Optical Coherence Tomography Novel Findings in Neoatherosclerosis

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Potential conflict of interest

Speaker's name: Michael Joner, MD

☑ I have the following potential conflicts of interest to report:

Consultant: Biotronik

Employment in industry: No

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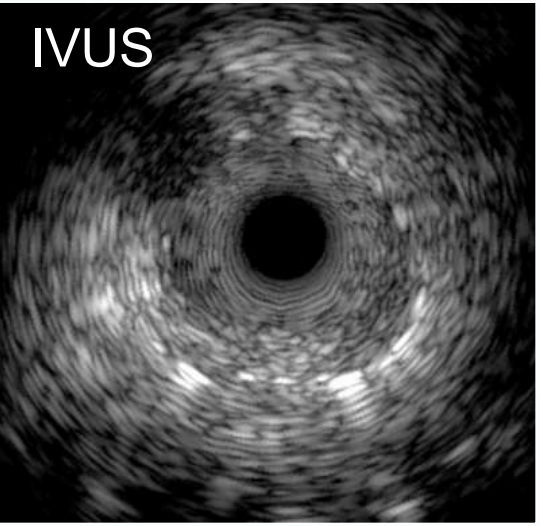
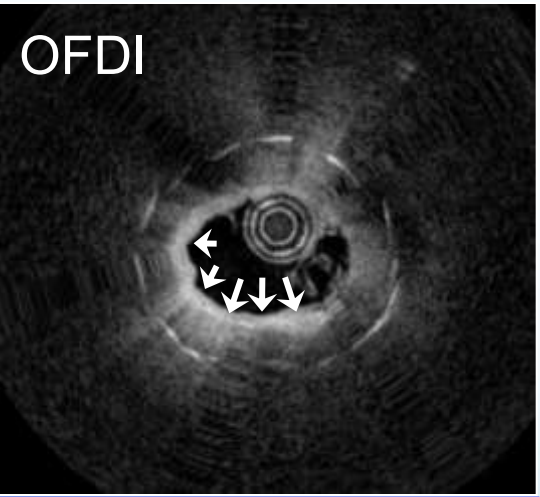
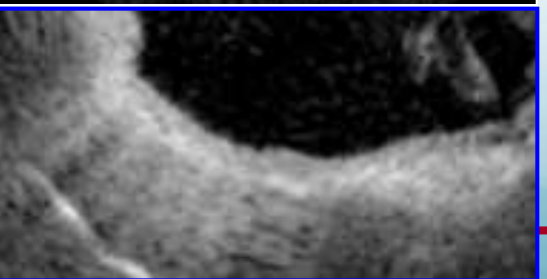
Owner of a healthcare company: No

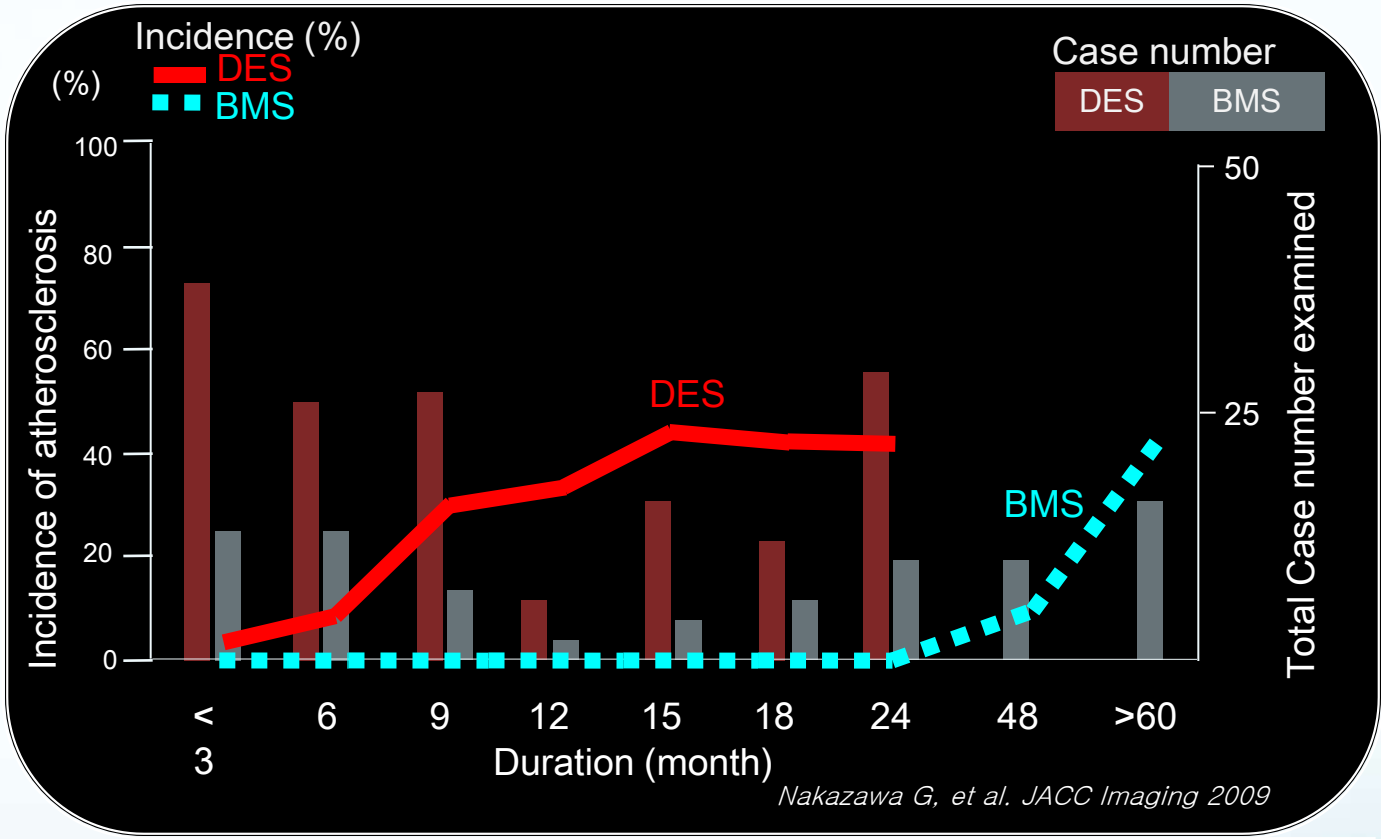
Stockholder of a healthcare company: No

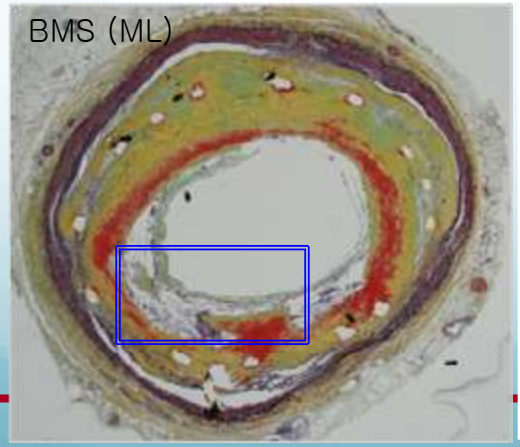
Incidence and Timing of Atherosclerotic Change



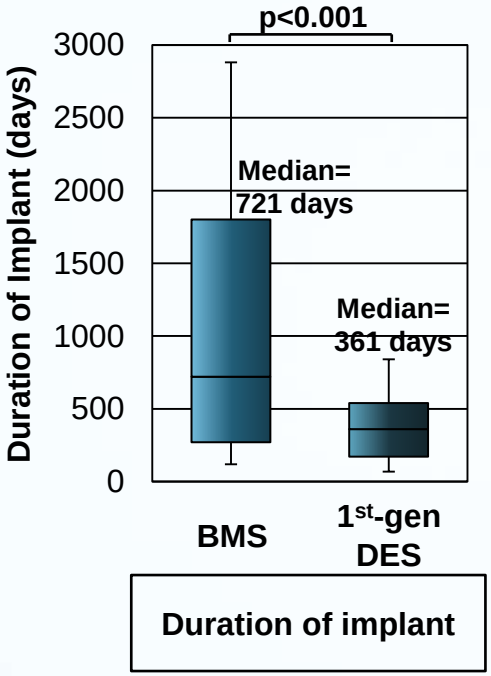




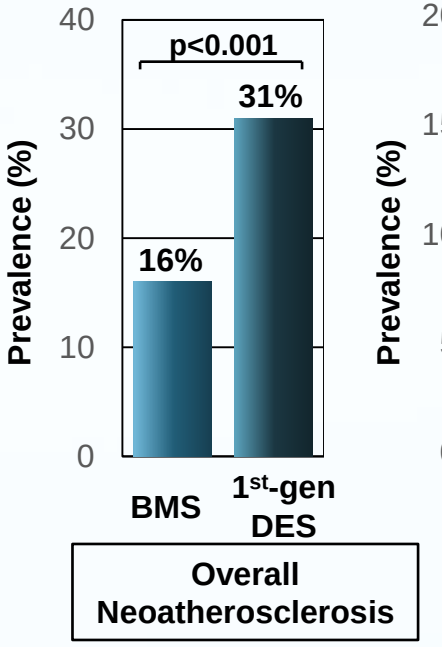




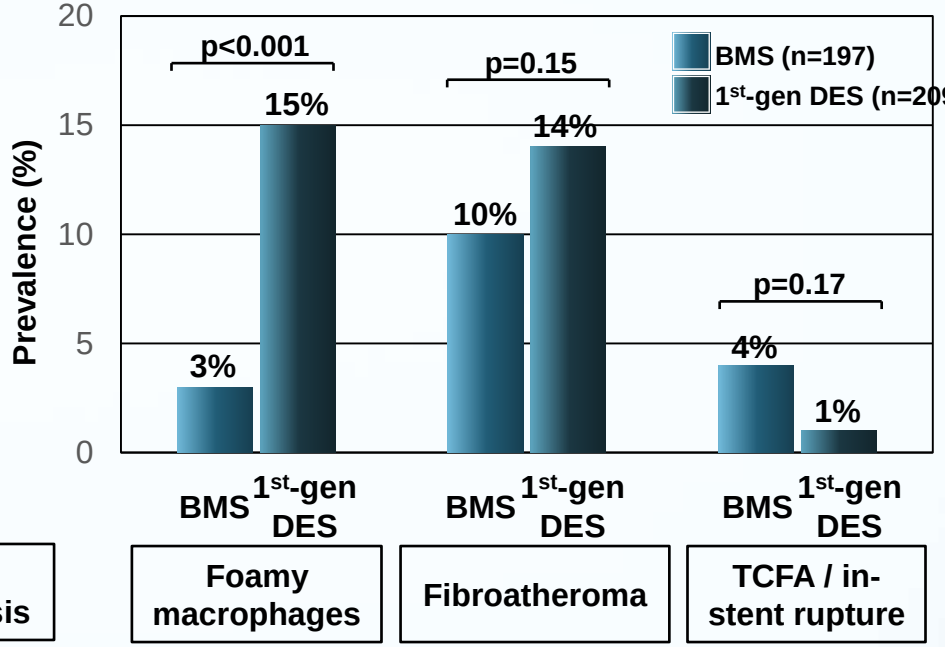
1st Generation DES



Duration of implant



Overall Neoatherosclerosis

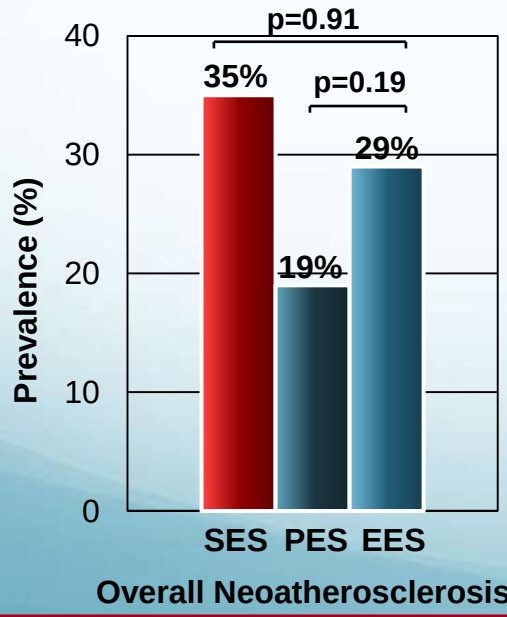


Foamy macrophages

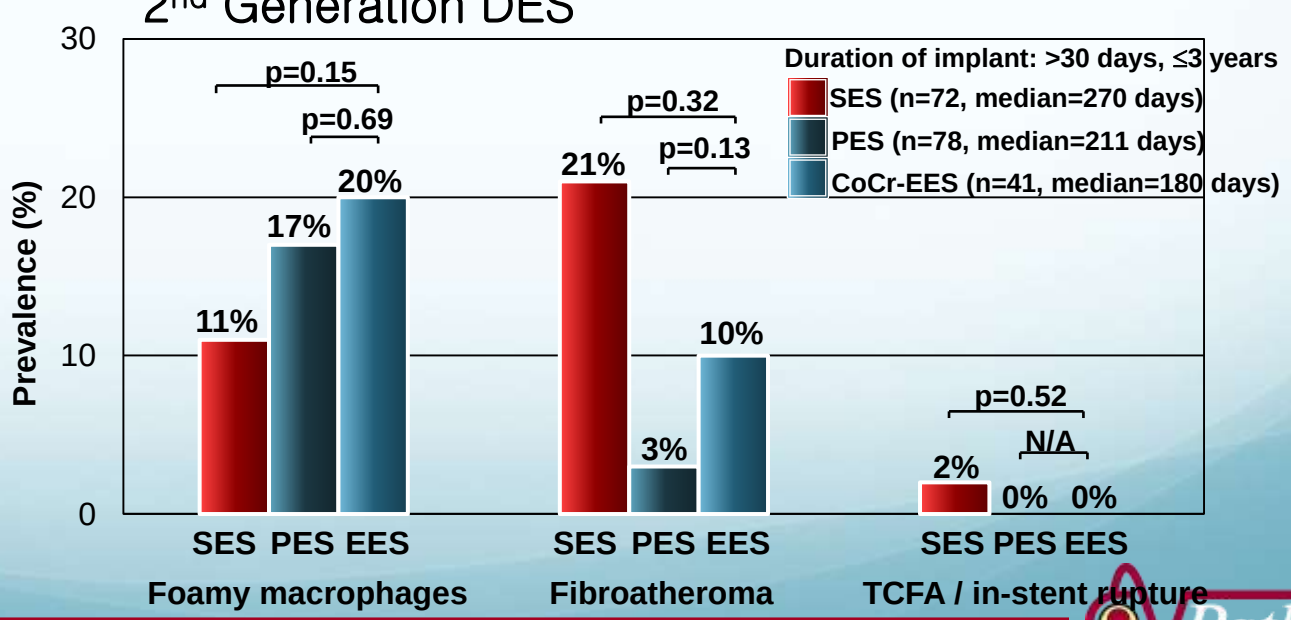
Fibroatheroma

TCFA / in-stent rupture

2nd Generation DES



Overall Neoatherosclerosis

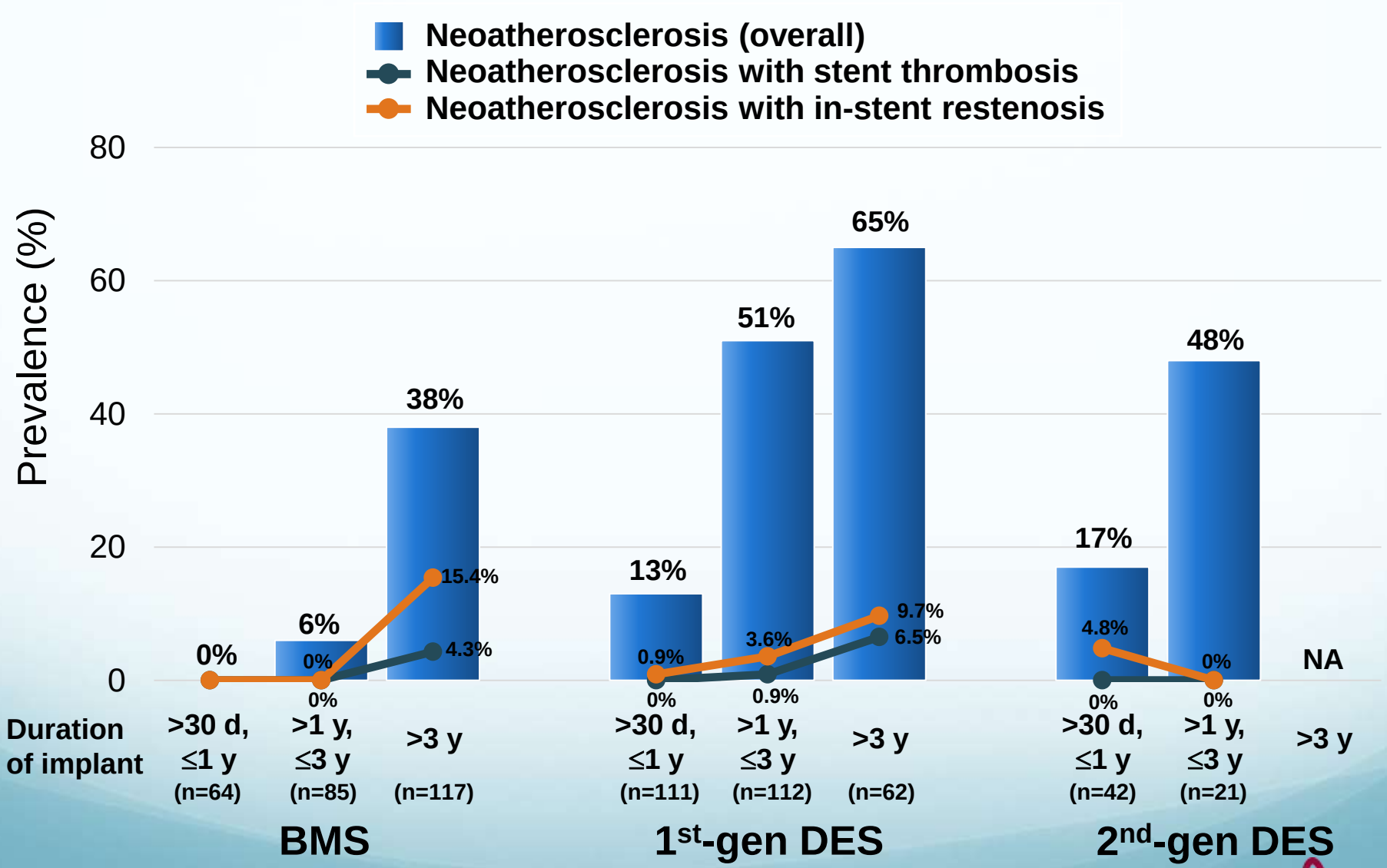


Foamy macrophages

Fibroatheroma

TCFA / in-stent rupture

Prevalence of Neoatherosclerosis at Autopsy: Overall, with Stent Thrombosis, and with Restenosis



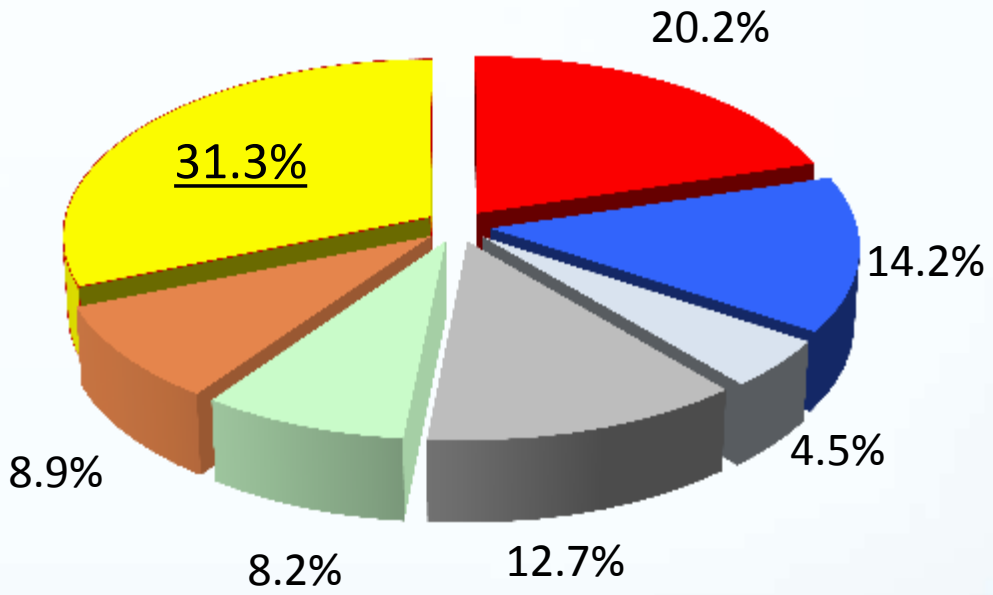
Otsuka et al., European Heart Journal May 2015, ahead of print

Prevalence of Neoatherosclerosis in clinical cases of VLST – PRESTIGE

OCT substudy

- 29 Centers with OCT capability
- Pts prospectively enrolled using a centralized telephone registration system
- Data collected according to a standardized protocol
- OCT before interventions (recommended)
- OCT immediately after emergent PCI (suggested)

- 217 patients comprised the primary study cohort for the current analysis.



Neoatherosclerosis was defined as presence of:

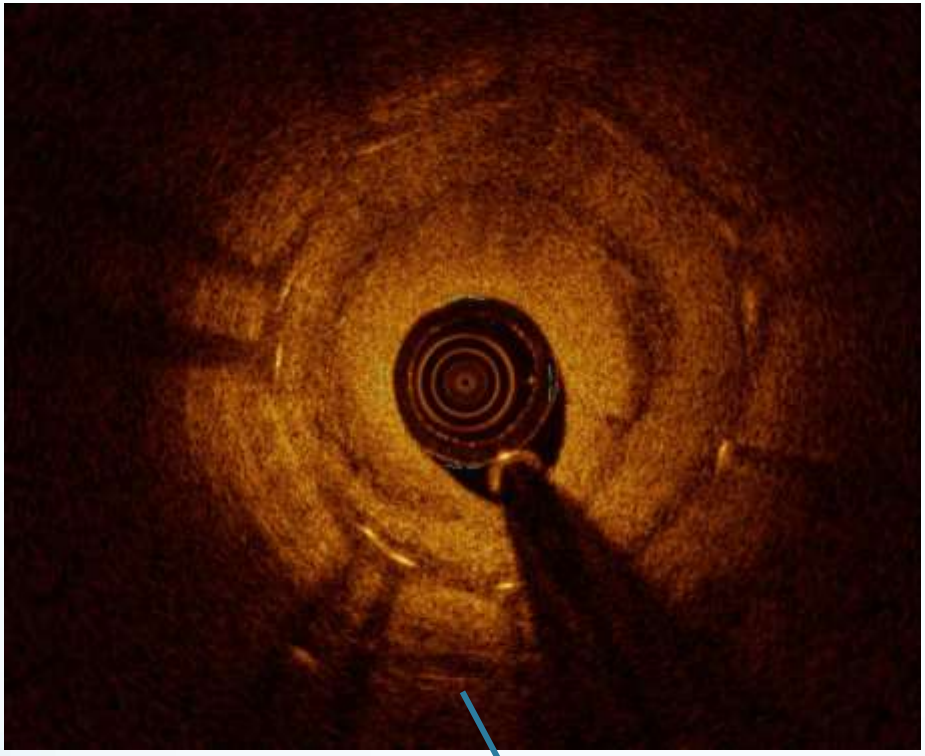
- *Lipid-laden tissue*
- *TCFA*
- *Rupture*
- *Calcification in neointima*

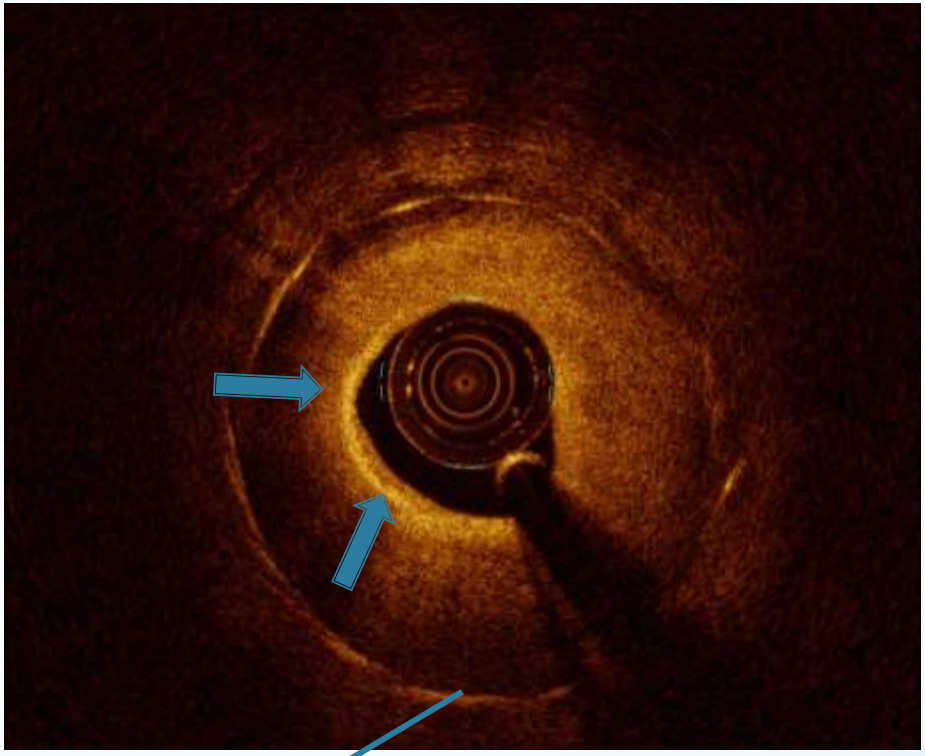
Guagliumi et al., TCT 2015

Prevalence of Neoatherosclerosis the Clinical Setting

Due to lack of standardization in definition, neoatherosclerosis has been substantially over-diagnosed by OCT

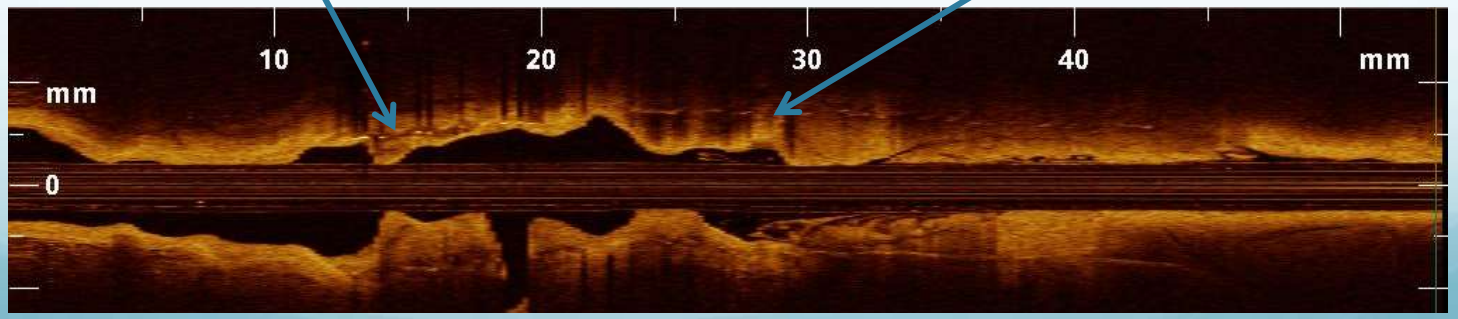
A 55-year old male patient presented with unstable angina 9 years after LAD stenting with a durable polymer paclitaxel-eluting stent. OCT imaging revealed diffuse high-grade in-stent restenosis of the stented segment



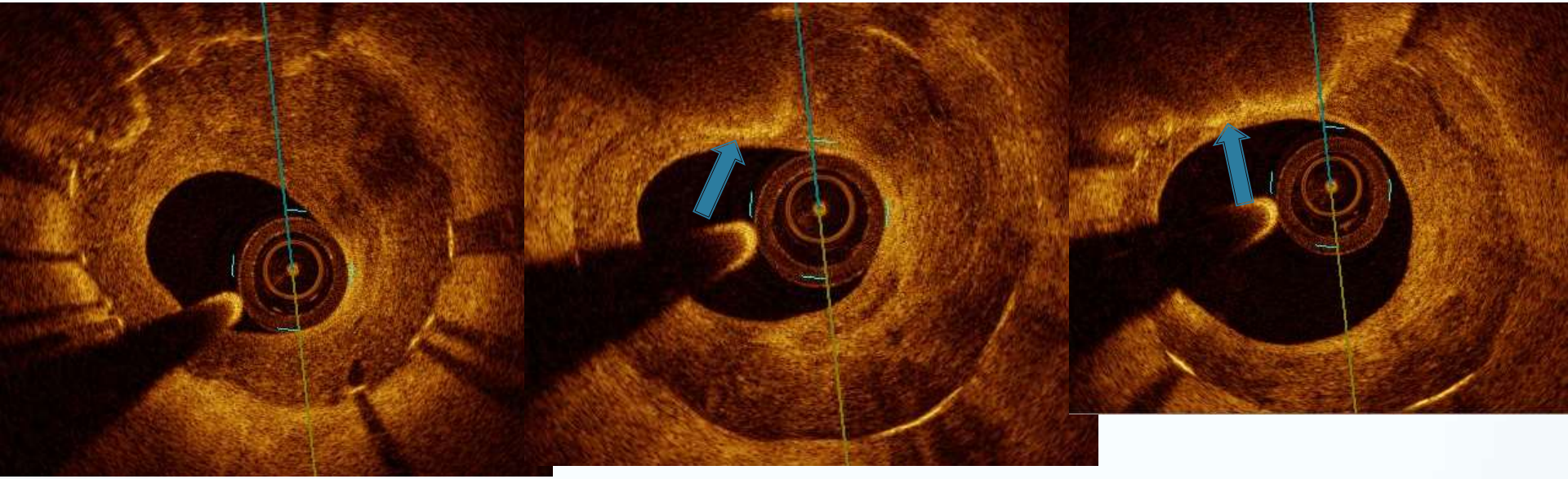


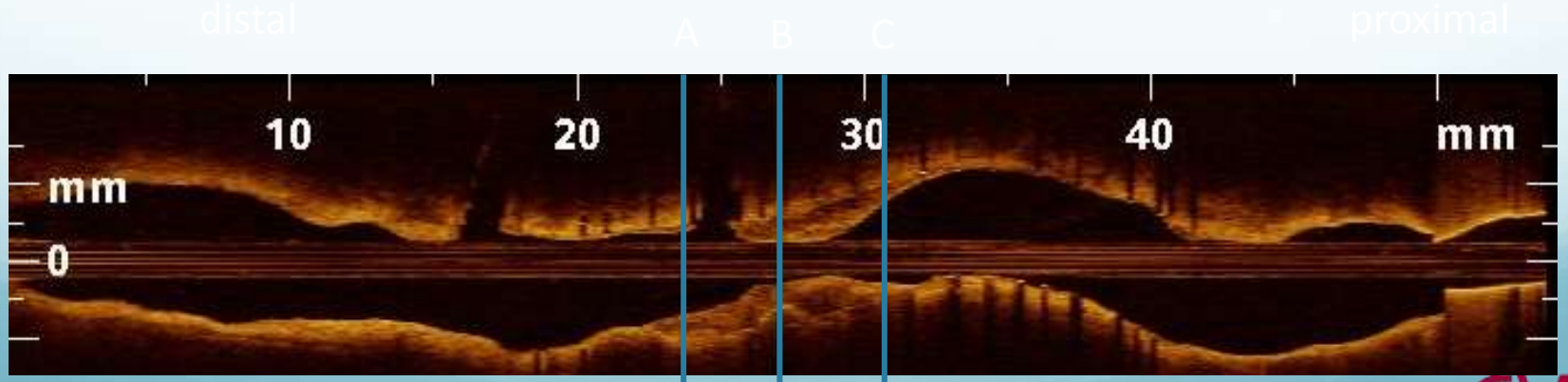
distal

proximal

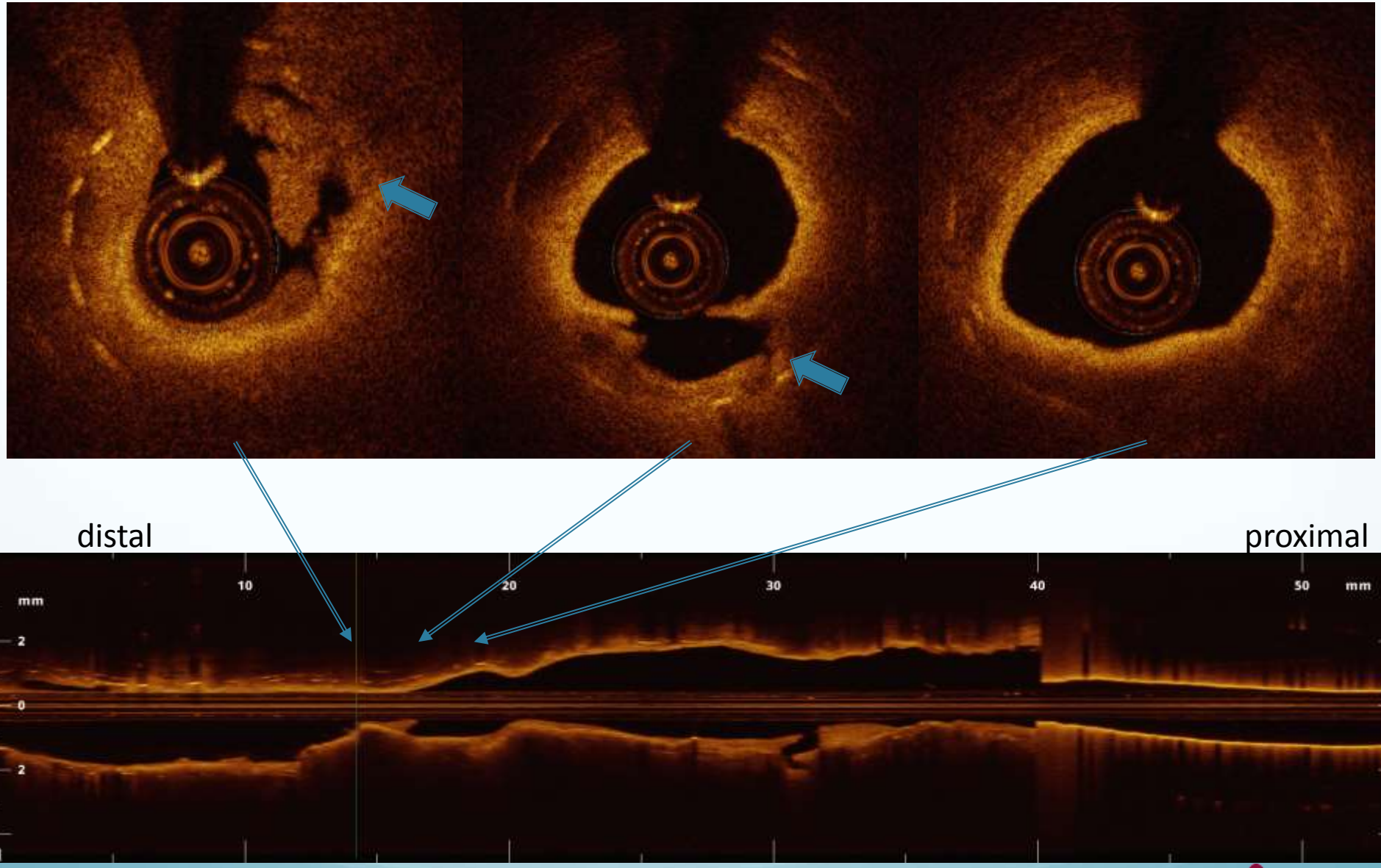


A 58-year old male patient presented with stable angina 7 months after implantation of a durable polymer everolimus-eluting stent. OCT imaging shows focal in-stent restenosis

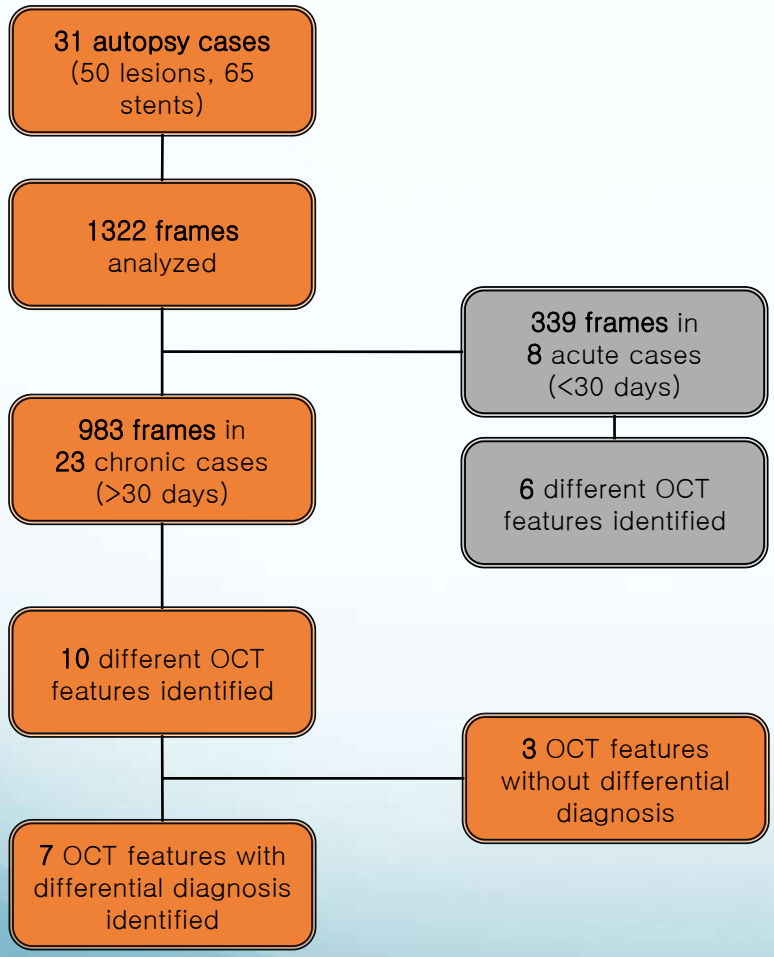




A 67-year old patient presented with stent thrombosis in the right coronary artery 3 years after implantation of a durable polymer drug-eluting stent.

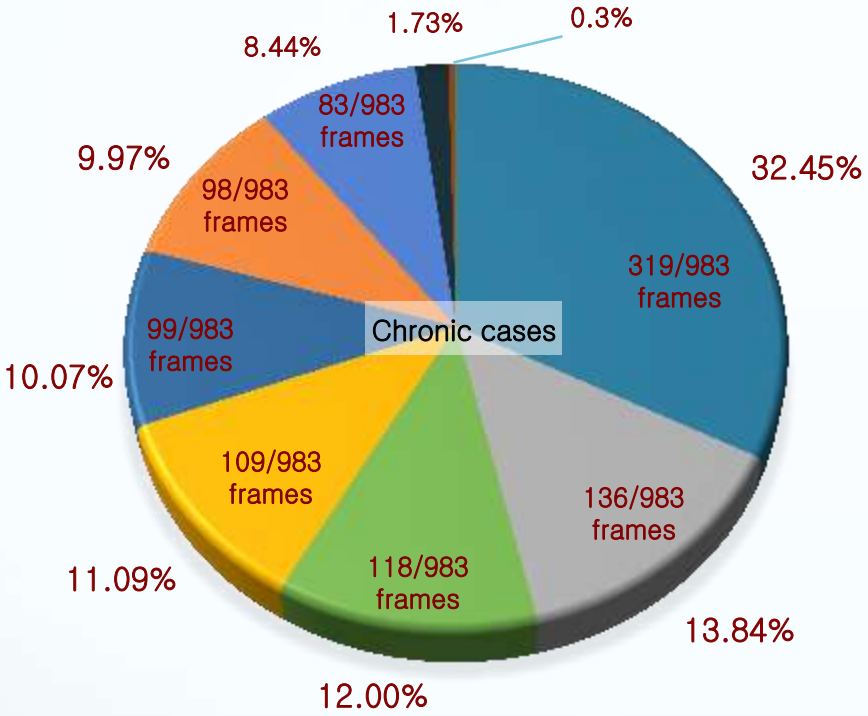


Differential Diagnosis of OCT Imaging Features in Human postmortem Hearts



OCT Finding	Overall Percentage N=1322 frames	Acute cases (< 30 days) N=339 frames	Chronic cases (> 30 days) N=983 frames
Heterogeneous/Layered neointima pattern (above struts)	24.1 %	0.0 %	32.5 %
Peri-strut low intensity (surrounding struts)	7.5 %	0.0 %	10.1 %
Neointimal evaginations	0.7 %	1.8 %	0.3 %
High attenuation surface	10.3%	0.0 %	13.8 %
Homogenous	8.9 %	0.0 %	12.0 %
Insufficient quality of frame	10.1 %	7.1 %	11.1 %

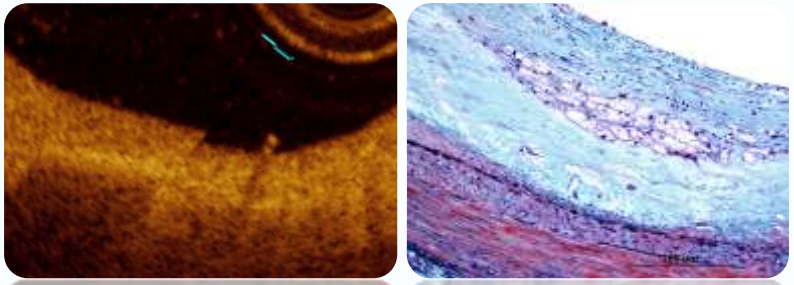
Differential Diagnosis of OCT Imaging Features in Human postmortem Hearts



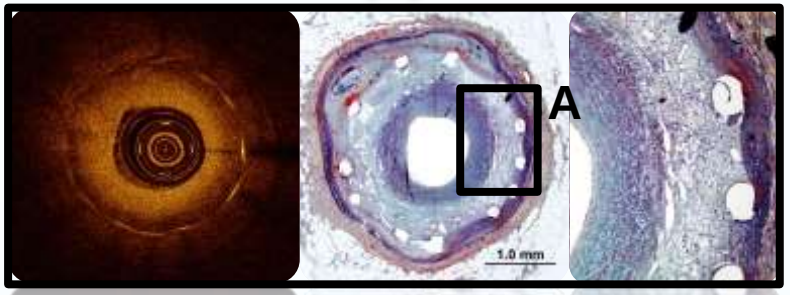
Patients	20 (6 female, 14 male)
Mean age	58.3 ± 15.73
Mean duration of stents	1439 days
Setting of implantation	ACS: 2 cases; Stable CAD: 18 cases
Stents	19x BMS, 10 x 1st DES, 12 x 2nd DES (10x RCA, 17x LAD, 2x LM to LAD, 2x LAD-LD1, 1x LOM1 and 1x LOM2)
Cause of death	5x Stent-related death; 12x non cardiac death; 3x cardiac but non-stent related death

Differential Diagnosis of OCT Imaging Features in Human postmortem Hearts

Layered backscatter ⟺ Foam cells deep in neointima

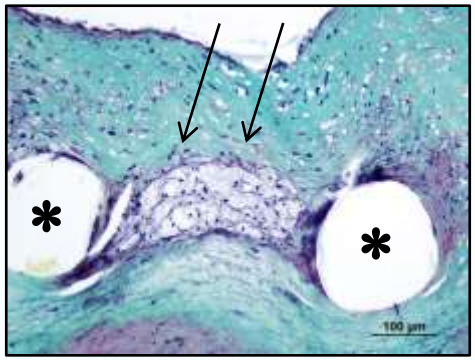


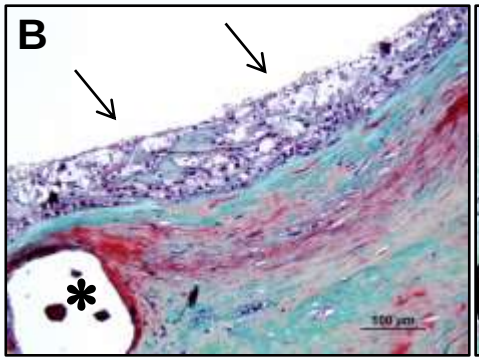
Layered backscatter ⟺ Neovascularization

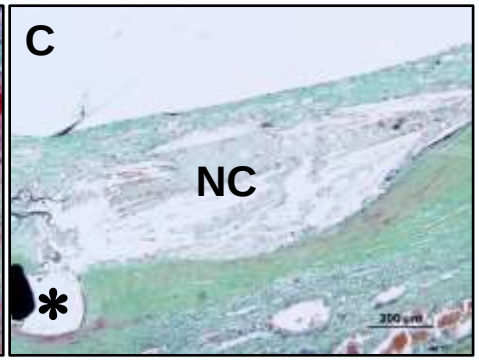


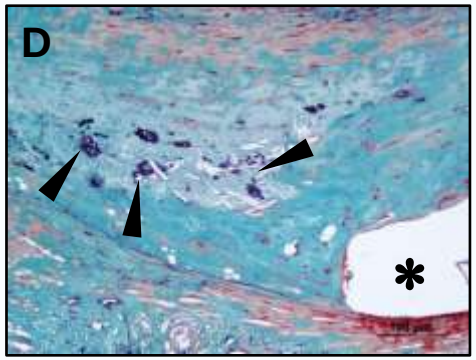
OCT imaging feature	Histological Differential Diagnosis				
Heterogeneous/Layered neointima pattern (above struts)	Peri-strut inflammatory reaction	Peri-strut neovascularisation	**Neoatherosclerosis (Lipid pool)**	-	-
Peri-strut low intensity (surrounding struts)	Fibrin accumulation	Peri-strut calcification	Peri-strut neovascularisation	Stent induced hypersensitiviy vasculitis	Foreign material (e.g. from jailed guidewire)
Neointimal evaginations	Stent induced hypersensitiviy vasculitis	Healed malapposition	-	-	-
High attenuation surface	**Superficial macrophage accumulation**	Neovascularisation with/without macrophages	-	-	-
Homogenous	Smooth muscle cells (SMC) within a proteoglycan-rich extracellular matrix.				

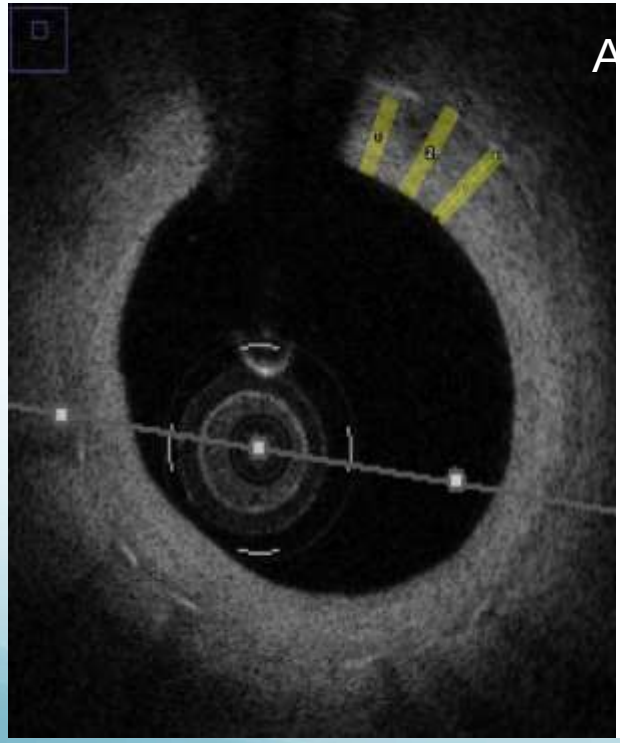
One Approach to Imaging Neoatherosclerosis











Methods:

1. Collection of stented arteries with presence of neoatherosclerosis at autopsy and from preclinical samples
2. OCT pullbacks were performed and co-registration of OCT frames with histological cross sections
3. Transformation of OCT image to 8-bit grey scale
4. Calibration of catheter size and signal intensity
5. Definition of regions of interest above and between stent struts
6. Analysis of Peak Intensity of Grey Scales and Attenuation rate
7. Correlation with histological findings

Comparison of Neoatherosclerosis at Autopsy and in Preclinical Animal Model

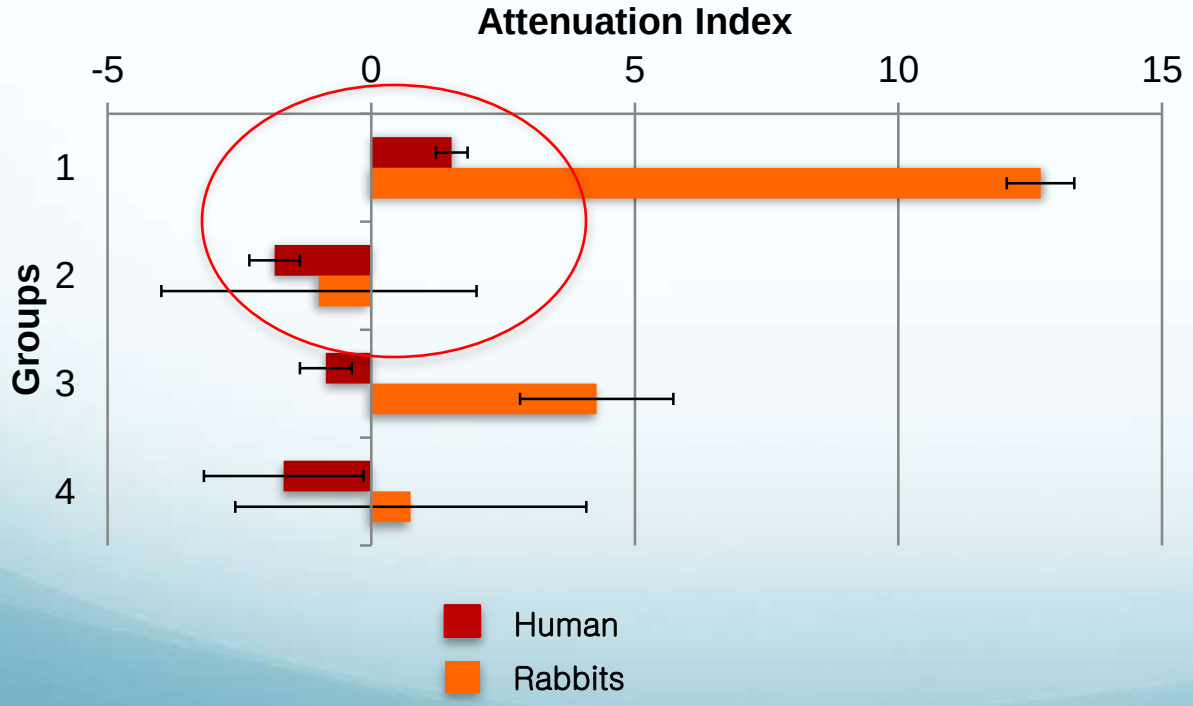
A total of 184 ROIs measured in autopsy samples and 725 in preclinical samples

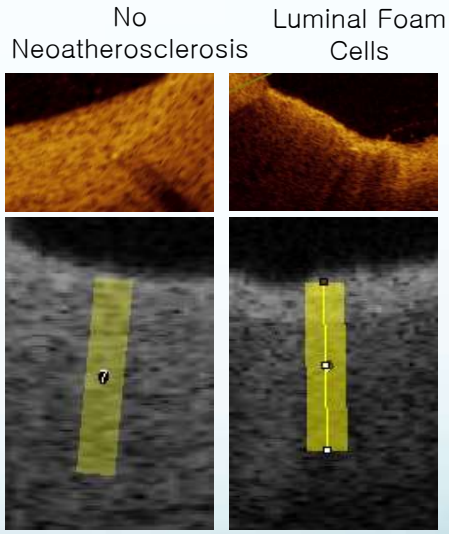
Detection of early stages of neoatherosclerosis is key!

Type	Neoatherosclerosis Group	Autopsy (n)	Preclinical (n)
1	No Neoatherosclerosis	102	568
2	Luminal Foam cells	40	26
3	Deep Foam cells	38	110
4	Luminal and deep Foam cells	4	21
	TOTAL:	**184**	**725**

Attenuation Index

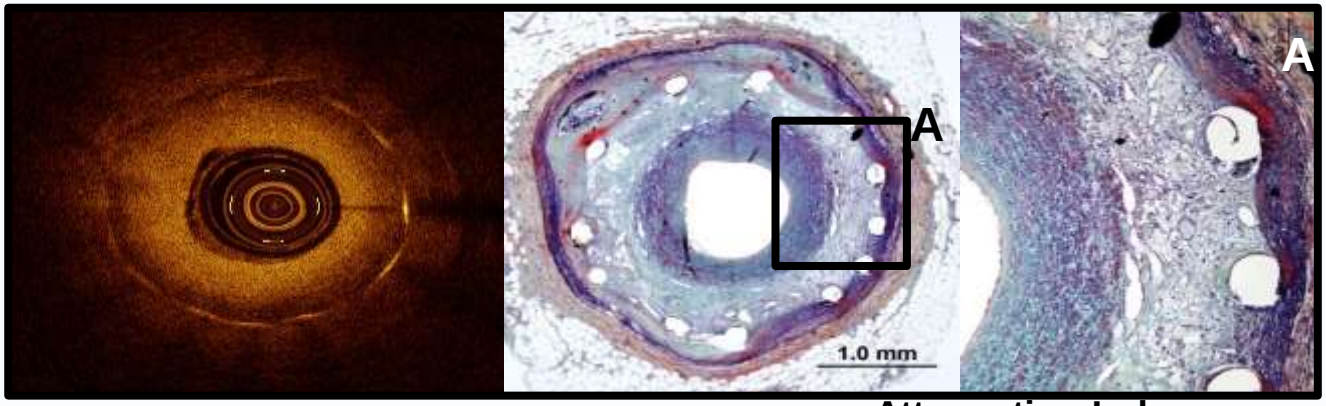
	Autopsy (n= 184 struts)		Preclinical (n= 725 struts)	
Neoatherosclerosis Group	**Attenuation - Mean**	**Std.dev.**	**Attenuation - Mean**	**Std.dev.**
1: No Neoatherosclerosis	1.5268 (n= 102)	0.30023	12.697 (n= 568)	0.64010
2: Luminal Foam Cells	-1.8350 (n= 40)	0.47943	-0.992 (n= 26)	2.99184
3: Deep Foam Cells	-0.8596 (n= 38)	0.49189	4.277 (n= 110)	1.45455
4: Lum.& deep Foam Cells	-1.6610 (n= 4)	1.51611	0.750 (n= 21)	3.32901



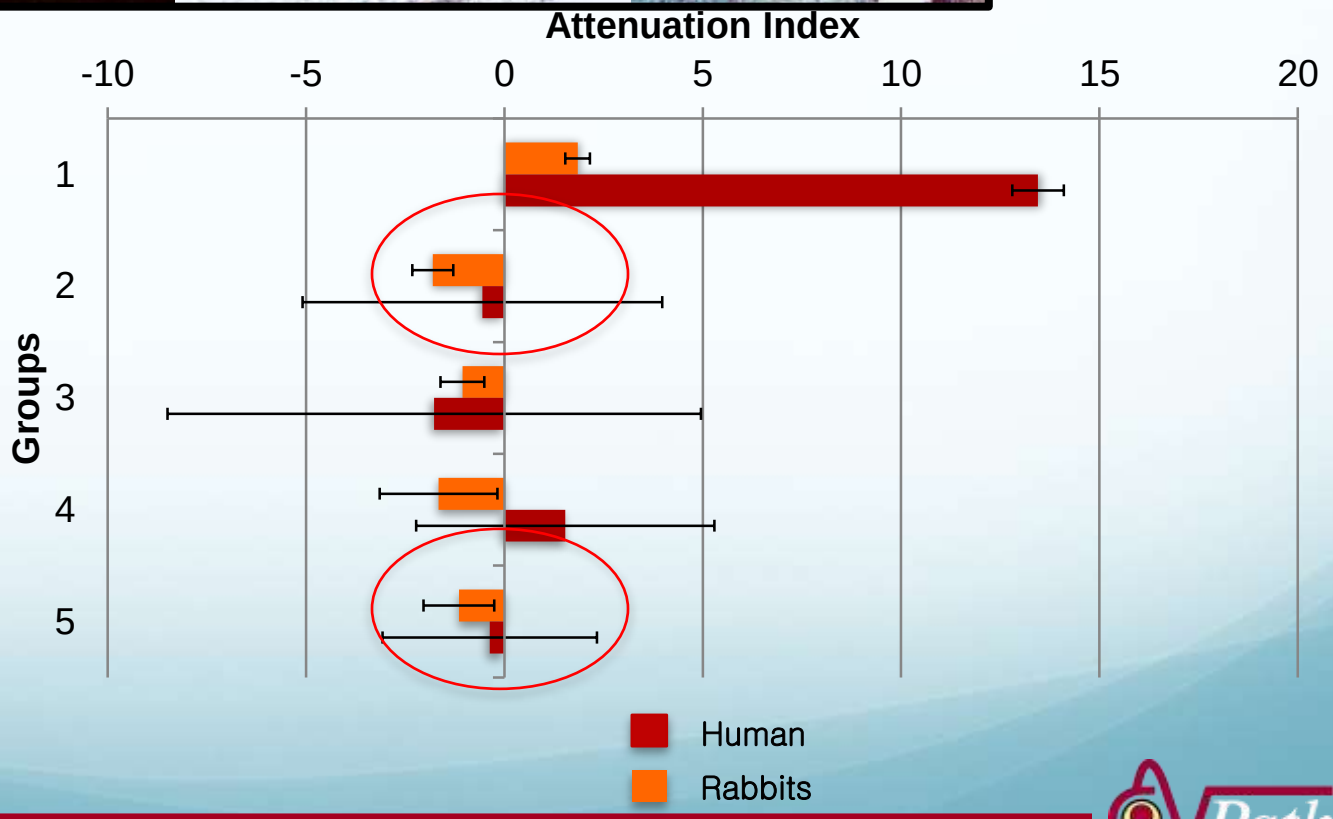


Foam Cells can be reliably distinguished by OCT

Neovascularization as Limitation

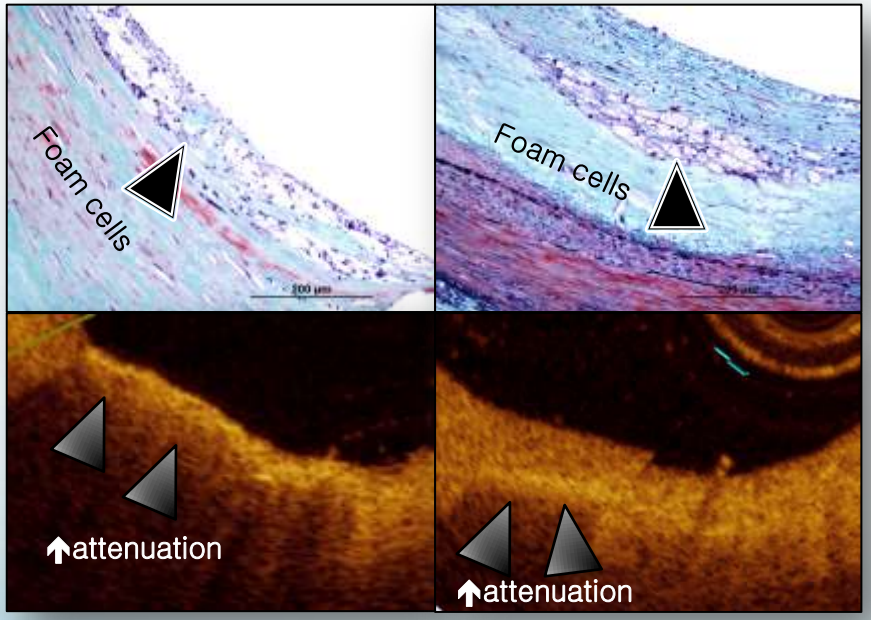


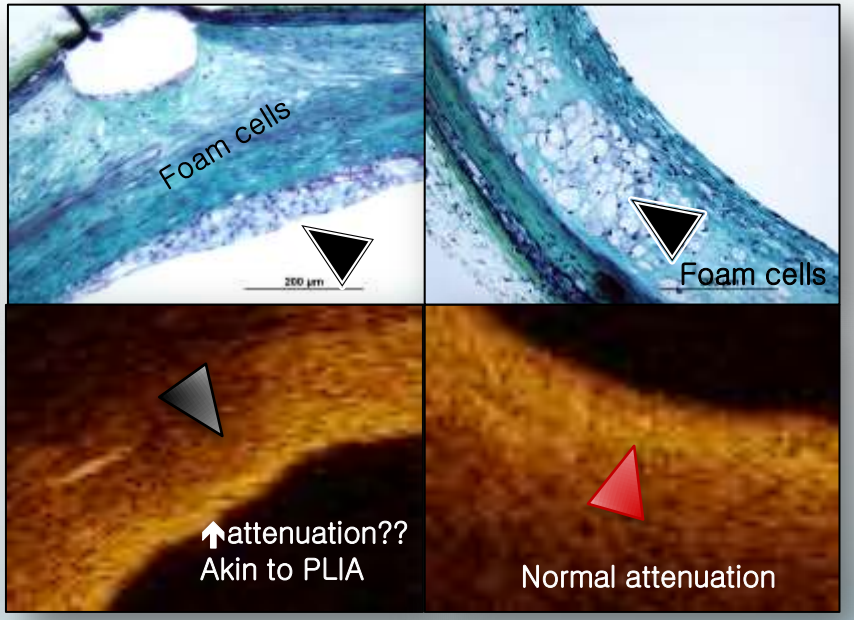
Neoatherosclerosis Group
1: No Neoatherosclerosis
2: Luminal Foam Cells
3: Deep Foam Cells
4: Lum.& deep Foam Cells
5: ***Neovascularization w/o neoatherosclerosis***



The Ratio of free to esterified Cholesterol and Location of Foam Cells determines Attenuates Rates in OCT Imaging

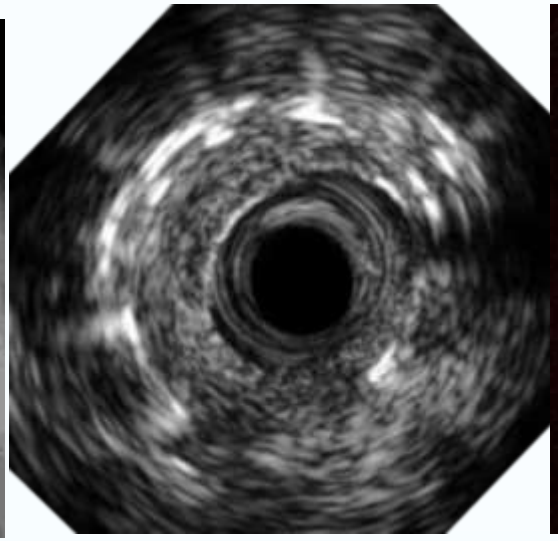
Foam cells do not necessarily always cause attenuation!
Free vs. esterified cholesterol is likely to play a role

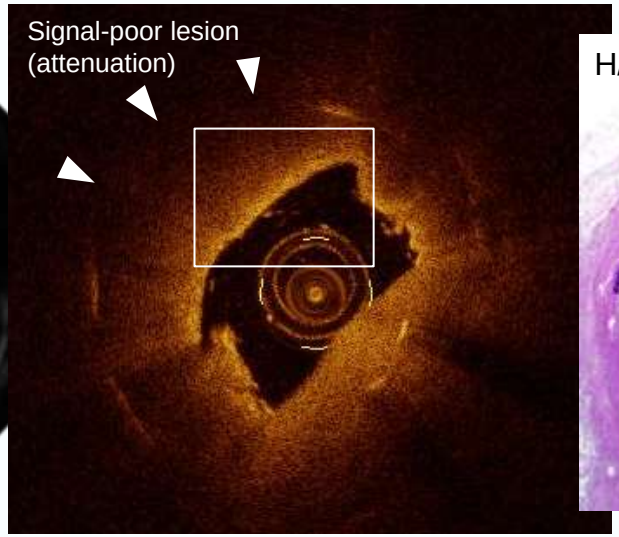


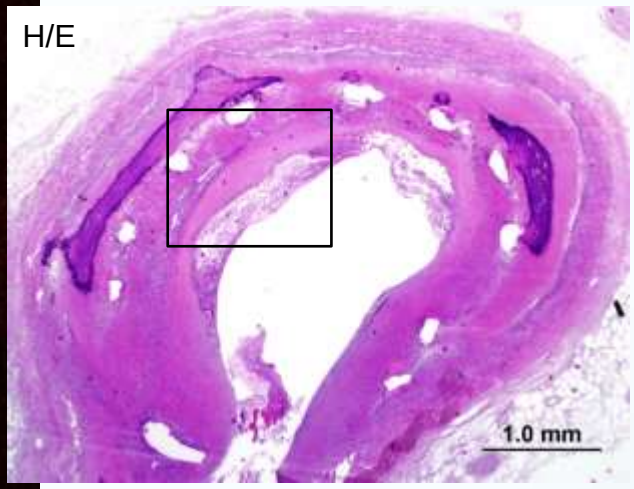


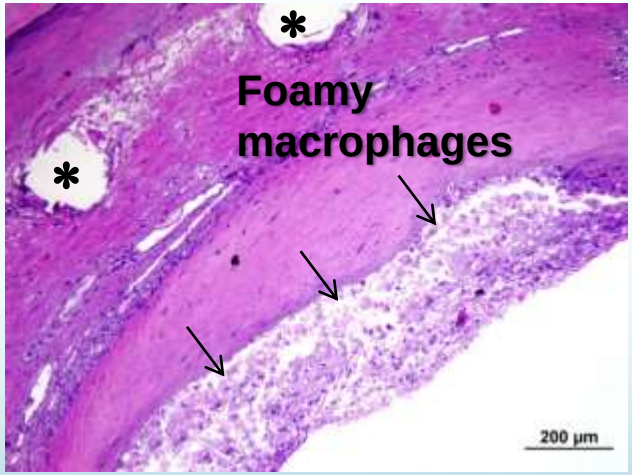
Foamy Macrophage Accumulation on Luminal Surface

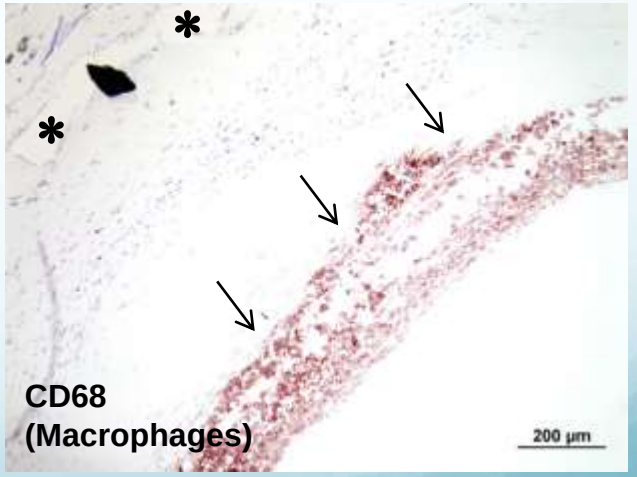
72-year-old female, BMS (Palmaz-Schatz stent) implanted in proximal RCA 10 years antemortem



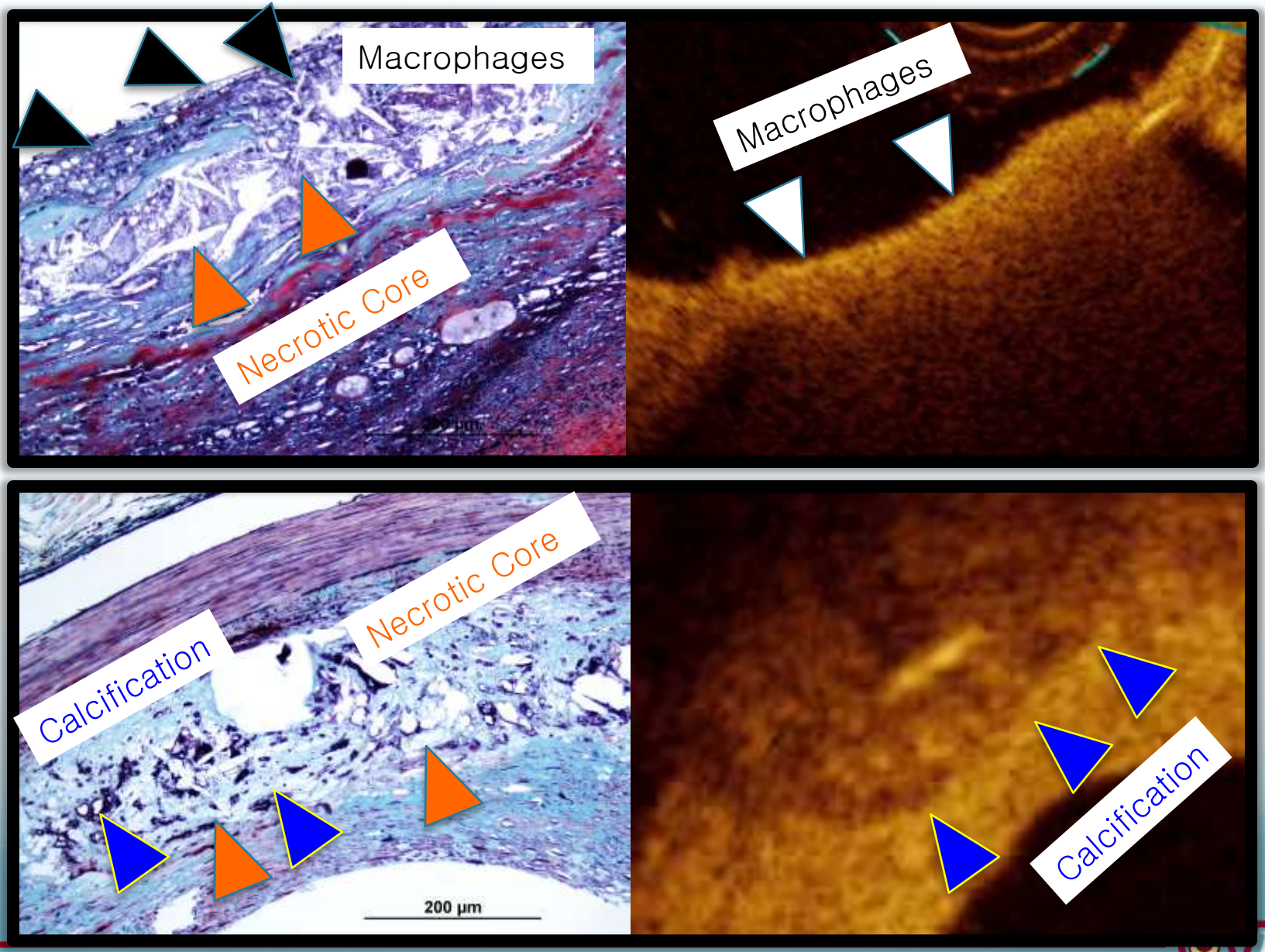




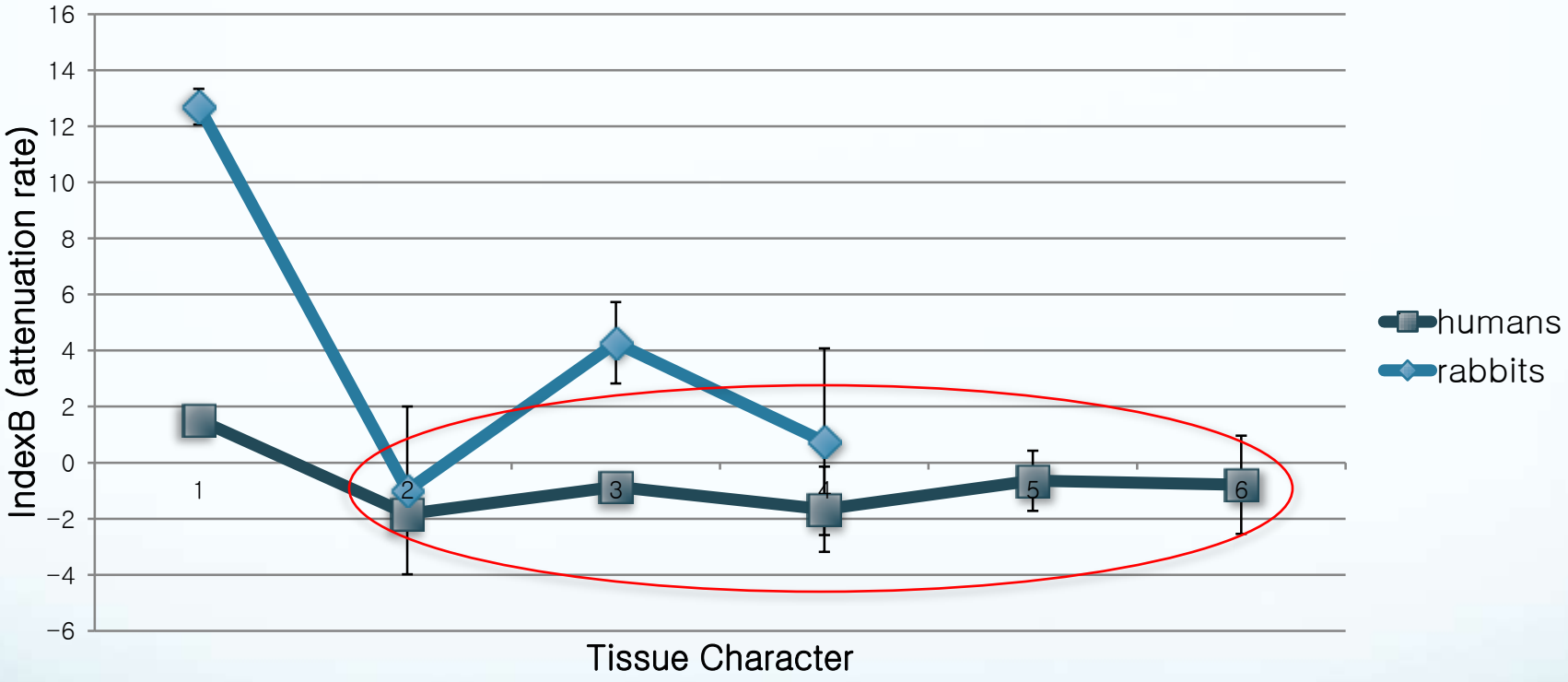




Necrotic Core and Calcification can only be detected in the absence of macrophages in the fibrous cap



Attenuation of OCT Signal in Neoatherosclerosis



1: healthy • 2: foam cells – luminal • 3: foam cells – deep • 4: foam cells – both • 5: Necrotic Core • 6: Necoritc Core with Calcifications

Summary

- Neoatherosclerosis frequently manifests as in-stent restenosis and stent thrombosis
- Secondary to absence of standardization in definition of neoatherosclerosis, it has been substantially over-estimated in the clinical setting
- Attenuation index can be used to detect neoatherosclerosis, where neovascularization close to stent struts represents an important limitation
- OCT is capable of detecting early stages of neoatherosclerosis (foam cell infiltration), while later stages (necrotic core) are difficult to discern.

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