

OCT Assessment of Neoatherosclerosis

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DISCLOSURE

1. Nothing to disclose regarding the slides

Today's Talk

1. Overview of “Neoatherosclerosis”

- Pathology study
- OCT studies

2. Serial OCT changes after DES implantation

3. Neoatherosclerosis

from YONSEI OCT registry

Today's Talk

1. Overview of “Neoatherosclerosis”

- Pathology study
- OCT studies

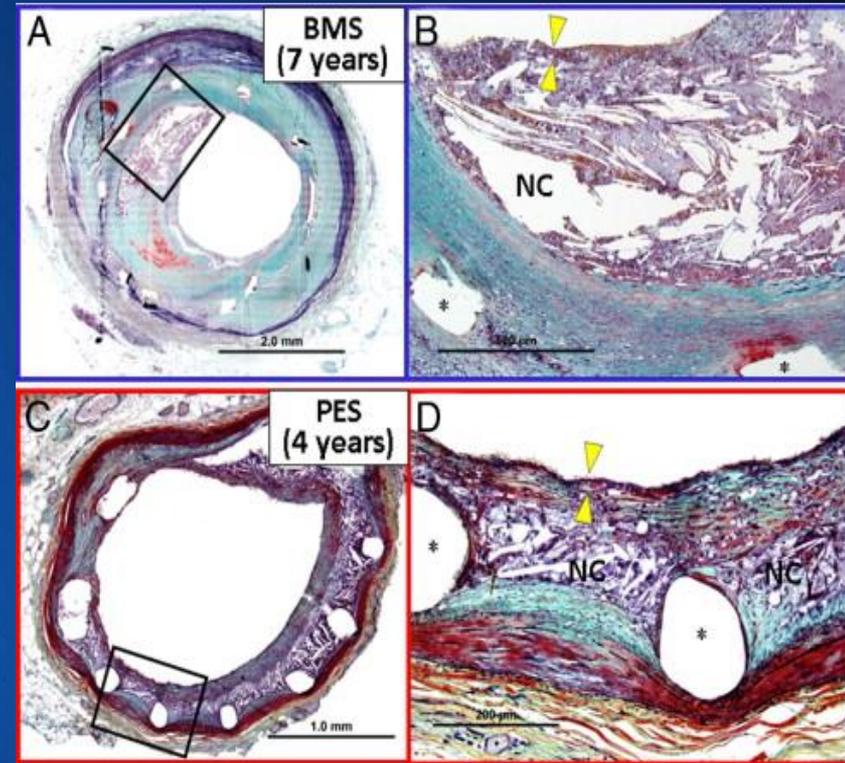
2. Serial OCT changes after DES implantation

3. Neoatherosclerosis

from YONSEI OCT registry

“Neo-atherosclerosis”

- Terminology from pathologic studies;
- Newly formed atherosclerotic changes within the neointimal tissue of stented segments, so called “Neoatherosclerosis”;

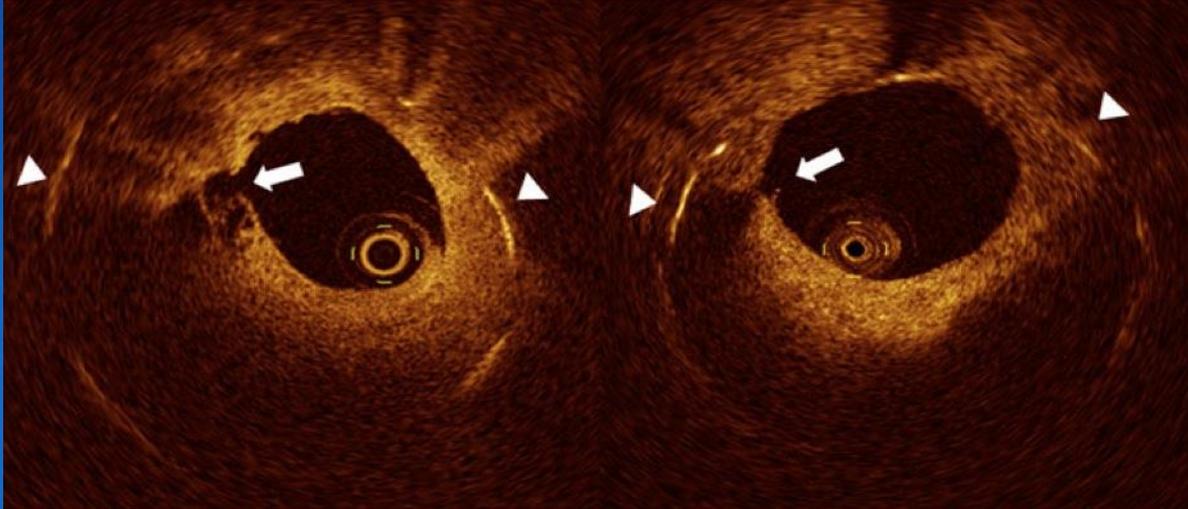


JACC 2012;59:2051-2057.

- ✓ **Necrotic core (NC) containing cholesterol crystals.**
- ✓ **Fibrous cap overlying the NC is infiltrated by numerous foamy macrophages and is markedly thinned.**

Implication of Neoatherosclerosis

- Related with late complication or failure of DES



Recently, a high-resolution imaging tool, OCT is enable to detect “newly developed atherosclerotic changes within stent segments” in living patients.

→ *Accelerating the studies regarding neoatherosclerosis*

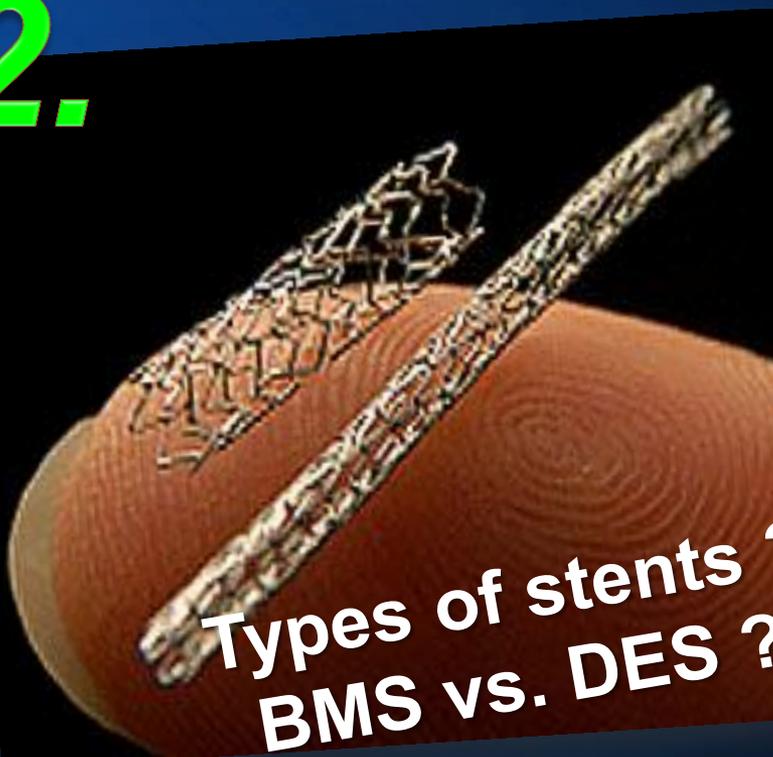
The most important factors in neoatherosclerosis?

1.

An hourglass with white sand falling from the top bulb to the bottom bulb, set against a blue background.

Time-interval
Evolution over time !

2.

A close-up of a metal stent resting on a person's finger, with a reddish-orange background.

Types of stents ?
BMS vs. DES ?

Incidence, duration of neo-atherosclerosis ?

EXPEDITED PUBLICATIONS

The Pathology of Neoatherosclerosis in Human Coronary Implants

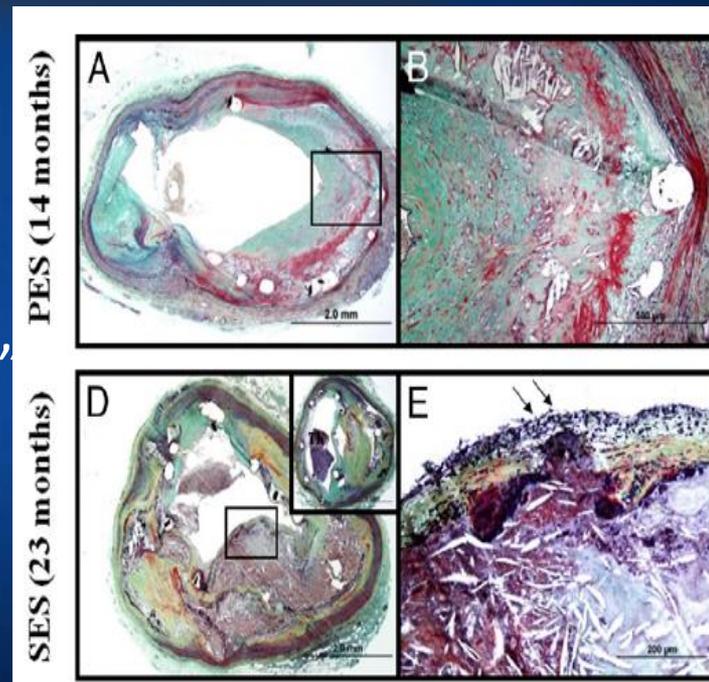
Bare-Metal and Drug-Eluting Stents

Gaku Nakazawa, MD,* Fumiuyuki Otsuka, MD,* Masataka Nakano, MD,* Marc Vorpahl, MD,*
Saami K. Yazdani, PhD,* Elena Ladich, MD,* Frank D. Kolodgie, PhD,* Alope V. Finn, MD,†
Renu Virmani, MD*

● CVPPath stent registry (n=299 autopsies),
with a total of 406 lesions (197 BMS, 209
DES (103 SES & 106 PES])—with implant
duration > 30 days

● Pathologic criteria of “neoatherosclerosis”

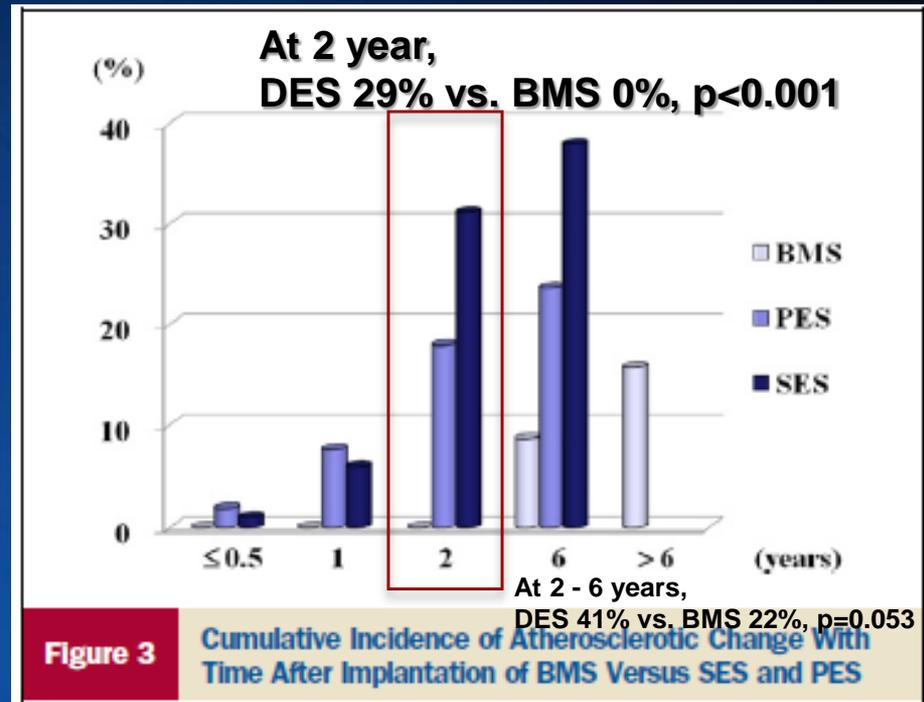
- *Peristrut foamy macrophage cluster*
- *Fibroatheroma*
- *Thin-cap fibroatheroma*
- *Rupture with thrombosis*



- **Incidence of neo-atherosclerosis;**
→ significantly greater in DES lesions (31%) than BMS lesions (16%; $p < 0.001$)

- **Median stent duration with neo-atherosclerosis**

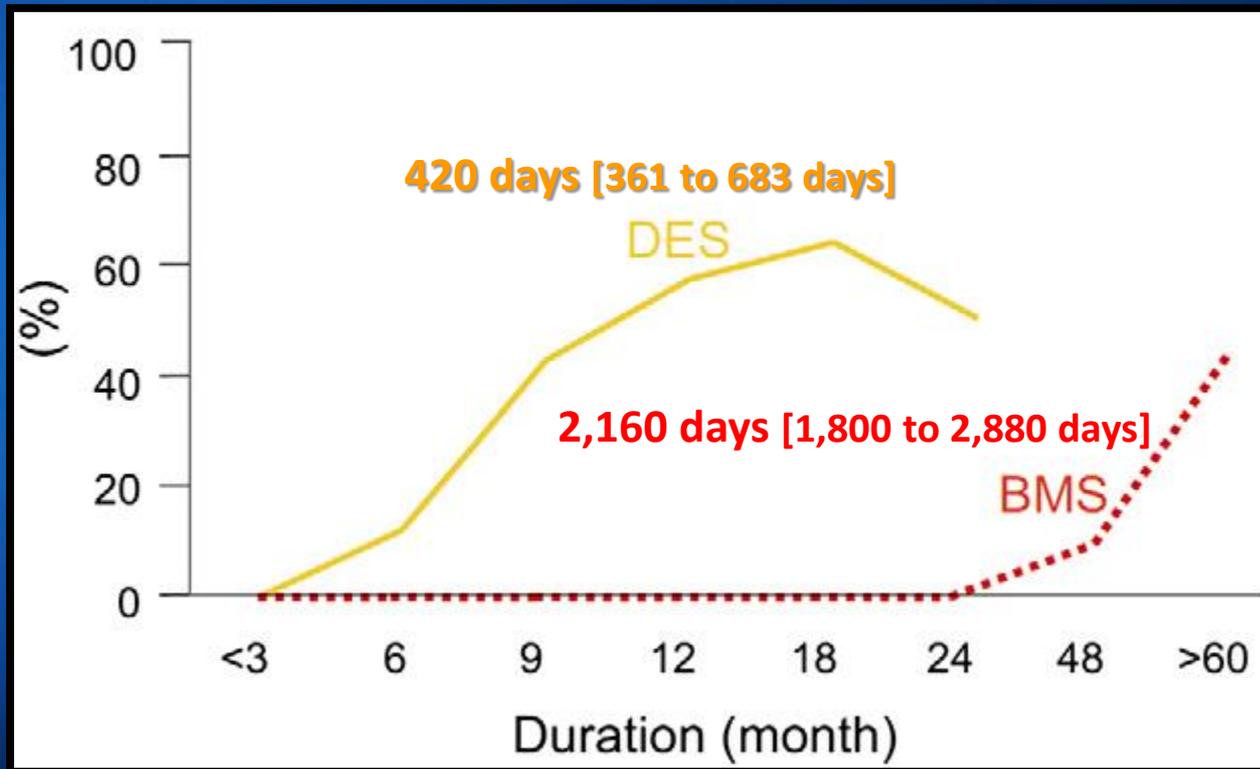
- shorter in DES than BMS (DES, 420 days vs. BMS, 2,160 days; $p < 0.001$).



- **Independent determinants of neo-atherosclerosis** (by multiple logistic regression)
→ included **longer implant durations** ($p < 0.001$) and **types of stents** [SES usage ($p < 0.001$), PES usage ($p = 0.001$)]

Neoatherosclerosis: DES and BMS

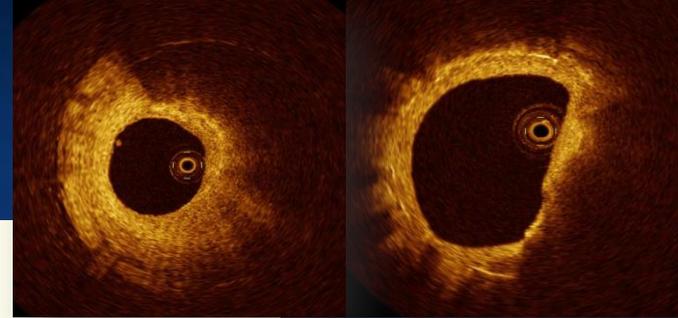
Cumulative incidence of Atherosclerotic Change with time after implantation of BMS vs. DES (SES and PES)



Nakazawa et al, JACC, 2011;57:1314-1322

In-vivo OCT studies after stent implantation ?

✓ BMS, Lipid-laden intima

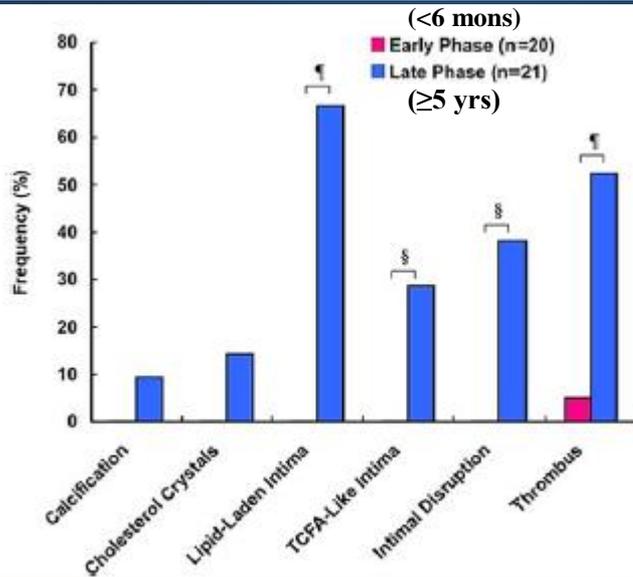


Appearance of Lipid-Laden Intima and Neovascularization After Implantation of Bare-Metal Stents

Extended Late-Phase Observation by Intracoronary Optical Coherence Tomography

(J Am Coll Cardiol 2010;55:26-32)

Masamichi Takano, MD,* Masanori Yamamoto, MD,† Shigenobu Inami, MD,*
Daisuke Murakami, MD,† Takayoshi Ohba, MD,† Yoshihiko Seino, MD,† Kyoichi Mizuno, MD*



- Lipid-laden intima was not observed in the early phase.
- In extended phase, lipid-laden intima, intimal disruption, and thrombus were frequently found.

→ Neointima transforms into lipid-laden atherosclerotic tissue in extended phase in BMS.

Figure 3 Frequencies of Atherosclerotic Findings

Difference of Tissue Characteristics Between Early and Very Late Restenosis Lesions After Bare-Metal Stent Implantation

An Optical Coherence Tomography Study

Maoto Habara, MD; Mitsuyasu Terashima, MD; Kenya Nasu, MD; Hideaki Kaneda, MD; Katsumi Inoue, MD; Tsuyoshi Ito, MD; Shigeru Kamikawa, MD; Tairo Kurita, MD; Nobuyoshi Tanaka, MD; Masashi Kimura, MD; Yoshihisa Kinoshita, MD; Etsuo Tsuchikane, MD; Hitoshi Matsuo, MD; Katsumi Ueno, MD; Osamu Katoh, MD; Takahiko Suzuki, MD

Habara M, et al. Circulation Cardiovasc interv 2011;4:232-238.

- Observational study of BMS restenosis
- **Very Late-ISR** (5 years, without restenosis within 1 year; n=43) vs. **Early-ISR** (within 1 year; n=39)
- Qualitative restenotic tissue analysis
 - *homogeneous vs. heterogeneous*

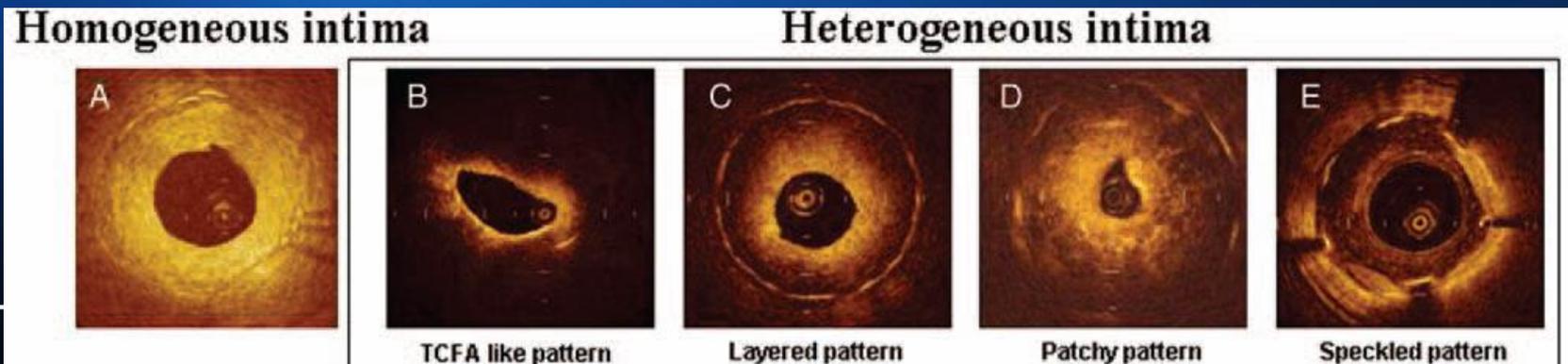
OCT study : BMS restenosis

	VL-ISR (n=43)	E-ISR (n=39)	P
Analysis at minimum lumen area site			
<u>Quantitative analysis</u>			
Minimum lumen area, mm ²	1.9±1.1	2.2±0.9	0.17
Stent area, mm ²	9.1±2.2	10.1±2.9	0.11
Mean neointimal hyperplasia area, %	79.0±10.0	77.6±7.1	0.46
<u>Qualitative analysis</u>			
Homogeneous intima	4 (9.3)	32 (82.1)	<0.0001
Heterogeneous intima	39 (90.7)	7 (17.9)	<0.0001
Microvessels, inraintima	7 (16.3)	0 (0)	0.01
Disrupted intima with visible cavity	6 (13.9)	0 (0)	0.03
Intraluminal material	7 (16.2)	0 (0)	0.01
With shadowing	6 (14.0)	0 (0)	0.03
Without shadowing	1 (2.3)	0 (0)	>0.99

Morphological differences of tissue characteristics between early, late, and very late restenosis lesions after first generation drug-eluting stent implantation: an optical coherence tomography study

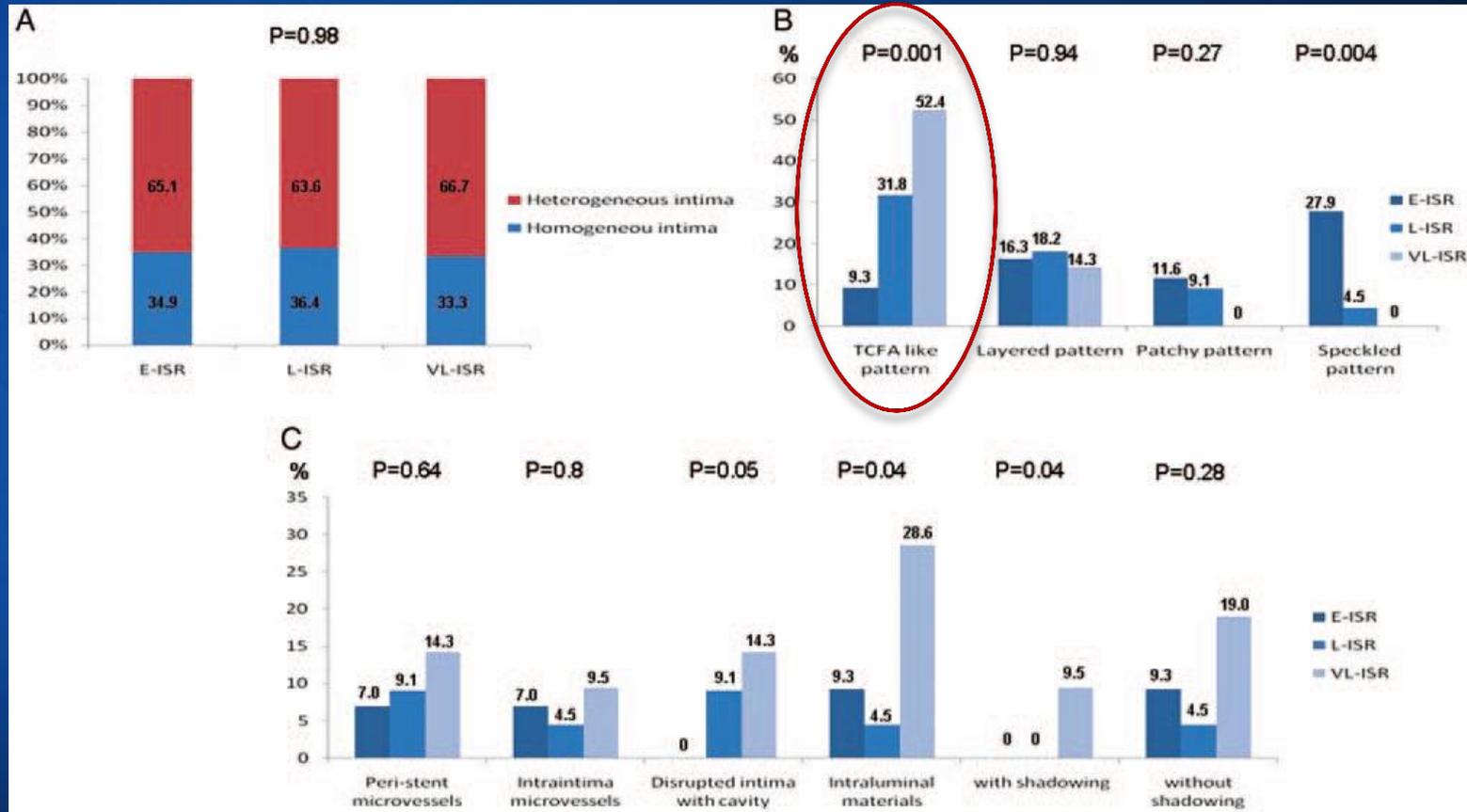
Maoto Habara¹, Mitsuyasu Terashima^{1*}, Kenya Nasu¹, Hideaki Kaneda², Daisuke Yokota¹, Tsuyoshi Ito¹, Tairo Kurita¹, Tomohiko Teramoto¹, Masashi Kimura¹, Yoshihisa Kinoshita¹, Etsuo Tsuchikane¹, Yasushi Asakura¹, and Takahiko Suzuki¹

- **Early-ISR** (<1 year, n = 43) vs. **Late-ISR** (1–3 years, n = 22) vs. **Very late-ISR** (>3 years, n = 21)
- Qualitative tissue analysis; homogeneous vs. heterogeneous



OCT study : DES restenosis

At the minimum lumen area site



Neoatherosclerosis might contribute to late catch-up phenomenon (L-ISR and VL-ISR) after DES implantation.

Today's Talk

1. Overview of “Neoatherosclerosis”

- Pathology study
- OCT studies

2. Serial OCT changes after DES implantation

3. Neoatherosclerosis

from YONSEI OCT registry

Quantitative and Qualitative Changes in DES-Related Neointimal Tissue Based on Serial OCT

Jung-Sun Kim, MD,* Myeong-Ki Hong, MD,*† Dong-Ho Shin, MD, MPH,*
Byeong-Keuk Kim, MD,* Young-Guk Ko, MD,* Donghoon Choi, MD,*
Yangsoo Jang, MD*†

- Little quantitative or qualitative in vivo data investigating serial changes in neointimal tissue characteristics of DES-treated lesions using an OCT.
- Therefore, we sought to evaluate serial changes in quantitative and qualitative characteristics of **neointimal tissue in DES-treated lesions between 9-month and 2-year follow-up.**

Methods

- **Study Population;**

Between Nov 2007 and Aug 2009 a total of 250 patients underwent follow-up OCT at 9 months (± 3 mon) after DES implantation.

→ Among these, a 2nd FU OCT at 2 years (± 3 mon) was performed in 72 patients with 76 DESs.

- **A total of 76 DESs were evaluated serially;**

- ✓ 23 sirolimus-eluting stents (SES, Cypher)
- ✓ 20 paclitaxel-eluting stents (PES, Taxus)
- ✓ 25 zotarolimus -eluting stents (ZES, Endeavor sprint)
- ✓ 8 everolimus-eluting stents (EES, Xience).

OCT Image Analysis

- OCT examination using a M2 OCT system
- **A total of 1,947 matched cross-sectional images** at both 9 months and 2 years analyzed at 1-mm intervals.

- **Quantitative analysis**

1. Thickness of neointimal hyperplasia
2. Stent strut coverage
3. Malapposition

- **Qualitative analysis**

1. Neointimal pattern (Homogeneous, heterogeneous, lipid laden)
2. Thin cap fibroatheroma (TCFA) like neointima
3. Thrombus
4. Neovascularization

OCT Data; Quantitative analysis

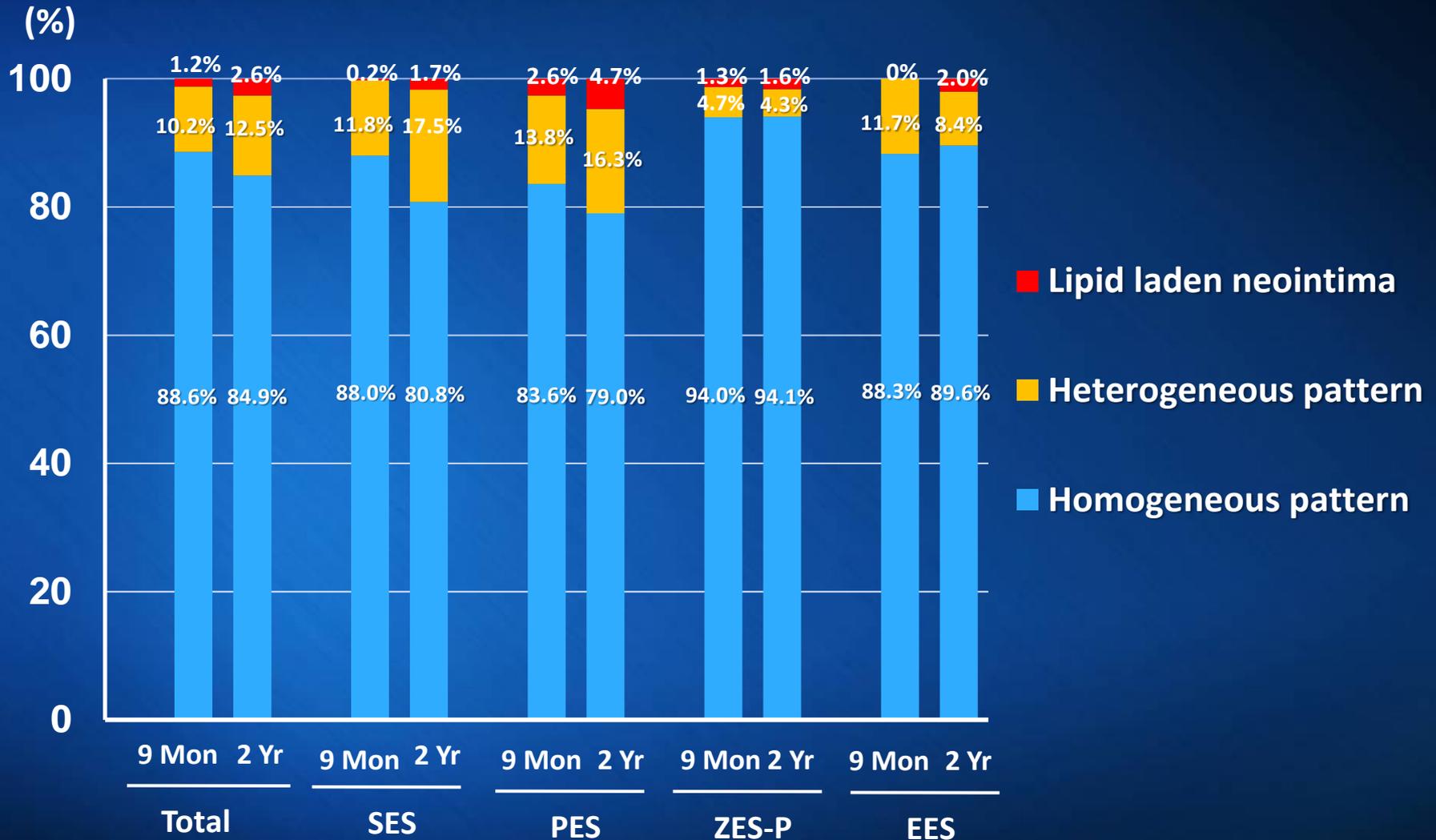
Total (n = 76)	9 months	2 years	P
<u>Cross-section level analysis</u>			
Mean lumen CSA (mm ²)	5.7 ± 1.4	5.4 ± 1.6	0.01
Mean NIH area (mm ²)	1.3 ± 0.9	1.7 ± 1.1	0.001
Percent NIH CSA (%)	18.7 ± 11.3	23.4 ± 14.5	<0.001
Cross-sections with uncovered strut ratio > 0.3	153 (7.9%)	91 (4.7%)	<0.001
Completely covered lesions (%)	44.7%	59.2%	0.07
<u>Strut level analysis</u>			
Mean NIH thickness (μm)	164 ± 95	214 ± 132	<0.001
Percentage of uncovered struts	787 (4.1%)	468 (2.4%)	<0.001
Percentage of malapposed strut	127 (0.7%)	183 (0.9%)	0.24

OCT data; Qualitative analysis

Total (n = 76)	9 months	2 years	P
Intracoronary thrombus	8 (10.5%)	7 (9.2%)	0.79
Lipid-laden neointima	11 (14.5%)	21 (27.6%)	0.047
TCFA-like neointima	3 (3.9%)	10 (13.2%)	0.04
Heterogeneous pattern	49 (64.5%)	47 (61.8%)	0.73
Neovascularization	34 (44.7%)	56 (73.7%)	<0.001
Extrastent lumen	15 (19.7%)	21 (27.6%)	0.25
Neointimal disruption	15 (19.7%)	26 (34.2%)	0.04

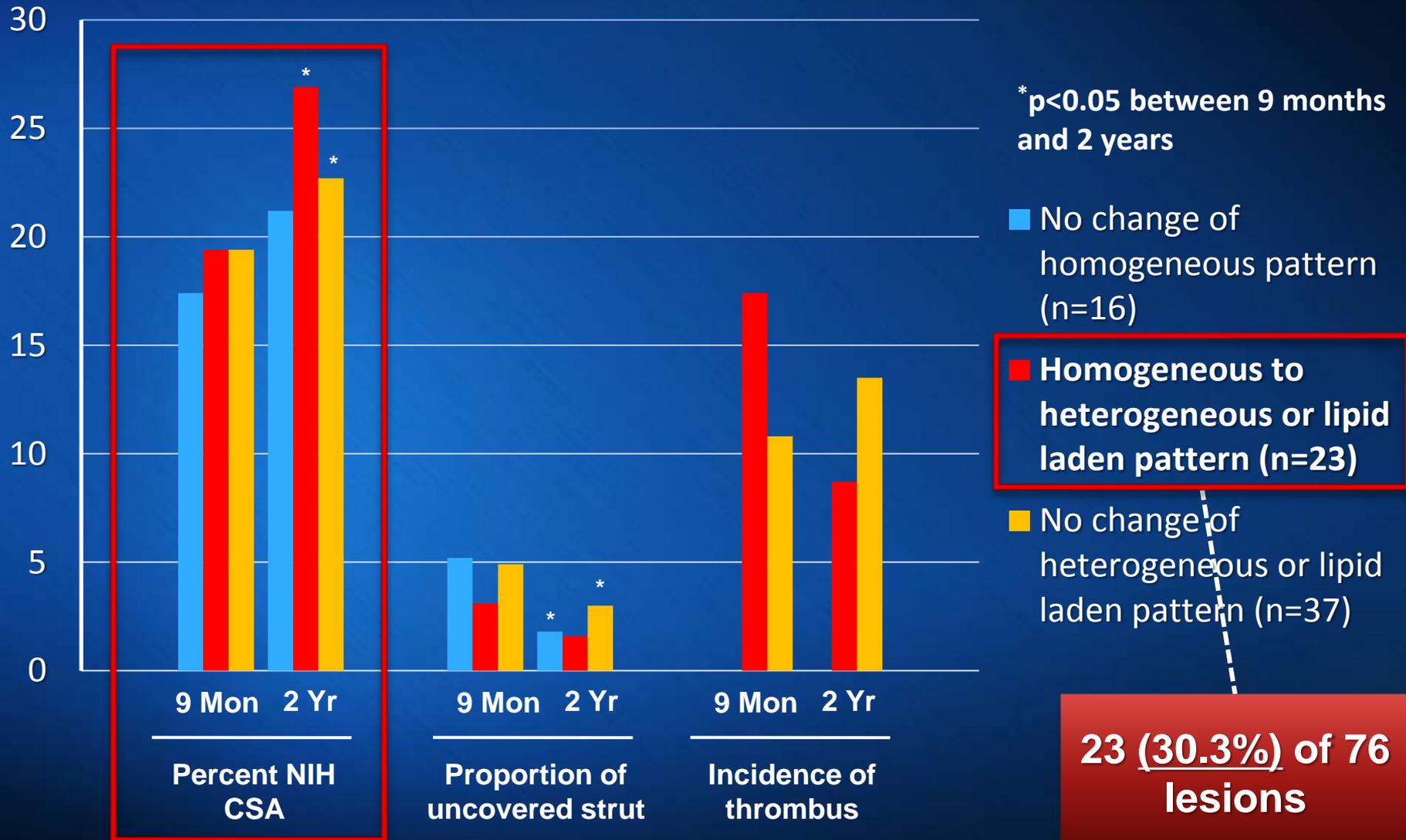
→ Supporting the presence of "neo-atherosclerosis"

Serial OCT : DES

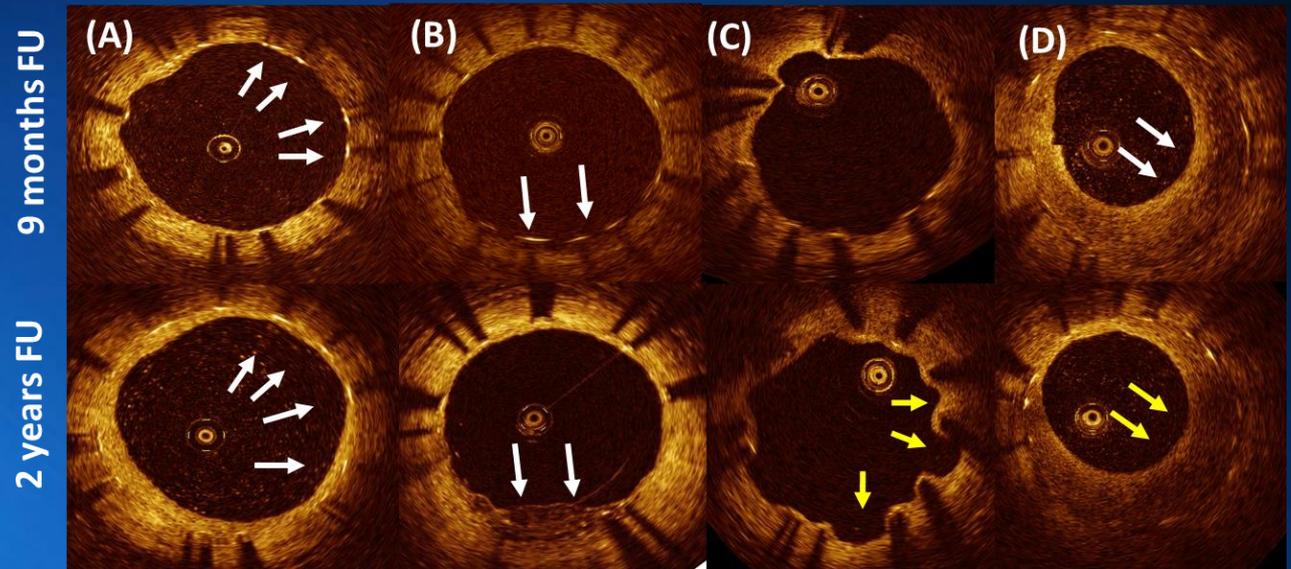


Irrespective of DES types, lipid-laden neointima was more frequently detected at 2-year f/u compared with 9 months (27.6% vs. 14.5%, p=0.009).

Matched cross-sectional evaluation



Conclusion of SERIAL OCT study



This Serial OCT study suggested that ...

1. neointimal coverage improved from 9 months to 2 years without significant changes in the incidence of malapposed struts and intracoronary thrombus.
2. **in-stent neoatherosclerosis** including transformation to lipid-laden neointima might ***progress during extended follow-up periods*** after DES implantation.

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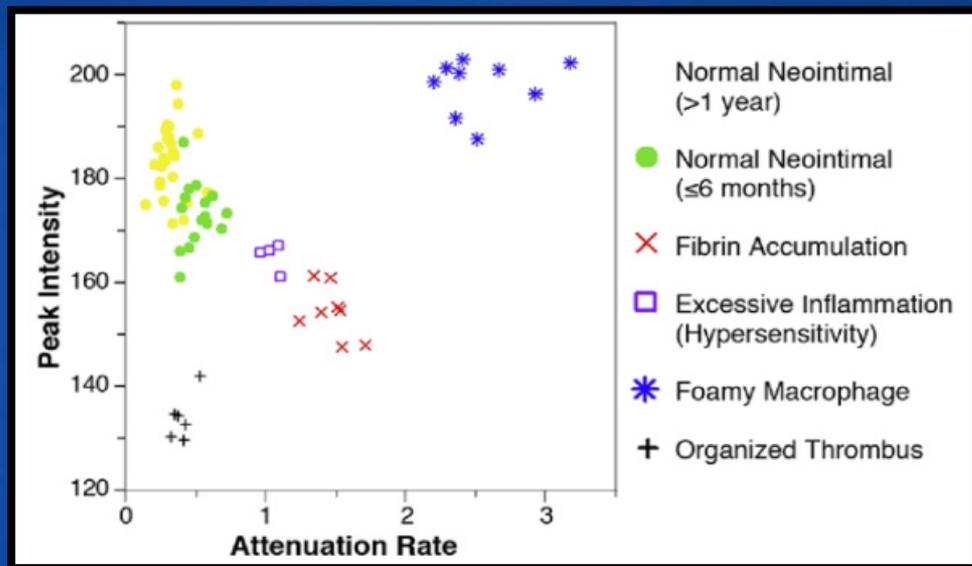
2. Serial OCT changes after DES implantation

3. Neoatherosclerosis

from YONSEI OCT registry

2. Limitation of Qualitative OCT assessment - I

Histology vs. OCT; accuracy of morphological measurements ?



- Foamy macrophage and organized thrombi constituted distinct groups, independent of other histological features.

- However, the some dark appearance of **fibrin accumulation**, **organized thrombus**, **excessive inflammation (hypersensitivity)**, and **mixture with fibrous tissue** create a heterogeneous or layered appearance
→ might impede direct discrimination of these tissues when they exist within neointima.

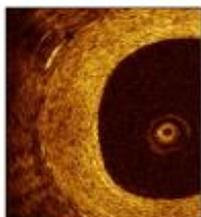
3. Limitation of Qualitative OCT assessment - II

Optical coherence tomography patterns of stent restenosis

(Am Heart J 2009;158:284-93.)

Nieves Gonzalo, MD, Patrick W. Serruys, MD, PhD, Takayuki Okamura, MD, PhD, Heleen M. van Beusekom, MD, PhD, Hector M. Garcia-Garcia, MD, MSc, Gijs van Soest, PhD, Wim van der Giessen, MD, PhD, and Evelyn Regar, MD, PhD
Rotterdam, The Netherlands

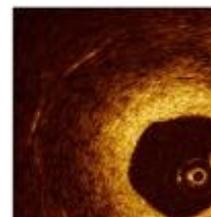
Restenotic tissue structure



Homogeneous: restenotic tissue has uniform optical properties and does not show focal variations in backscattering pattern.



Heterogeneous: restenotic tissue has focally changing optical properties and shows various backscattering patterns

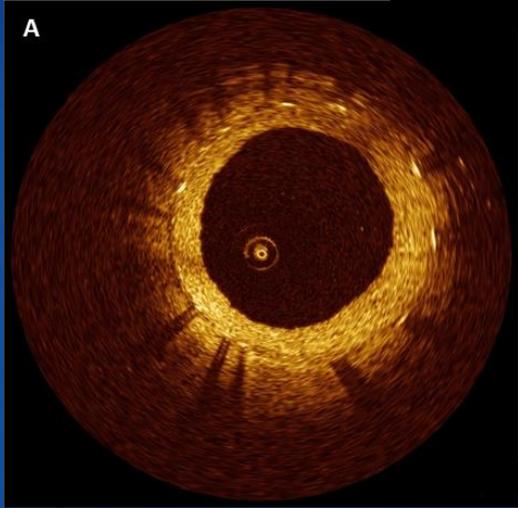


Layered: restenotic tissue consists of concentric layers with different optical properties: an adluminal high scattering layer and an abluminal low scattering layer

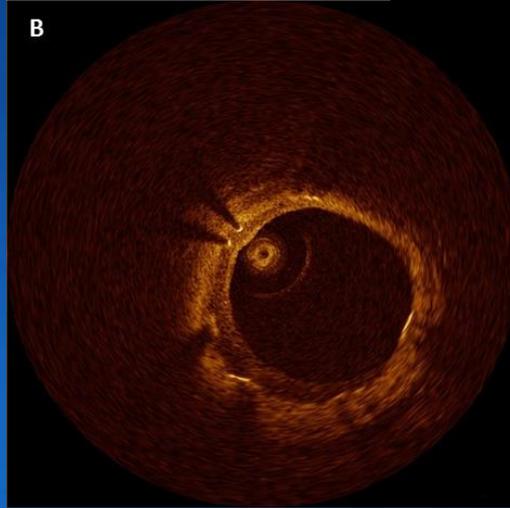
- ✓ This OCT classification was not enough for the characterization of neointima.
- ✓ Especially, the classification and characterization of 'neoatherosclerosis' was not considered.

Types of Neointima

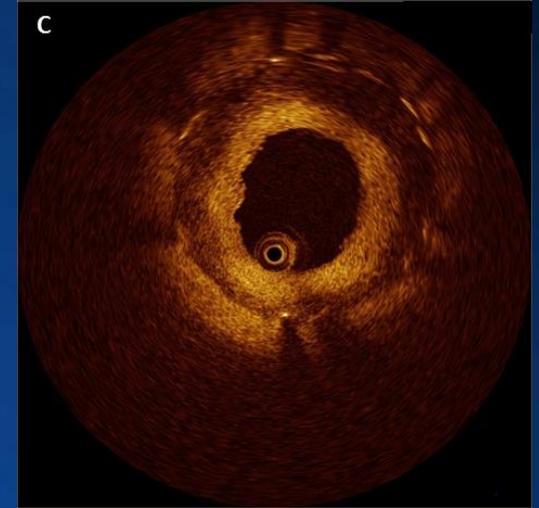
Classical 3 classification;



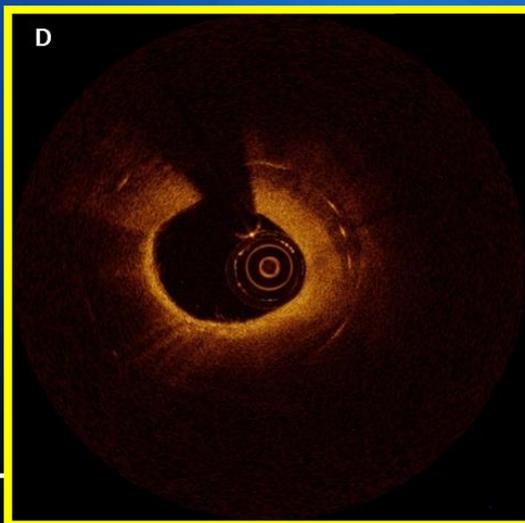
Homo



Hetero



Layered



Additional classification;
Neoatheroma

From ... **YONSEI OCT REGISTRY**

Backgrounds

- ✓ The impact of **different time courses** and **the degree of neointimal growth** on neointimal morphology have not been sufficiently investigated.

Objectives

- ✓ We sought to investigate morphological features of neointimal tissue in a large number of study patients with various burden of neointimal tissue.

METHODS - I

- From YONSEI OCT registry 418 patients of **507 DESs** (2007 - 2012)
- Inclusion Criteria :
 - >100 μ m of mean neointimal thickness on follow-up OCT**
- Exclusion Criteria :
 1. Complex lesions as following: significant left main coronary artery diseases; highly tortuous vessels; Ostial or very proximal lesions (< 15 mm from ostium)
 2. Angioplasty before acquiring OCT image
 3. Poor left ventricular function (< 30% of ejection fraction)
 4. Renal insufficiency with baseline serum creatinine > 1.5 mg/dL

METHODS - II

- **OCT procedure**

Model M2 imaging system or C7-XR™ imaging system

- **Analyzed lesions**

5 consecutive cross-sections at 1-mm intervals with maximal percentage of neointimal CSA stenosis

- **Qualitative analysis**

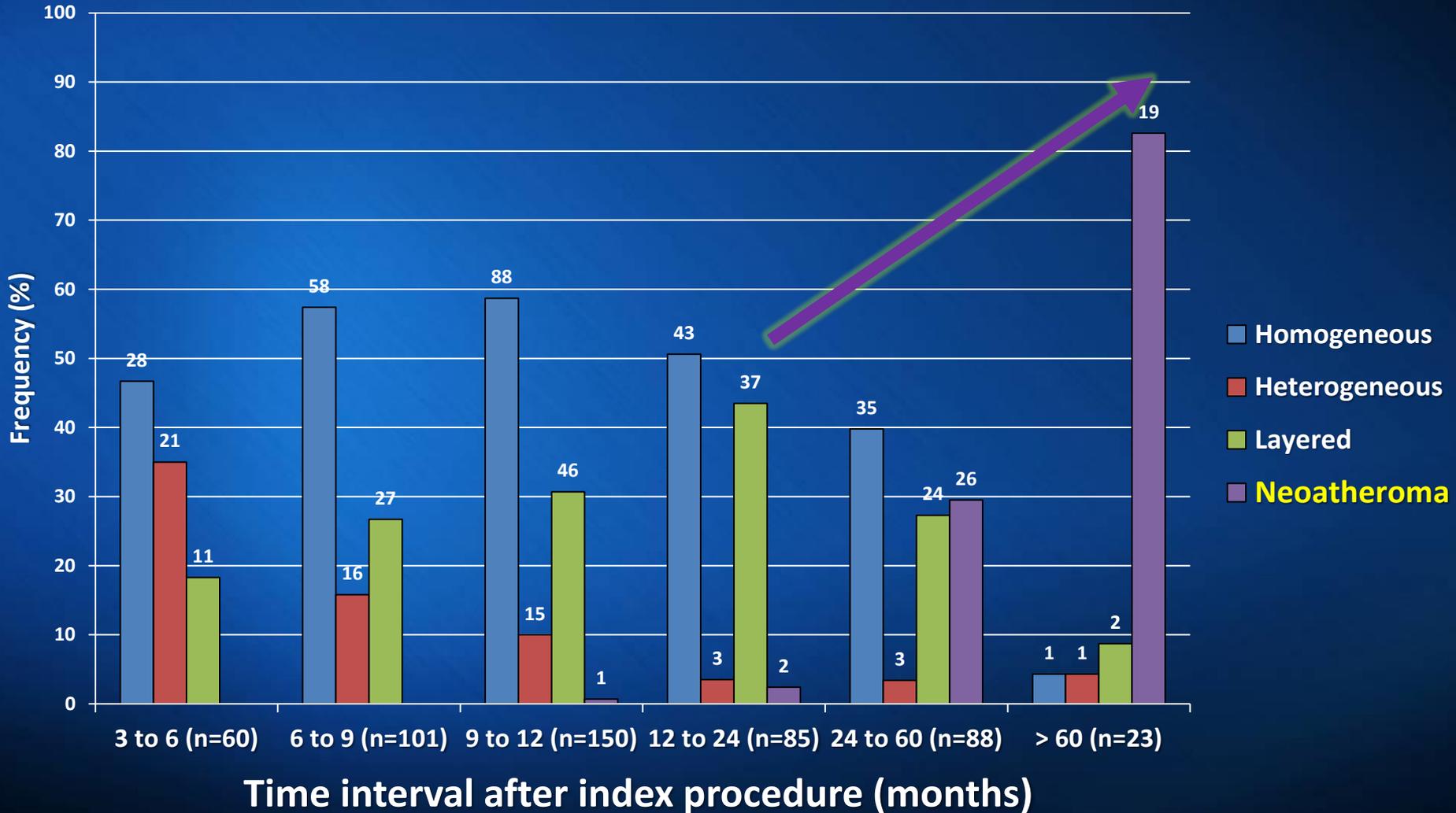
1. Homogeneous : an uniform signal rich band
2. Heterogeneous : focally changing optical properties
3. Layered : abluminal high scattering layer and luminal low scattering layer
4. **Neointimal hyperplasia:** lipid-laden neointima or calcification

Baseline Characteristics

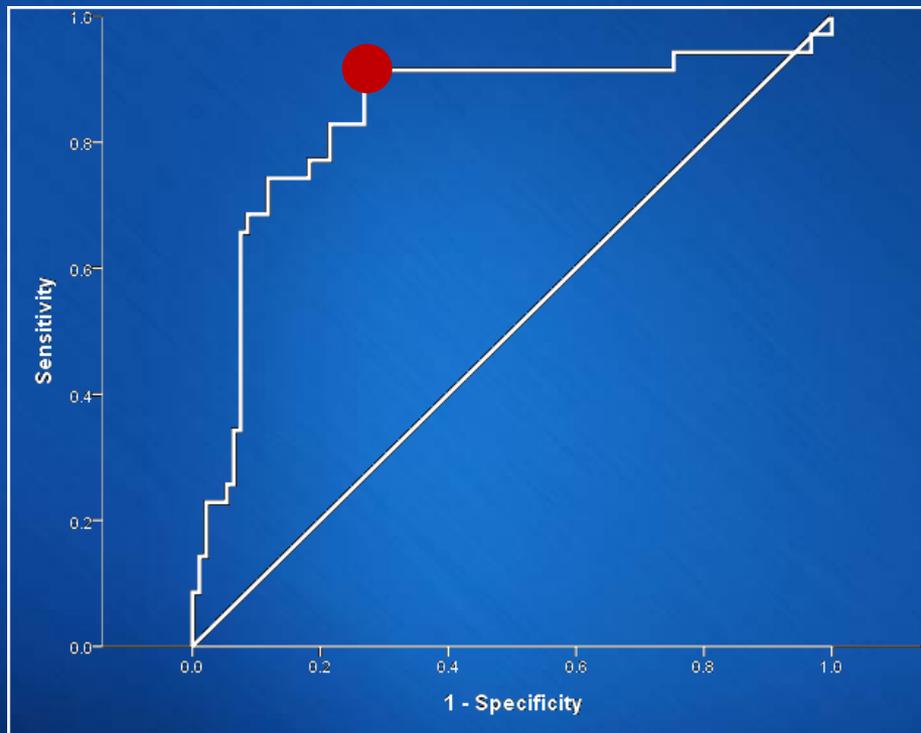
Total (<u>418 patients of 507 DESs</u>)	N (%)
Age	62 ± 9
DM	139 (33%)
Initial clinical presentation, ACS	107 (26%)
Types of DESs	
Sirolimus-eluting stent	117 (23%)
Paclitaxel-eluting stent	102 (20%)
Zotarolimus-eluting stent	204 (40%)
Everolimus-eluting stent	67 (13%)
Biolimus-eluting stent	17 (3%)
Stent age	
< 9 months	161 (32%)
9 – 24 months	235 (46%)
> 24 months	111 (22%)

Distribution of neointima according to stent age

Grouped by stent age



Best cut-off time predicting the presence of neoatherosclerosis



Optimal cut-off time: **30 months**

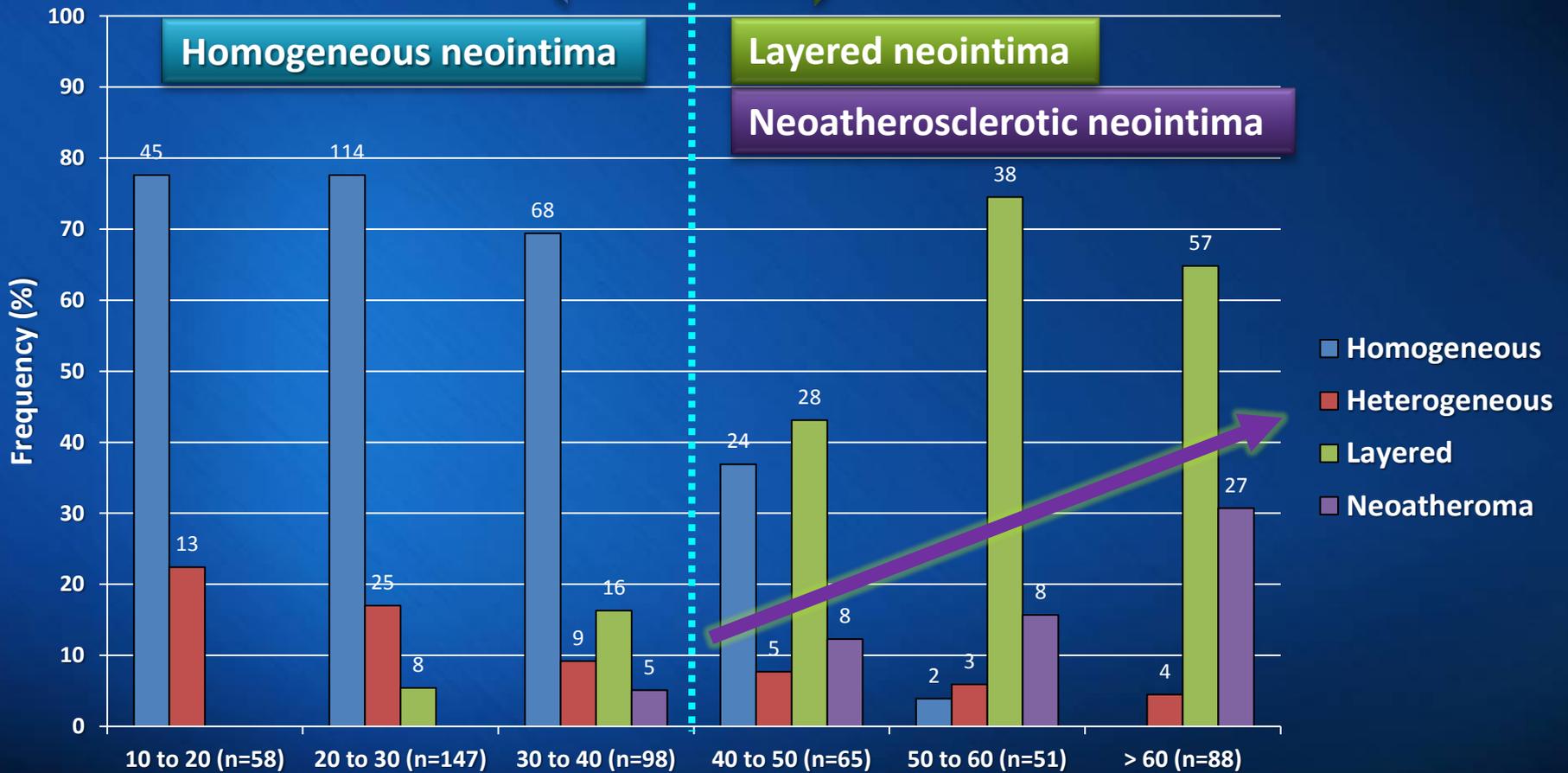
Area Under Curve: 0.839, $p < 0.001$
95% CI: 0.764 - 0.898

Sensitivity: 91.4% / Specificity: 72.0%

Distribution of neointima

Grouped by CSA stenosis

40-50%



Percentage of cross-sectional area stenosis of neointima (%)

CONCLUSION

- This OCT study showed that
 - ✓ Morphological pattern of neointimal tissue after DES implantation depended on the burden of neointimal hyperplasia and stent age.
 - Homogeneous neointima was the most common type in lesions $<50\%$ of neointimal CSA stenosis.
 - In lesions $\geq 50\%$ of neointimal CSA stenosis, layered and neoatherosclerotic neointima were frequently detected.
 - ✓ Best cut-off time for the prediction of the presence of “neoatherosclerosis” was 30 months.
 - ✓ Neoatherosclerotic neointima contributed to neointimal growth in DES ≥ 30 months after implantation.

Neo-atherosclerosis in BMS Restenosis at 10 Years

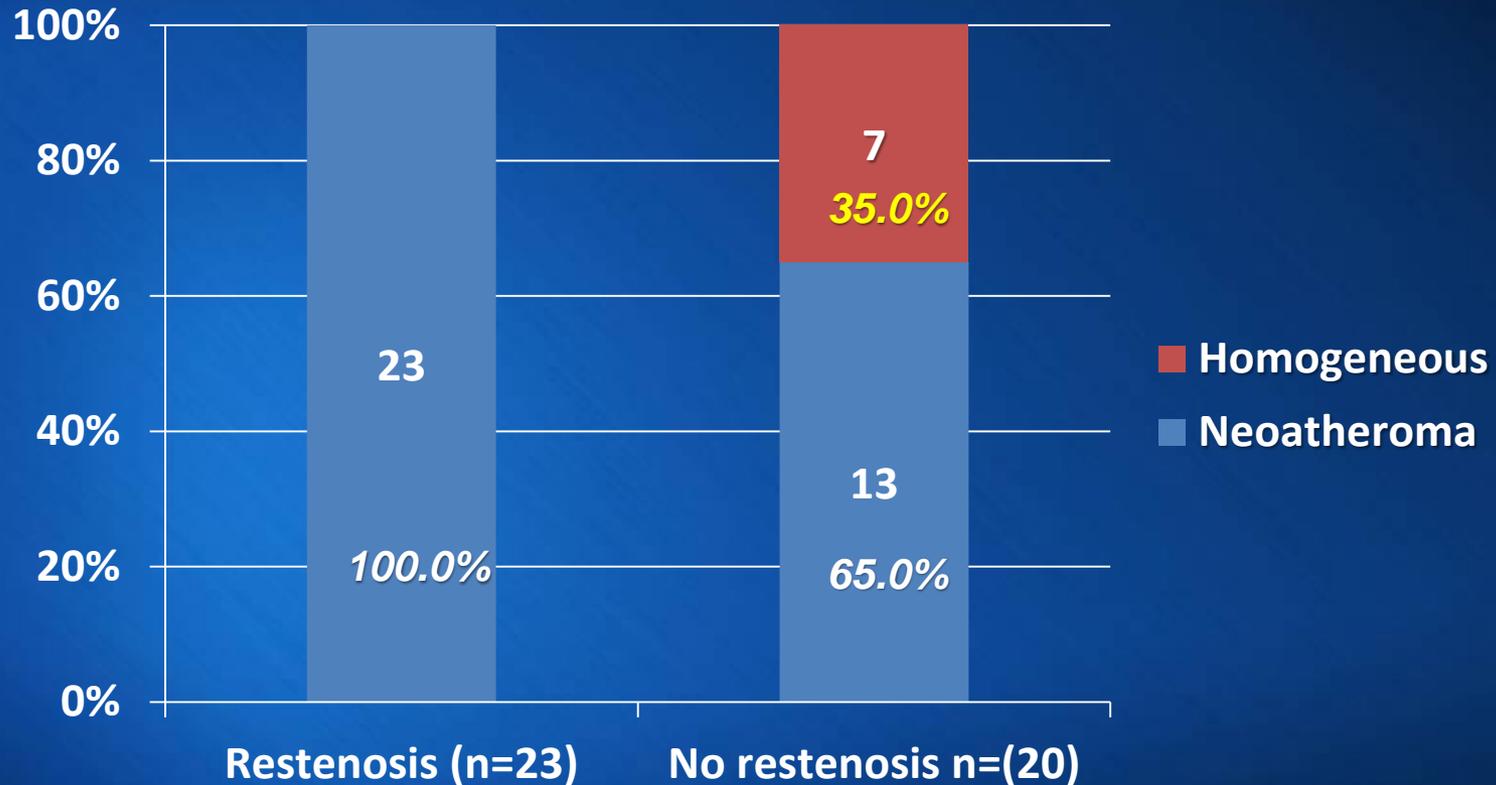
Brief report

OCT data	N = 22
Strut coverage	
Completely embedded at all frames	20 (90%)
Malapposition seen at ≥ 1 frame	1 (5%)
OCT-measured MLA, mm ²	1.6 (1.0–2.4)
Stent area at the MLA site, mm ²	9.0 (7.9–11.2)
Lipidic neointima	22 (100%)
Calcium-containing	7 (32%)
Thickness of fibrous cap, μm	50 (50–60)
OCT-defined intimal rupture	13 (59%)
TCFA-containing neointima	15 (68%)
OCT-defined thrombi	17 (77%)
OCT-defined red thrombi	12 (55%)

Kang SJ, et al. JACC Cardiovasc Imaging 2012

YONSEI OCT Registry : BMS

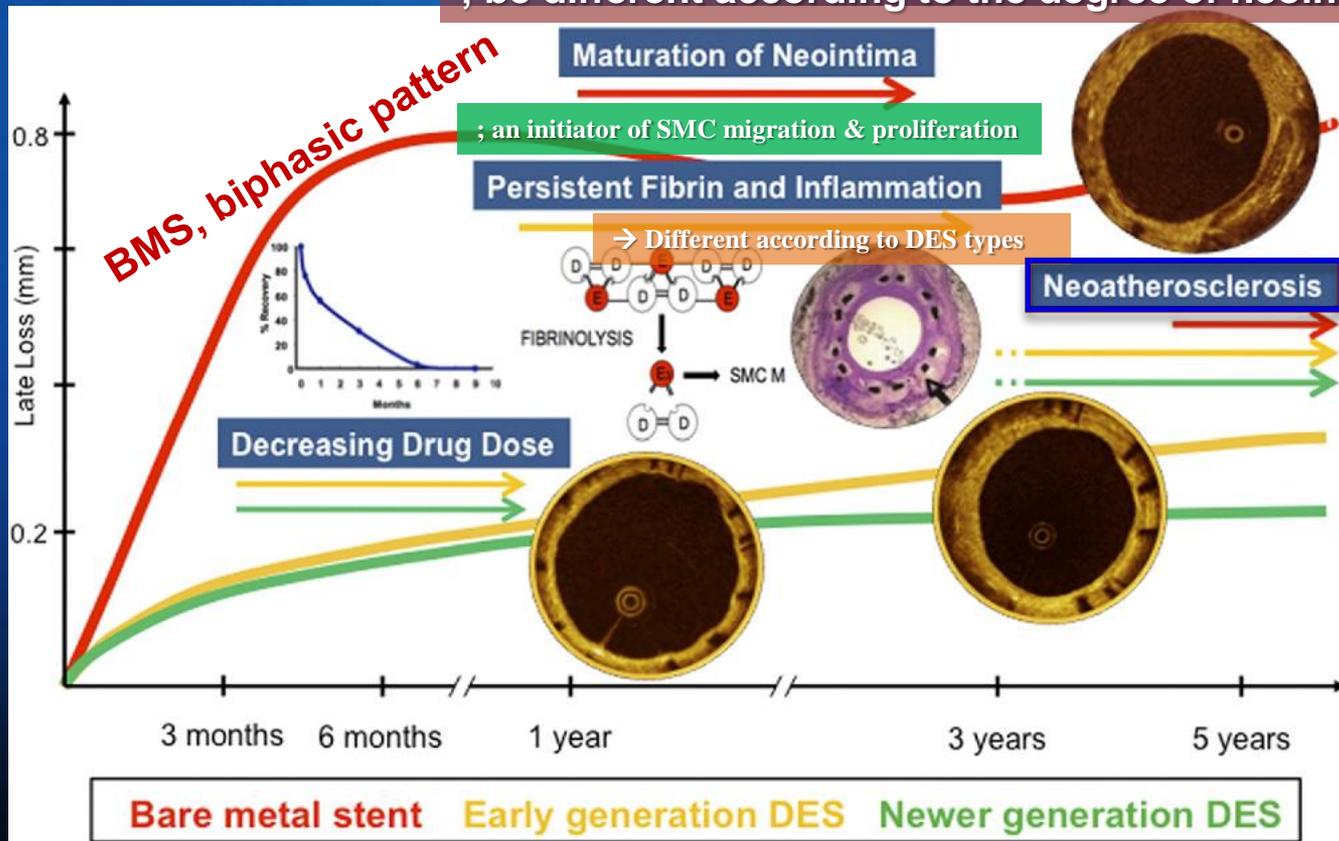
Mean time interval after stent implantation : 11.3 years



- ✓ Neointimal growth of BMS might be affected by the burden of neointimal growth.
- ✓ Despite longer followed duration, neointimal growth might not be occurred in BMS without restenosis

Mechanisms of Late Intimal Growth;
Different Time Course of the Neointimal Growth for BMS and for DESs throughout 5 Years

; occur at extended late period
 ; be different according to the degree of neointimal burdens



Characterized by in-stent TCFA-containing neointima & calcifications.
 → Reflect a contributing factor that arises later in the time course.

Early- vs. New-DES ?
 → Extended late responds might be different according to the types of DES.
 ; late catch-up, incidence and timing of neoatherosclerosis

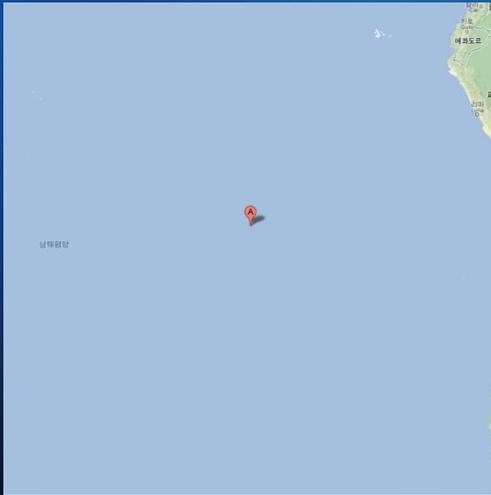
CONCLUSION

- Neoatherosclerosis ...

- is a frequent finding in DES and BMS.
- occurs earlier in DES than in BMS
- Contributed to luminal narrowing during extended follow-up periods after stent implantation
- Responses might be different according to the types of DESs.

Moai Statues

; located on Easter Island, Chile; 7대 불가사의의 중 하나.

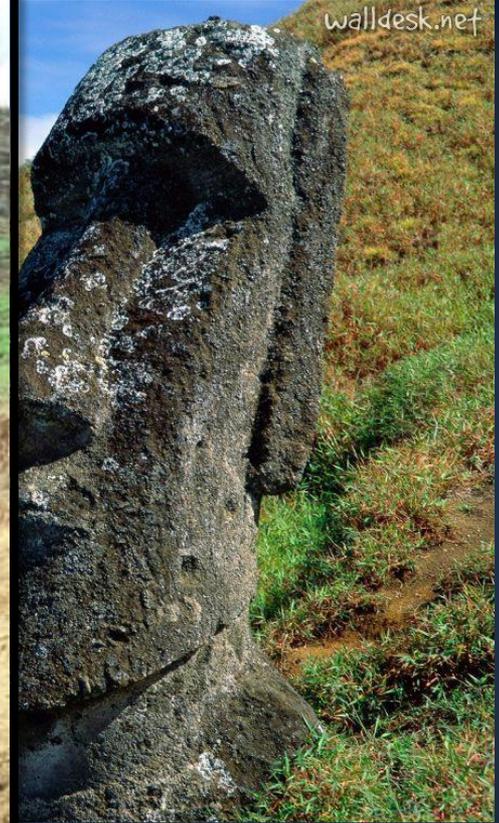


모아이 석상의 실체?
... 알고 보니 통다리 !!!

빙산의 일각?
모아이의 일각이라
불러...

Current Imaging tools

Future Imaging tools...
can see "real one" without digging!!



The image shows a large, modern multi-story hospital building with a glass facade and a traditional Korean pavilion in the foreground. The text "Thank you for your attention" is overlaid in large yellow font. The building has "YONSEI UNIVERSITY" and "SEVERANCE CARDIOVASCULAR HOSPITAL" written on it. The pavilion has a traditional tiled roof and wooden structure. There are trees and a lawn in the foreground.

Thank you for
your attention

Back-up slides

Potential solutions for the prevention of stent thrombosis

Early (<30days)

Late (1 – 12 months)

Very late (> 12 months)

Procedural

Delayed healing

Abnormal vascular responses

Underexpansion

Uncovered struts

Hypersensitivity

Edge dissection

Fibrin deposition

Extensive fibrin deposition

Residual plaque rupture

Late malapposition

Neo-atherosclerosis

Solution;

- Prevention of sub-optimal results of PCI
- Detailed evaluation of procedures

- Use of DAPT
- Determined by new imaging modalities

• *Currently, DAPT might only solution for prevention*

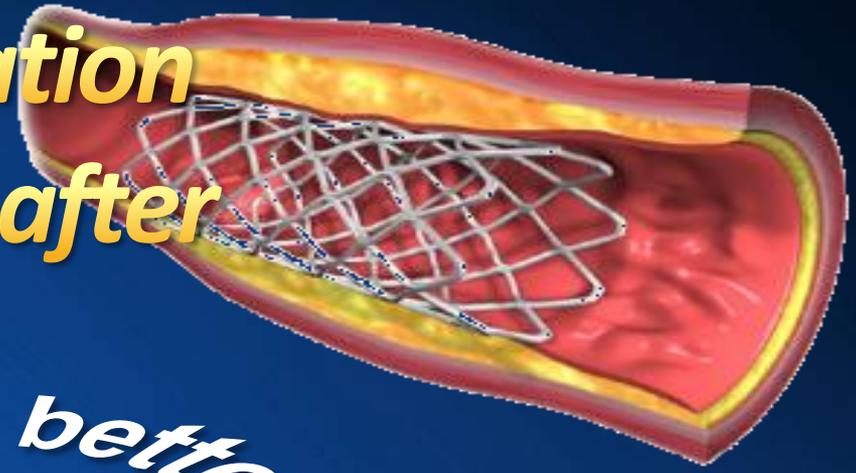
We should await the results of

- ✓ New antiplatelets
- ✓ Antiplatelet resistance

1. Conclusion

- Detailed OCT assessment, especially qualitative OCT analysis provides various new information regarding restenosis.
- The clinical implication regarding OCT parameters should be clearly established in the future.
- Neoatherosclerosis, shown at pathologic and OCT studies, increases neo-intimal vulnerability and contributes to the development of late stent failure.
→ This would be one of the major mechanisms.

IVUS vs. OCT in evaluation of vascular responses after stent implantation



IVUS better



OCT better !

Characterization of neointimal tissues.



Optical coherence tomography patterns of stent restenosis

Nieves Gonzalo, MD, Patrick W. Serruys, MD, PhD, Takayuki Okamura, MD, PhD, Heleen M. van Beusekom, MD, PhD, Hector M. Garcia-Garcia, MD, MSc, Gijs van Soest, PhD, Wim van der Giessen, MD, PhD, and Evelyn Regar, MD, PhD
Rotterdam, The Netherlands

Background Stent restenosis is an infrequent but poorly understood clinical problem in the drug-eluting stent era. The aim of the study was to evaluate the morphologic characteristics of stent restenosis by optical coherence tomography (OCT).

Methods Patients (n = 24, 25 vessels) presenting with angiographically documented stent restenosis were included. Quantitative OCT analysis consisted of lumen and stent area measurement and calculation of restenotic tissue area and burden. Qualitative restenotic tissue analysis included assessment of tissue structure, backscattering and symmetry, visible microvessels, lumen shape, and presence of intraluminal material.

Results By angiography, restenosis was classified as diffuse, focal, and at the margins in 9, 11, and 5 vessels, respectively. By OCT, restenotic tissue structure was layered in 52%, homogeneous in 28%, and heterogeneous in 20%. The predominant backscatter was high in 72%. Microvessels were visible in 12%. Lumen shape was irregular in 28% and there was intraluminal material in 20%. The mean restenotic tissue symmetry ratio was 0.58 ± 0.19 . Heterogeneous and low scattering restenotic tissue was more frequent in focal (45.5% and 54.5%, respectively) than in diffuse (0 and 11.1%) and margin restenosis (0 and 0%) ($P = .005$ for heterogeneous, $P = .03$ for low scattering). Restenosis patients with unstable angina symptoms presented more frequently irregular lumen shape (60 vs 6.7%, $P = .007$). Stents implanted ≤ 12 months ago had more frequently restenotic tissue with layered appearance (84.6% vs 16.7%, $P = .003$).

Conclusions We demonstrate the ability of OCT to identify differential patterns of restenotic tissue after stenting. This information could help in understanding the mechanism of stent restenosis. (Am Heart J 2009;158:284-93.)

Optical coherence tomography patterns of stent restenosis

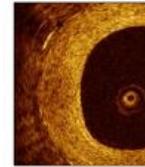
(Am Heart J 2009;158:284-93.)

Nieves Gonzalo, MD, Patrick W. Serruys, MD, PhD, Takayuki Okamura, MD, PhD, Heleen M. van Beusekom, MD, PhD, Hector M. Garcia-Garcia, MD, MSc, Gijs van Soest, PhD, Wim van der Giessen, MD, PhD, and Evelyn Regar, MD, PhD
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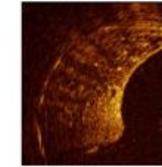
- In this OCT study, the systemic approach was applied to describe the restenosis using the **five categories** by qualitative OCT assessment;

- 1) Tissue structure,
- 2) Backscatter,
- 3) Microvessels,
- 4) Lumen shape,
- 5) Intraluminal material.

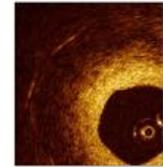
Restenotic tissue structure



Homogeneous: restenotic tissue has uniform optical properties and does not show focal variations in backscattering pattern.

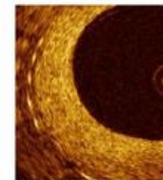


Heterogeneous: restenotic tissue has focally changing optical properties and shows various backscattering patterns

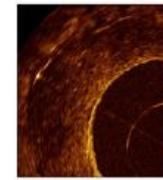


Layered: restenotic tissue consists of concentric layers with different optical properties: an adluminal high scattering layer and an abluminal low scattering layer

Restenotic tissue backscatter

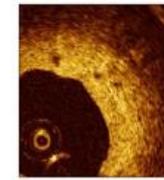


High: the majority of the tissue shows high backscatter and appears bright

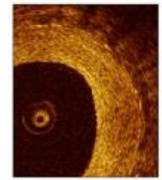


Low: the majority of the tissue shows low backscatter and appears dark or black

Microvessels visible

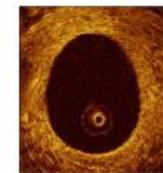


Yes: microvessels appear as well delineated low backscattering structures less than 200 micron in diameter that show a trajectory within the vessel

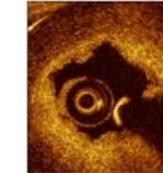


No

Lumen shape



Regular: lumen border is sharply delineated, smooth and circular

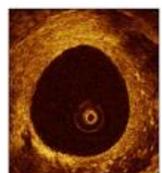


Irregular: lumen border irregular with tissue protrusions from the vessel wall into the lumen

Presence of intraluminal material



Yes: there is visible material inside the vessel lumen.



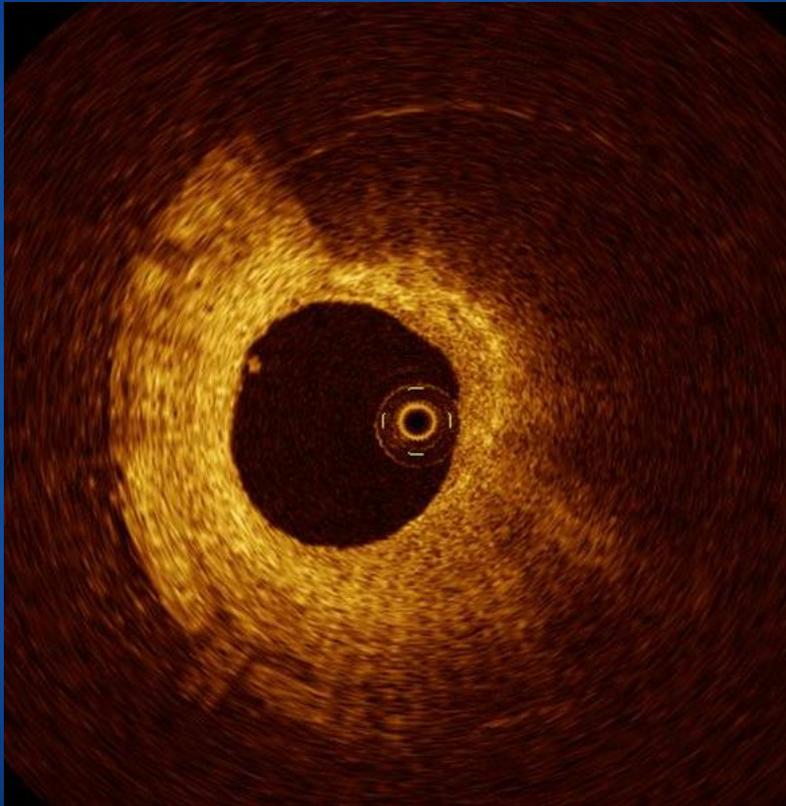
No

Optical Coherence Tomographic Analysis of In-Stent Neoatherosclerosis After Drug-Eluting Stent Implantation

Soo-Jin Kang, MD; Gary S. Mintz, MD; Takashi Akasaka, MD, PhD; Duk-Woo Park, MD, PhD; Jong-Young Lee, MD; Won-Jang Kim, MD; Seung-Whan Lee, MD, PhD; Young-Hak Kim, MD, PhD; Cheol Whan Lee, MD, PhD; Seong-Wook Park, MD, PhD; Seung-Jung Park, MD, PhD

- OCT & VH-IVUS in 50 patients (30 stable, 20 unstable angina) with 50 DES ISR lesions.
 - 26 lesions (52%) had OCT-defined in-stent TCFA-containing neointima and 29 (58%) had in-stent neointimal rupture.
 - As compared to stable angina, patients presenting with unstable angina showed a thinner fibrous cap (55 vs. 100 μ m, P=0.006) and higher incidence of OCT-defined TCFA-containing neointima (75% vs. 37%, P=0.008), intimal rupture (75% vs. 47%, P=0.044), and thrombi (80% vs. 43%, P=0.010).
- suggest that in-stent neo-atherosclerosis assessed by OCT may be an important mechanism of DES failure, especially late after implantation.**

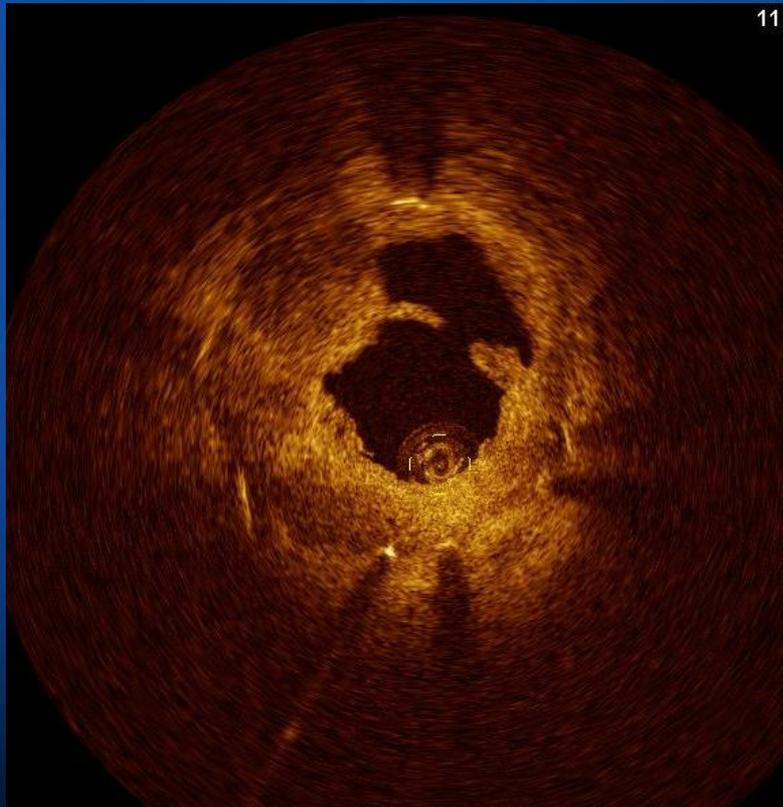
✓ Lipid pool & Thin-cap fibroatheroma (TCFA)



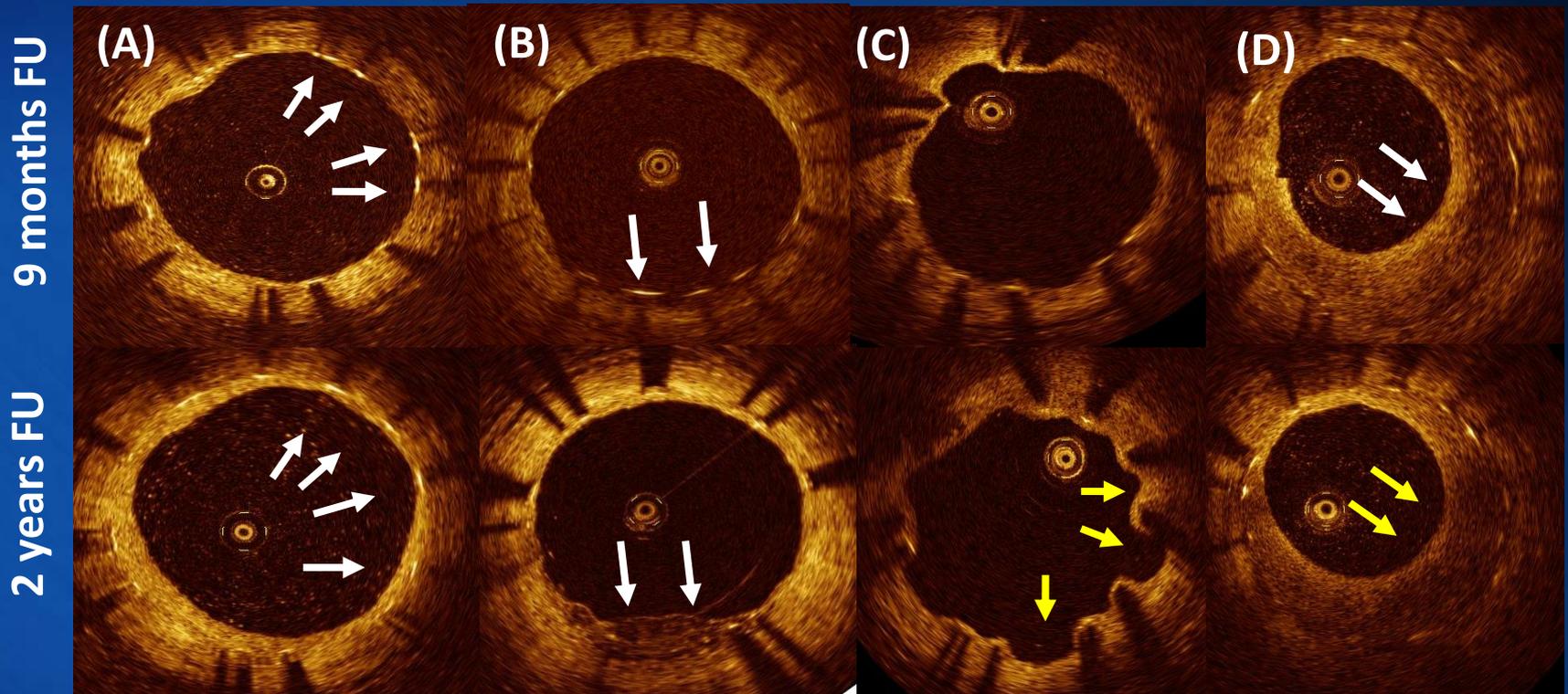
TCFA-containing intima; fibrous cap thickness at the thinnest part $\leq 65\mu\text{m}$ and an angle of lipidic tissue 180° .

✓ *Neointimal rupture*

; a break in the fibrous cap that connected the lumen with the underlying lipid pool



Conclusion of SERIAL OCT study



- A. Uncovered struts at 9 months were covered with neointima on 2 yr FU (white arrow).
- B. Appearance of a low density abnormal tissue structure over uncovered struts during serial follow-up (white arrow).
- C. Extrastent lumen not present at 9 months was noted at 2 year FU (yellow arrow).
- D. Increase in the low density within heterogeneous neointima between 9 months (white arrow) and 2 years (yellow arrow).