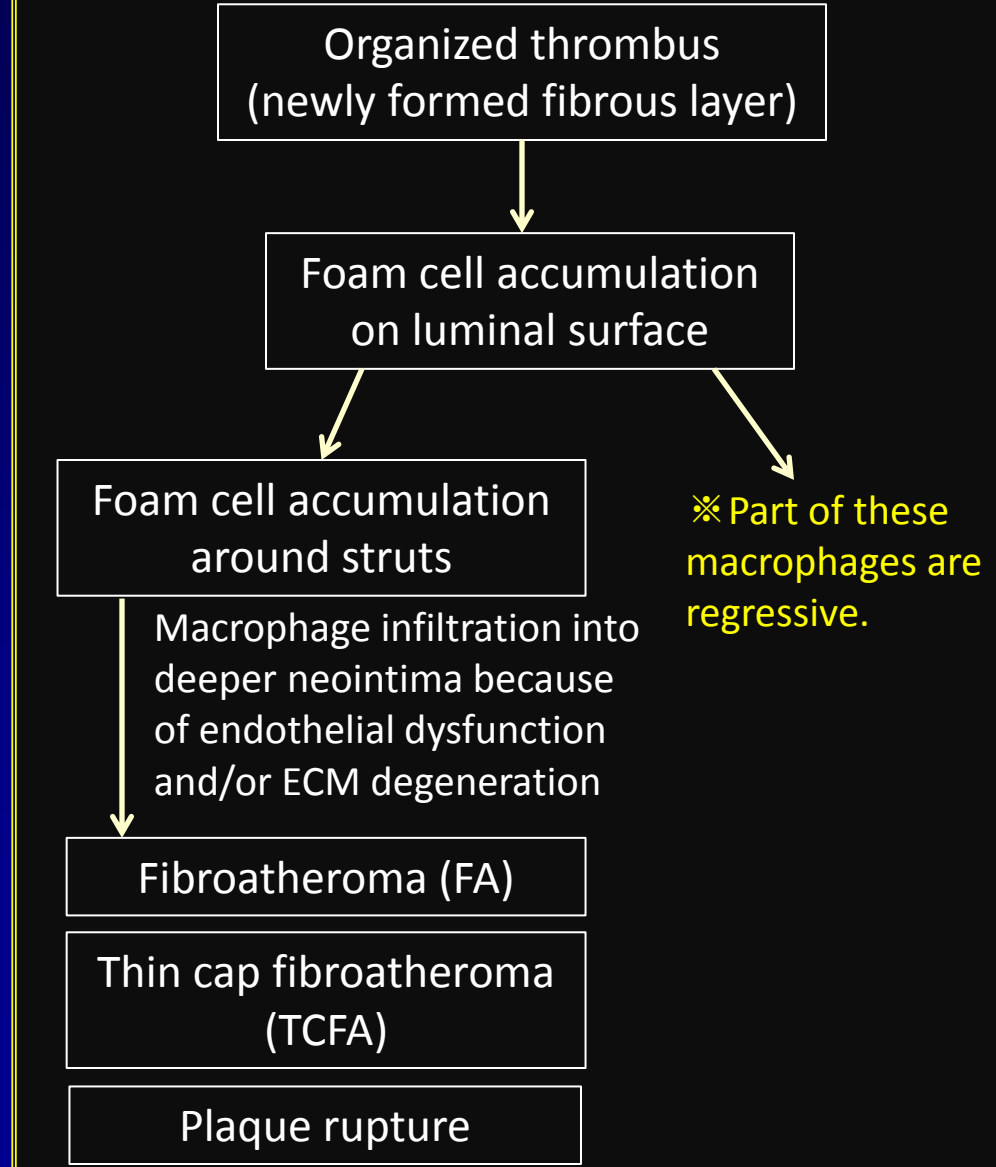
# Speculative Pathway of Neoatherosclerosis

Different from Atherosclerosis in Native Coronary Artery

## Native Atherosclerosis



## Neoatherosclerosis



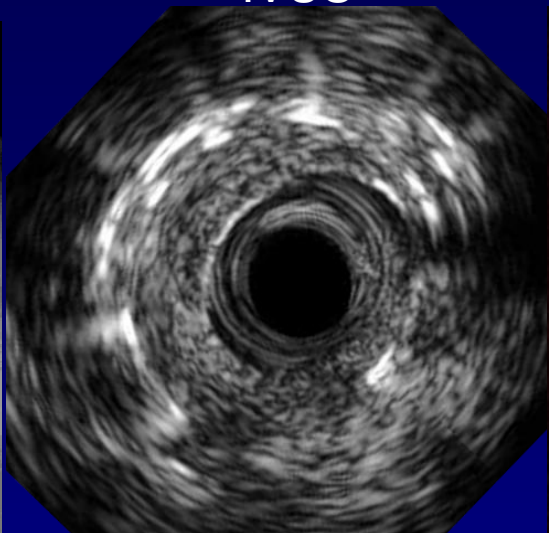
# Foamy Macrophage Accumulation on Luminal Surface

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

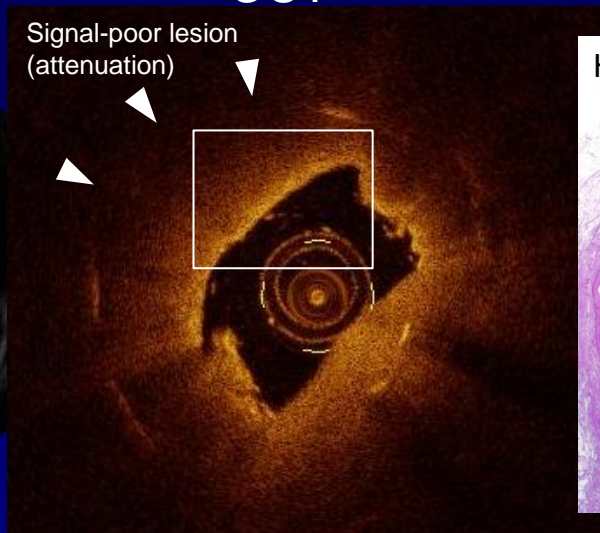
X-ray



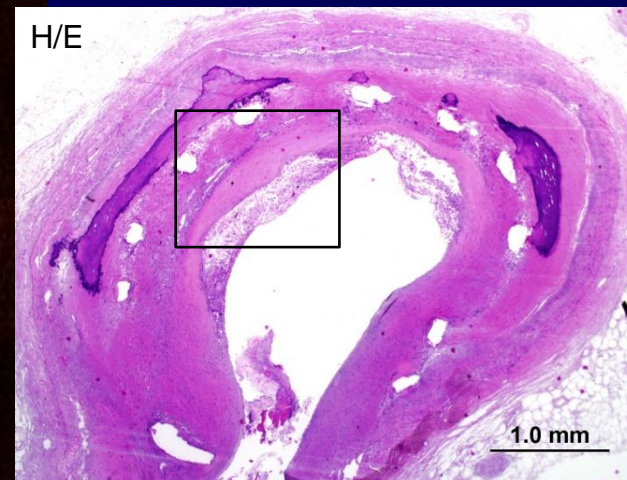
IVUS



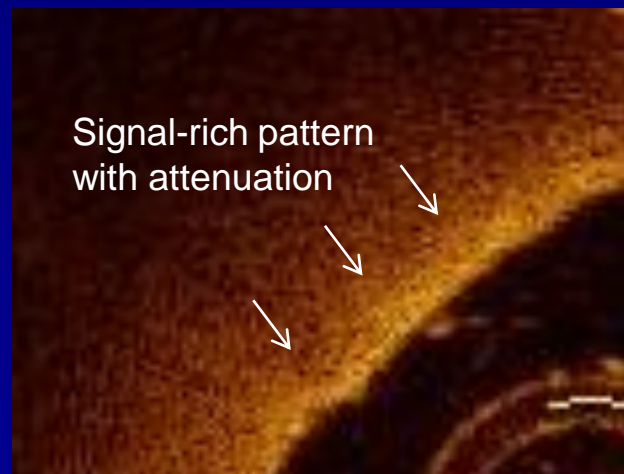
OCT



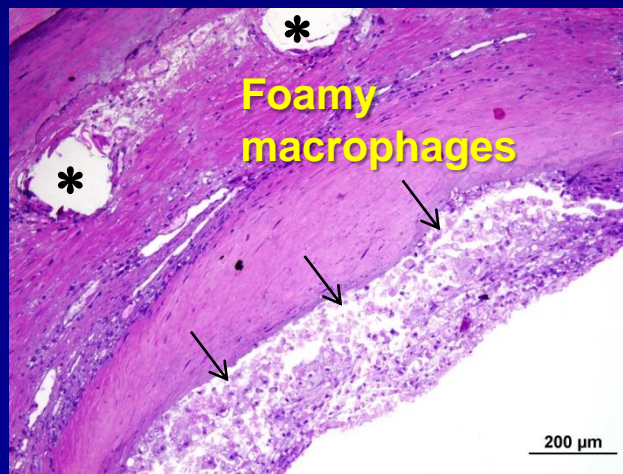
Histology



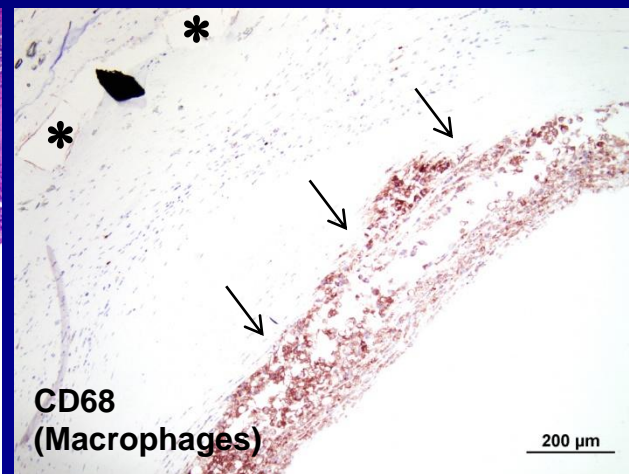
Signal-rich pattern with attenuation



Foamy macrophages



CD68 (Macrophages)



Neointimal hyperplasia: Newly formed atherosclerotic change within the neointima.

\* Stent strut



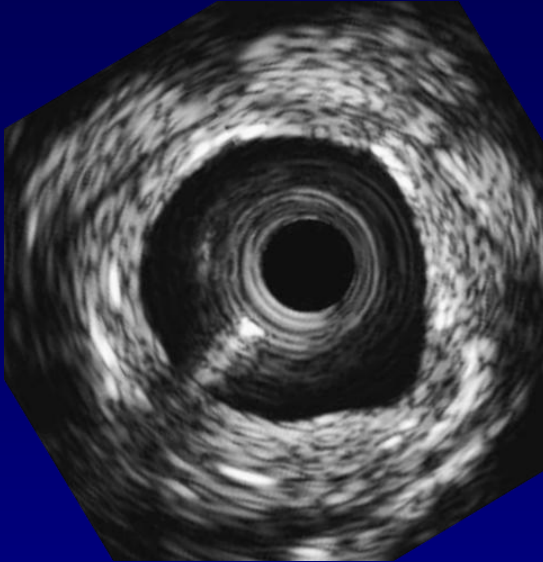
# Neoatherosclerosis with Necrotic Core

48-year-old man, Sirolimus-eluting stent implanted in proximal LAD, Non-coronary death (suicide)

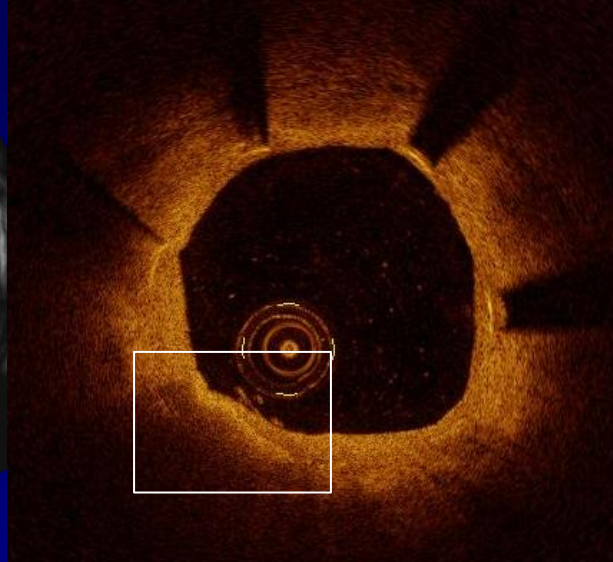
X-ray



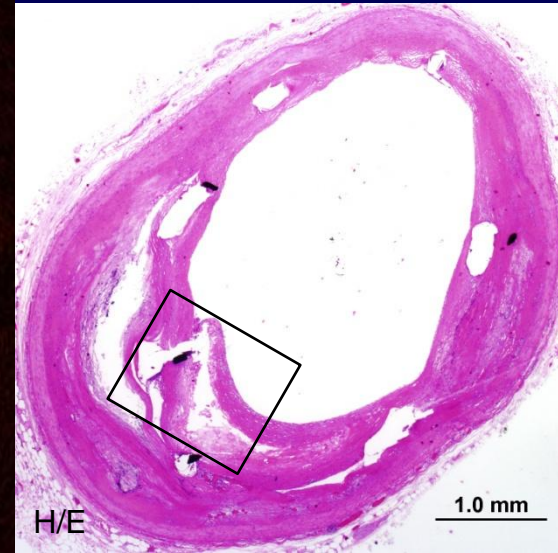
IVUS



OCT



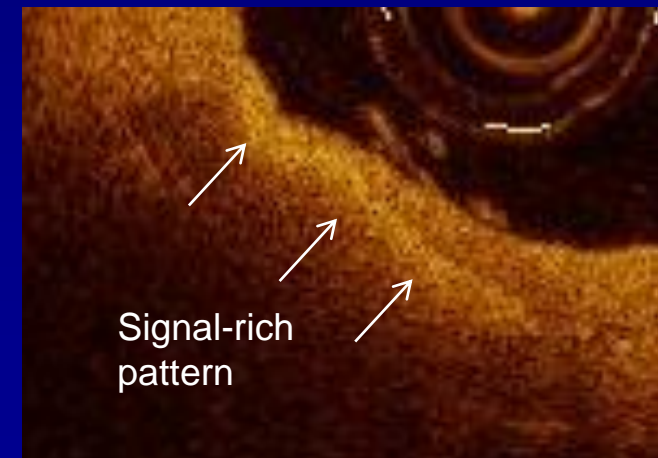
Histology



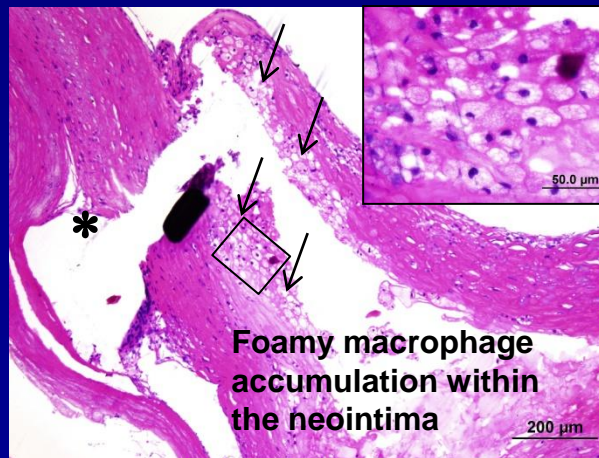
H/E

1.0 mm

Signal-rich pattern

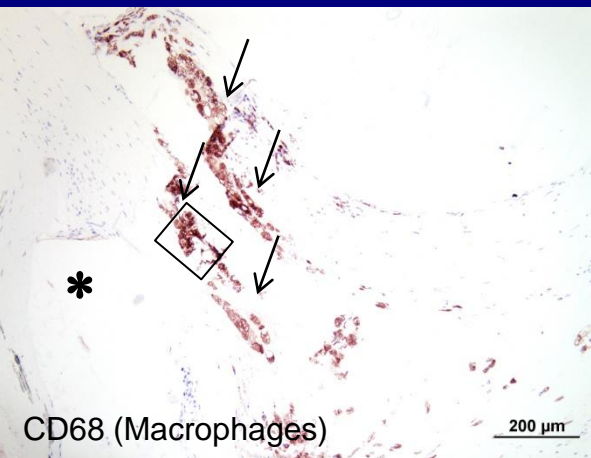


Foamy macrophage accumulation within the neointima



50.0 μm

200 μm



CD68 (Macrophages)

200 μm

Neoatherosclerosis: Newly formed atherosclerotic change within the neointima.

\* Stent strut

# Summary: Neoatherosclerosis

- In-stent neoatherosclerosis is characterized by foamy macrophage accumulation with or without necrotic core formation, and occurs both in BMS and DES. However, DES shows more frequent and rapid development of neoatherosclerosis as compared to BMS.
- In-stent plaque rupture from neoatherosclerosis is an important cause of VLST in both BMS and DES, which can occur with shorter duration of implant for DES as compared to BMS.
- Incompetent endothelium following stent implantation is characterized by poorly formed cell junctions, reduced expression of antithrombotic molecules, and decreased nitric oxide production, which may be associated with more accelerated neoatherosclerosis in 1<sup>st</sup>-gen DES as compared to BMS.
- Second-generation DES also shows neoatherosclerosis but the incidence and characteristics of neoatherosclerosis in newer-generation DES is as yet too early to establish in autopsy studies as the number of cases are too few
- OCT appears to be a better tool for the detection of neoatherosclerosis as compared to IVUS, while it is also important to understand the limitation of this technology.

# Acknowledgments

## Funding

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## CVPath Institute

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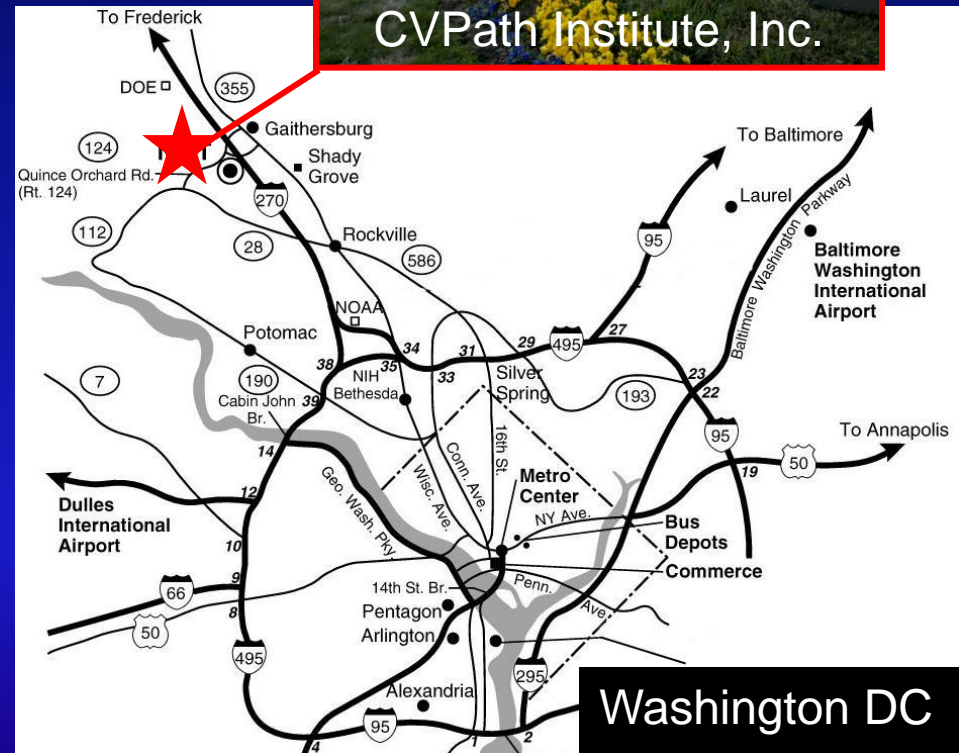
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Lila Adams, HT

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Washington DC