APPAC

Comment évaluer l'endothélialisation?

Biarritz 8 Juin 2017

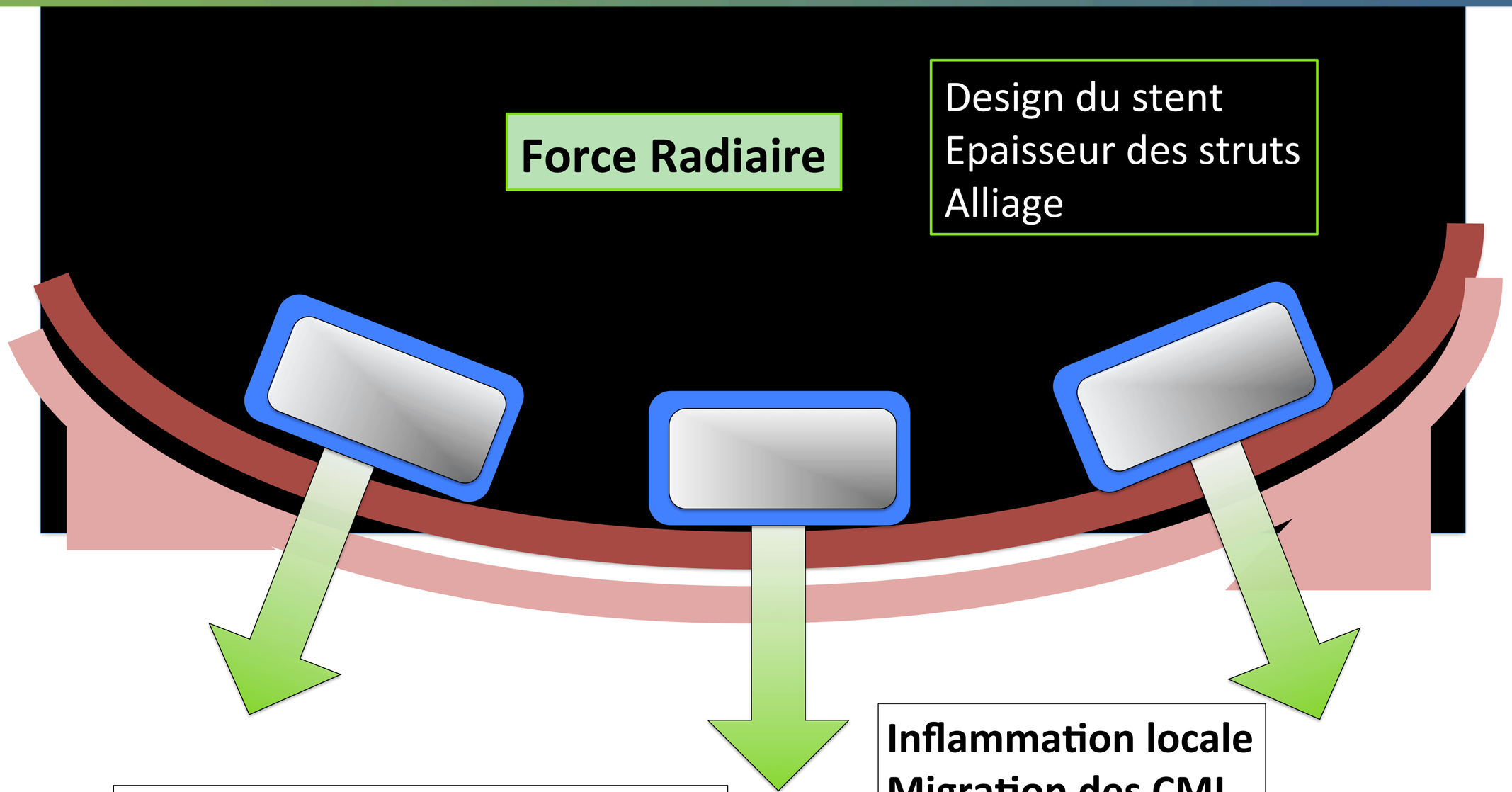
Géraud SOUTEYRAND

Endothélialisation

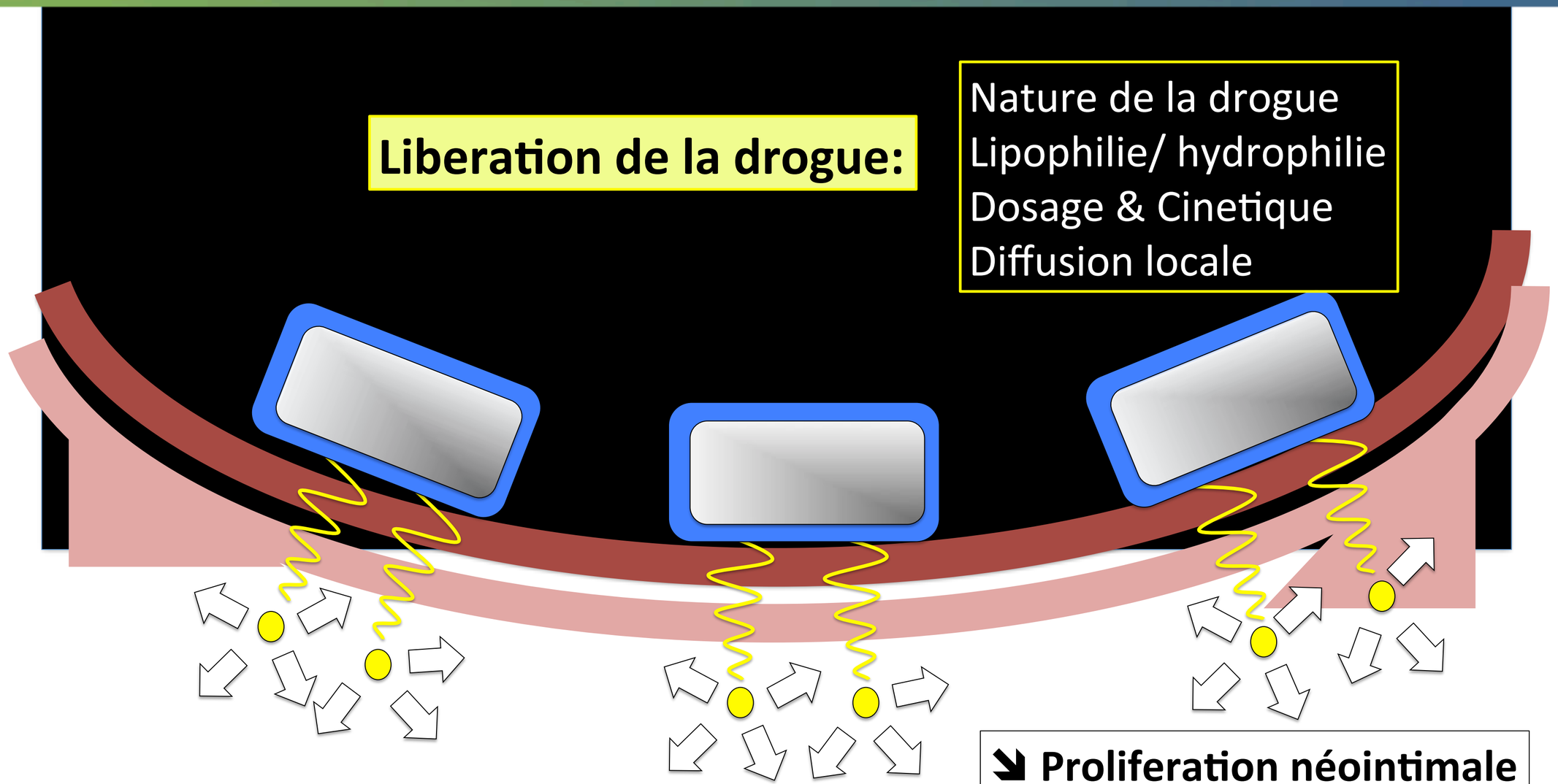
Pourquoi évaluer endothélialisation?

Avec quel outil?

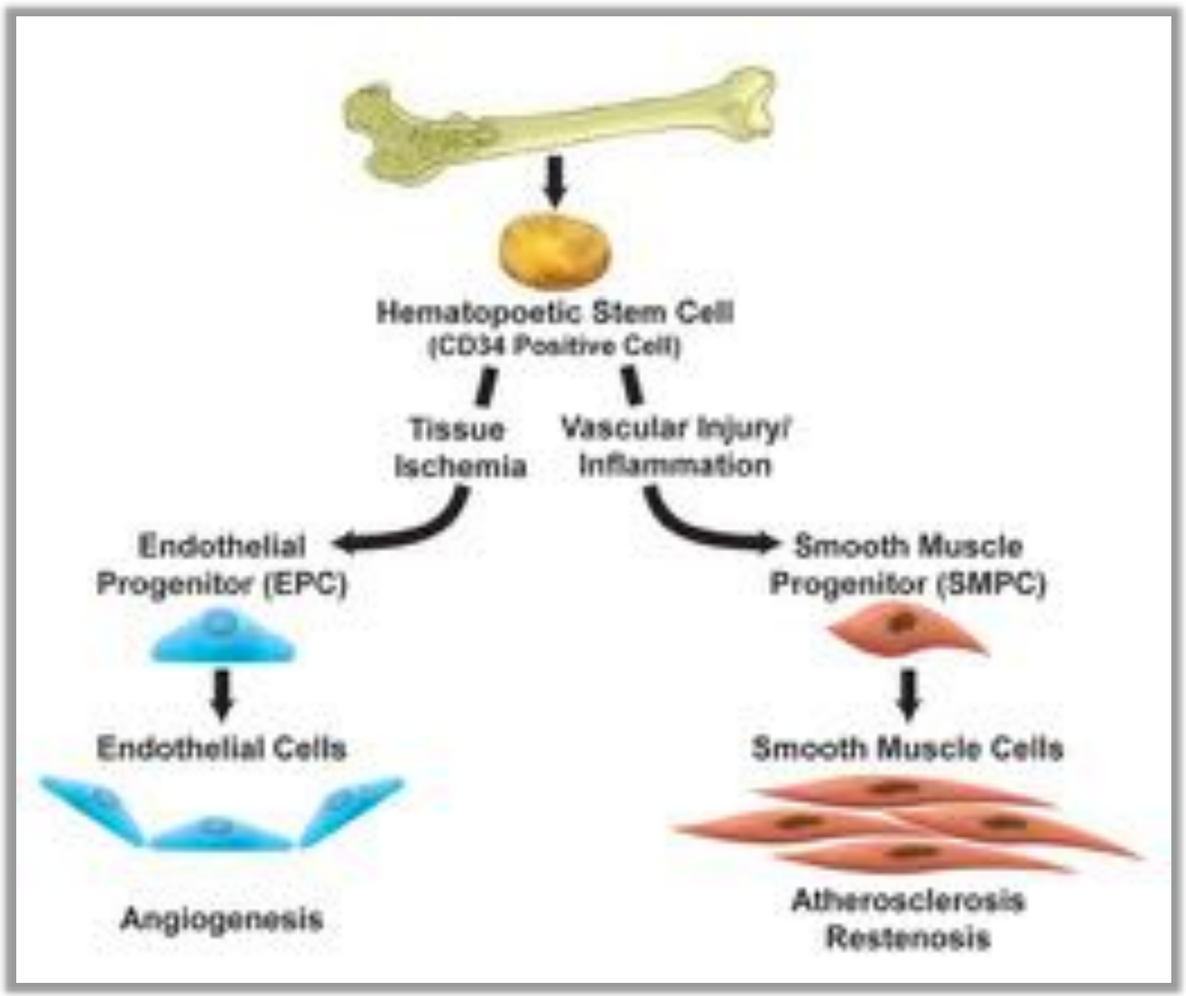
Endothélialisation



Endothélialisation

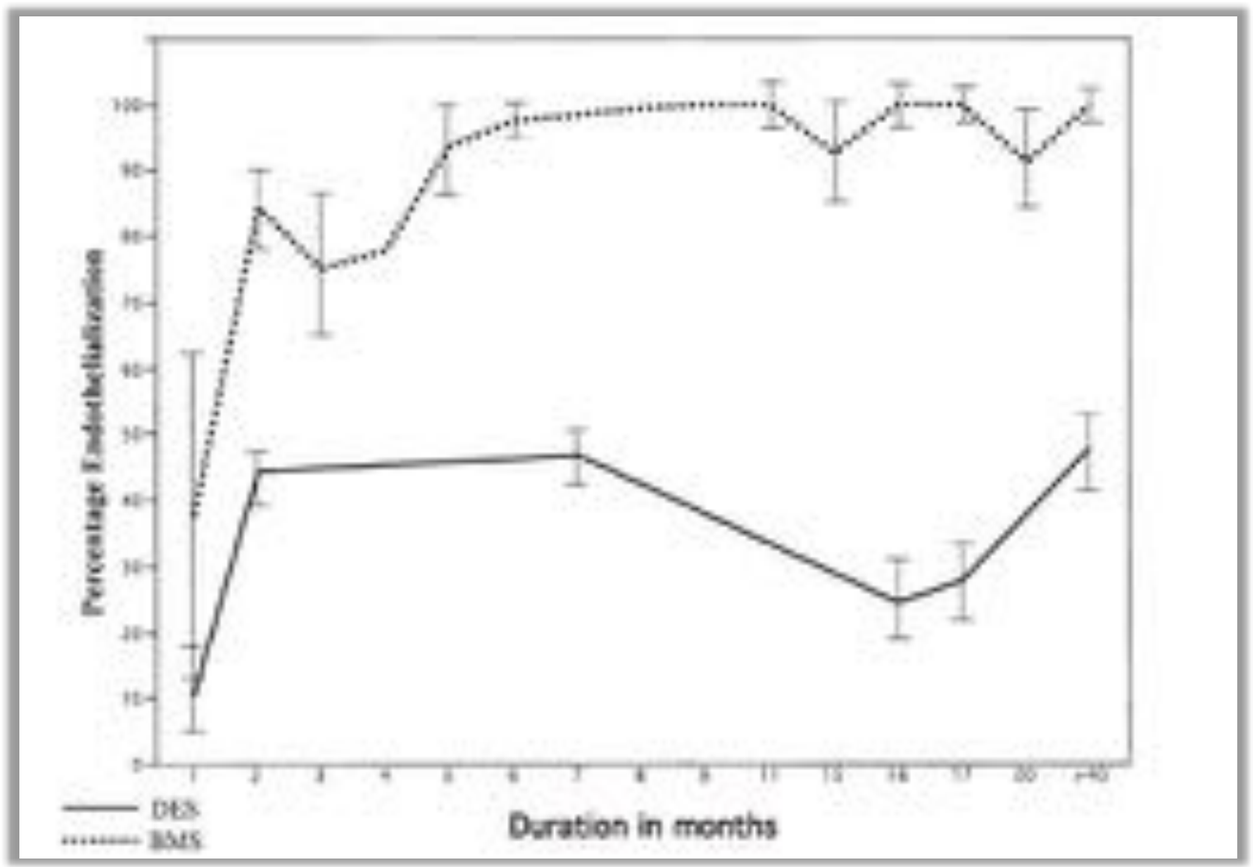


Non couverture des mailles



Non couverture des mailles

DES 1ère génération

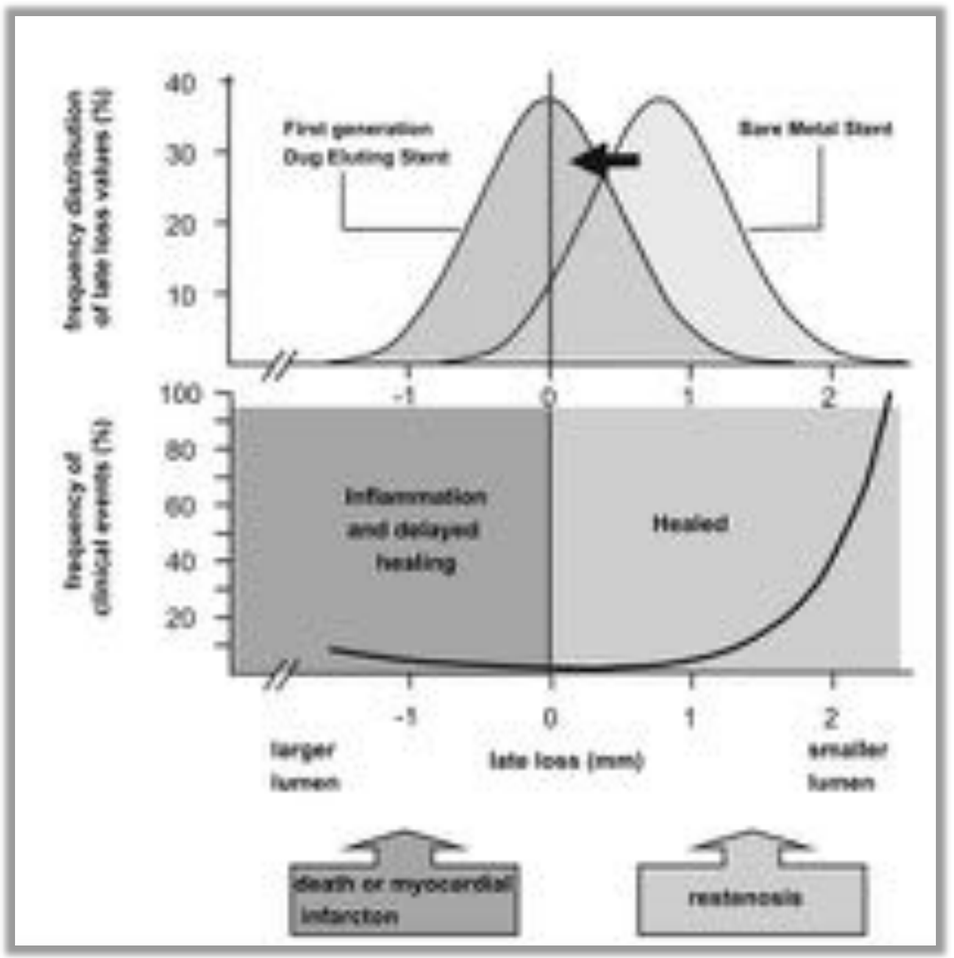


Joner M JACC 2006

Stent Thrombosis Late After Implantation of First-Generation Drug-Eluting Stents

A Cause for Concern

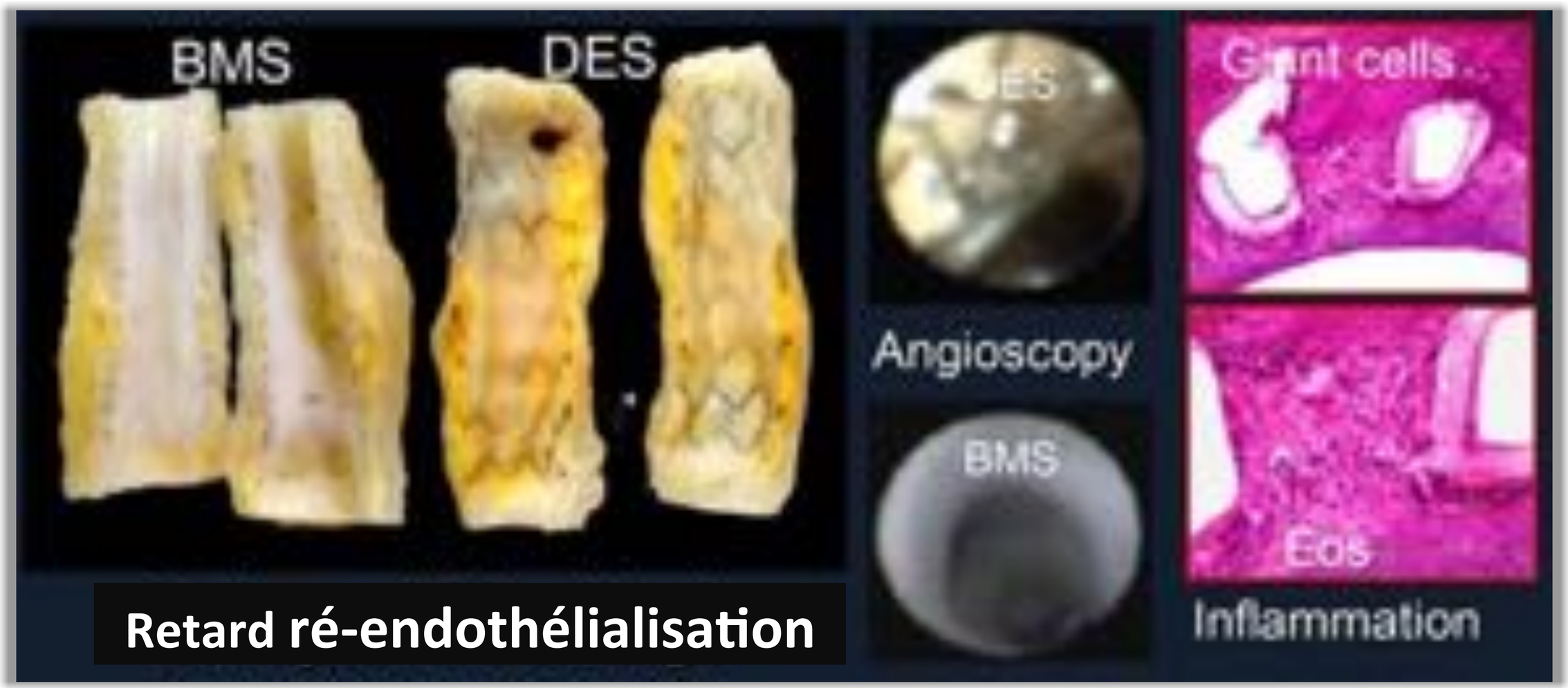
Edoardo Camenzind, MD; P. Gabriel Steg, MD; William Wijns, MD



Circulation 2007

Non couverture des mailles

DES 1ère génération/risque thrombose de stent

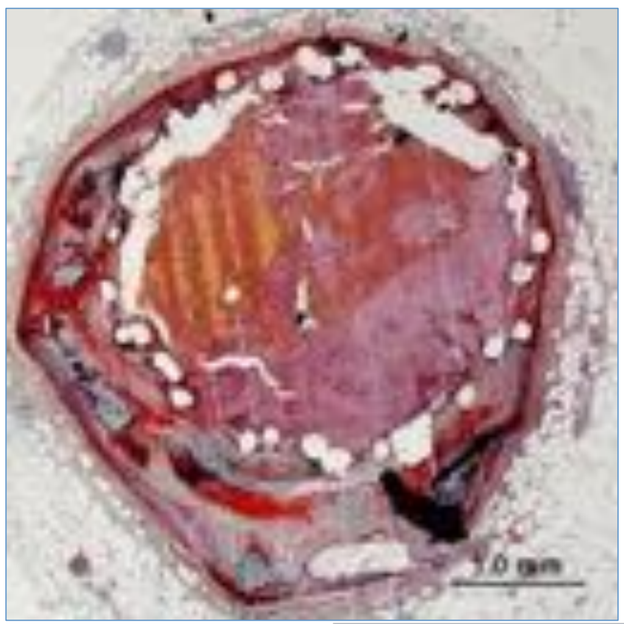


Non couverture des mailles

Facteurs associés à la thrombose de stent

Non couverture des mailles

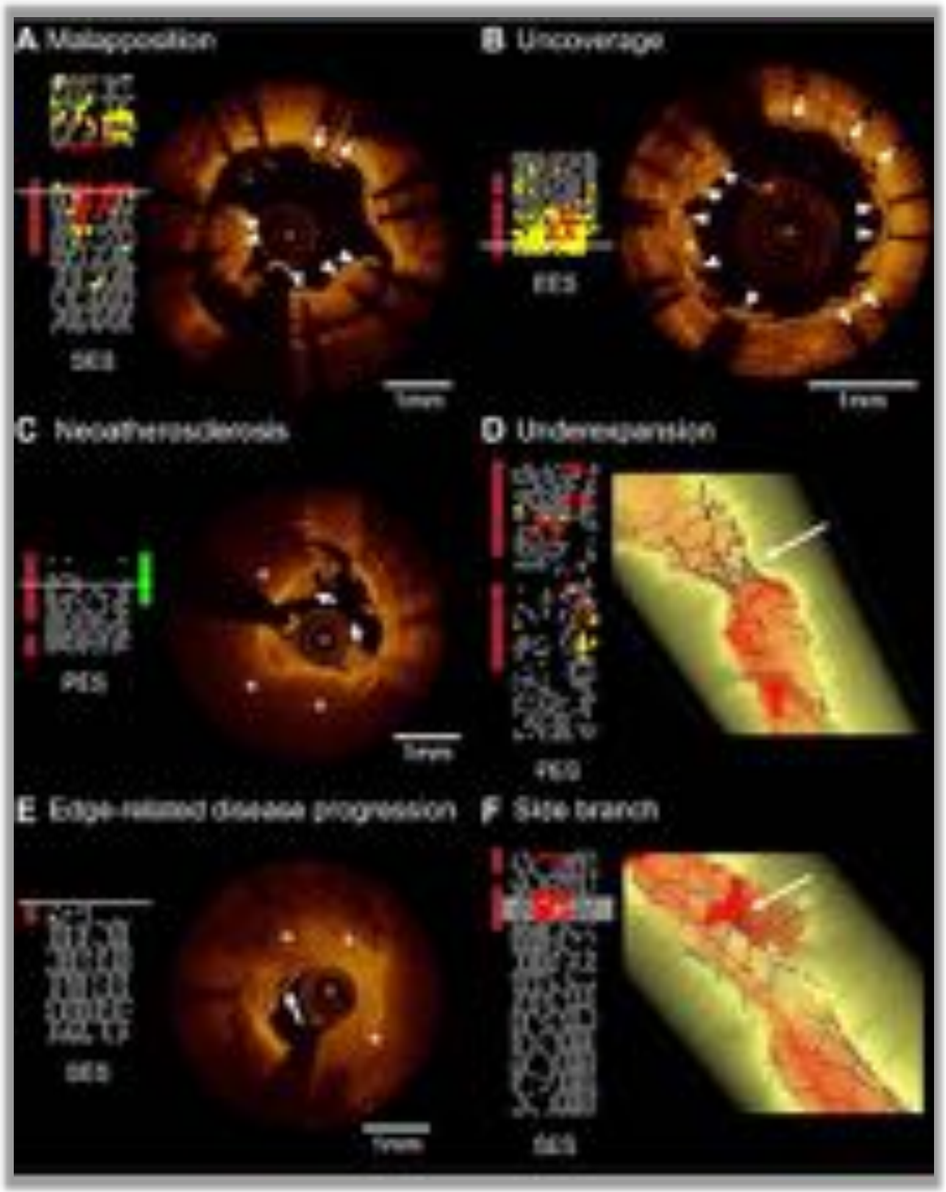
Pb lié traitement antiagrégant plaquettaire



Transformation athéromateuse néointima

Profil de patient :
Diabète, insuffisance rénale, dysfonction VG

OCT et thrombose de stent



Mechanisms of Very Late Drug-Eluting Stent Thrombosis Assessed by Optical Coherence Tomography

58 patients avec thrombose très tardive
38 DES 1ère génération – 20 DES 2ème génération

Causes de thromboses :

- **Malapposition 33%**
- **Rupture néoathérosclérose 26%**
- **Non couverture 10%**
- **Sous expansion 5%**

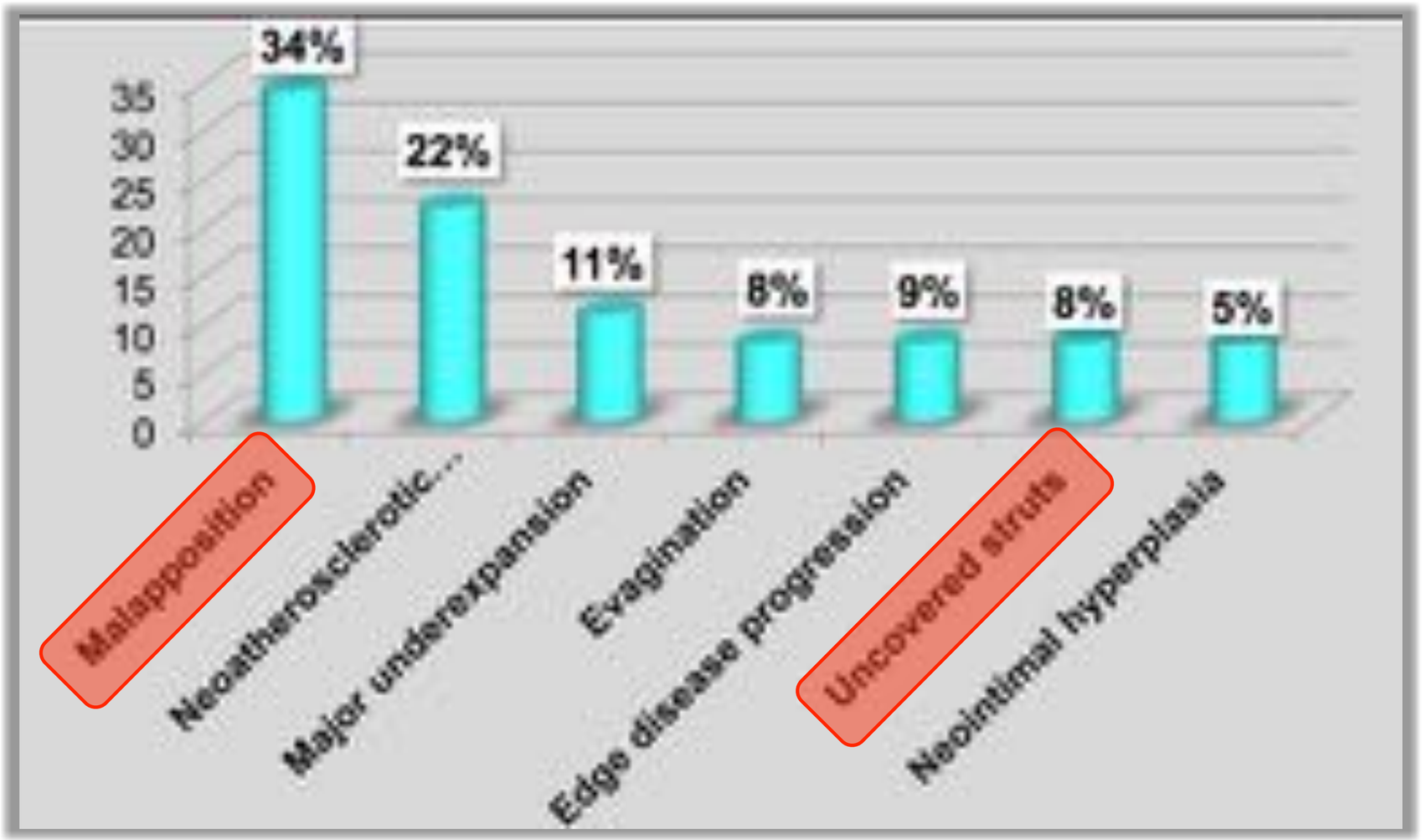
Taniwaki M. Circulation 2016

OCT et thrombose de stent

PESTO

Analyse OCT

Causes de thrombose

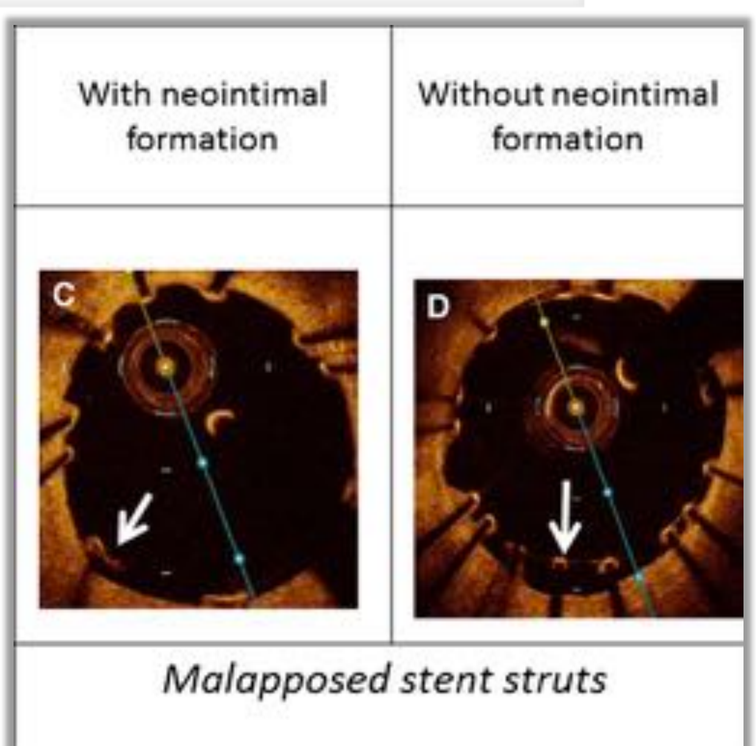


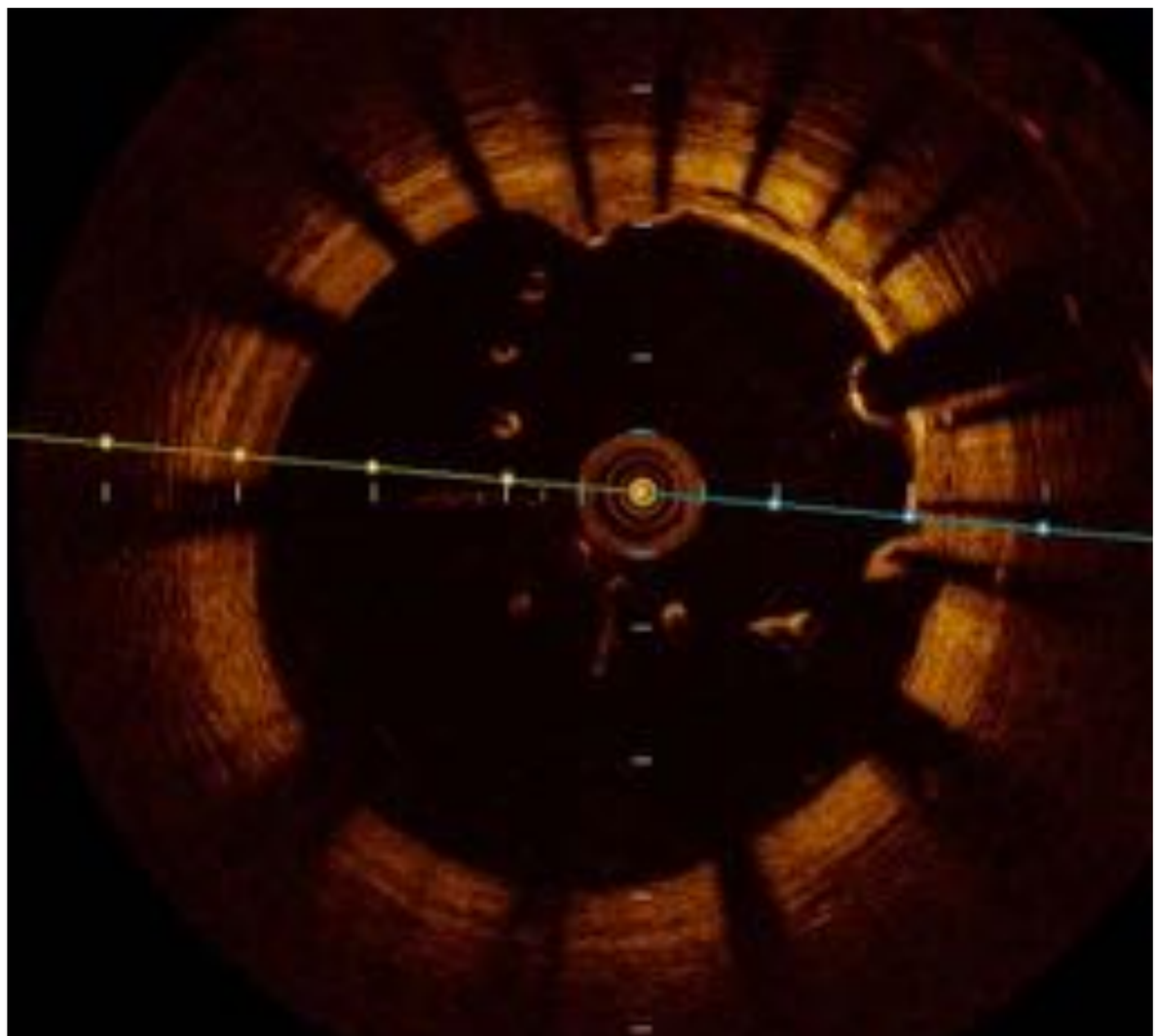
Eur Heart Journal 2016

OCT et thrombose de stent

PESTO

Malapposition et non couverture souvent associés



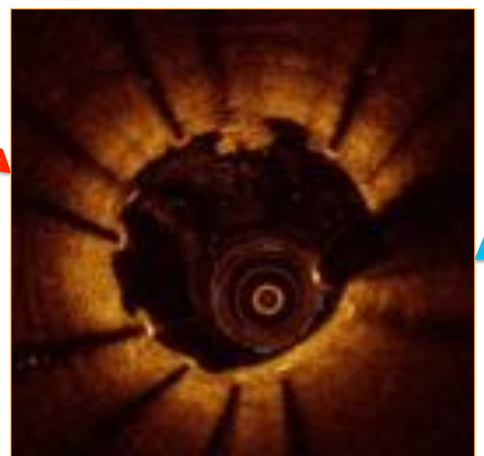


Eur Heart Journal 2016

Couverture néointimale

Facteurs influençant la couverture néointimale

<u>Caractéristiques du stent</u>
Biocompatibilité / Allergie
Combinaison Polymère/Drogue
Réponse inflammatoire locale
Design



<u>Caractéristiques de l'Angioplastie</u>
Longueur de lésion
Overlapping
Sous-expansion, Malapposition
Bifurcation
ANTC Brachytherapie

<u>Caractéristiques du patient</u>:
Diabète (augmente la couverture)

Endothélialisation

Pourquoi évaluer endothélialisation?

Avec quel outil?

Couverture néointimale

Ex Vivo Assessment of Vascular Response to Coronary Stents by Optical Frequency Domain Imaging

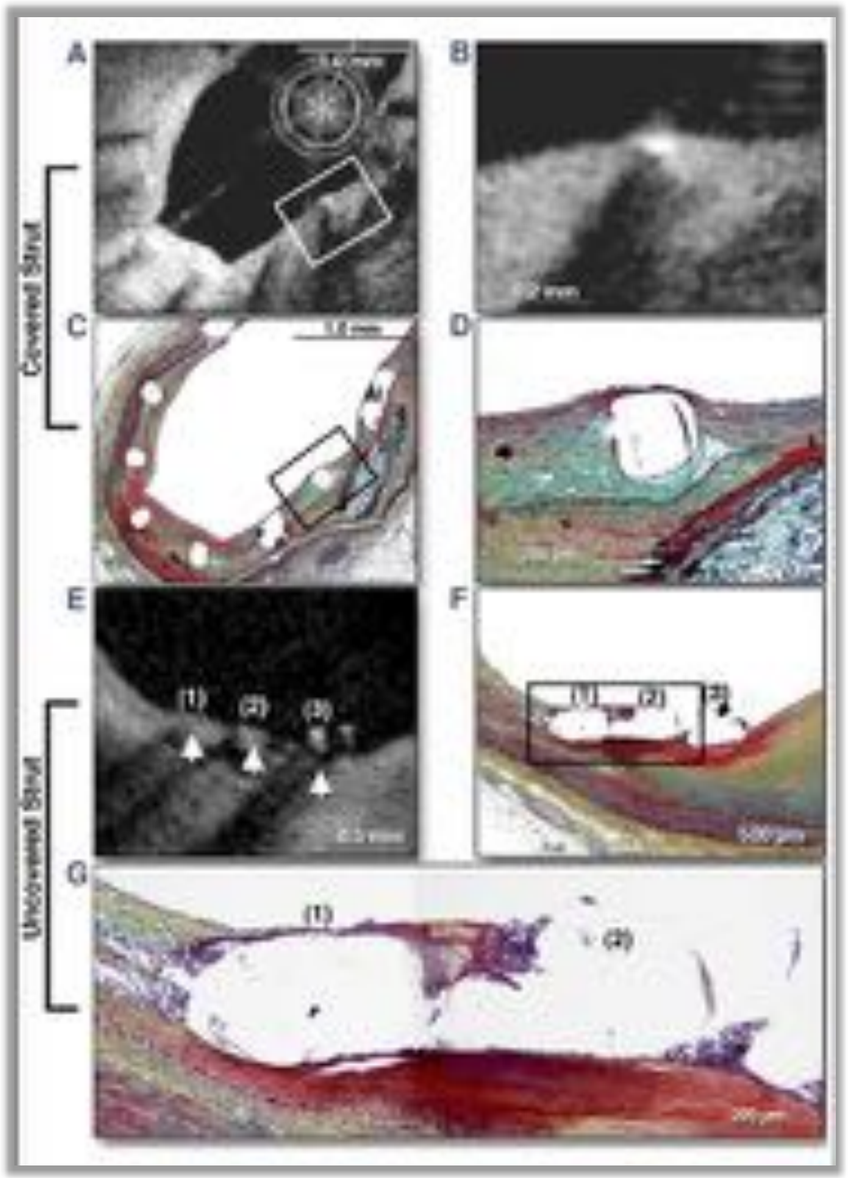
Analyse comparative OFDI, IVUS et histologie sur 134 segments stentés

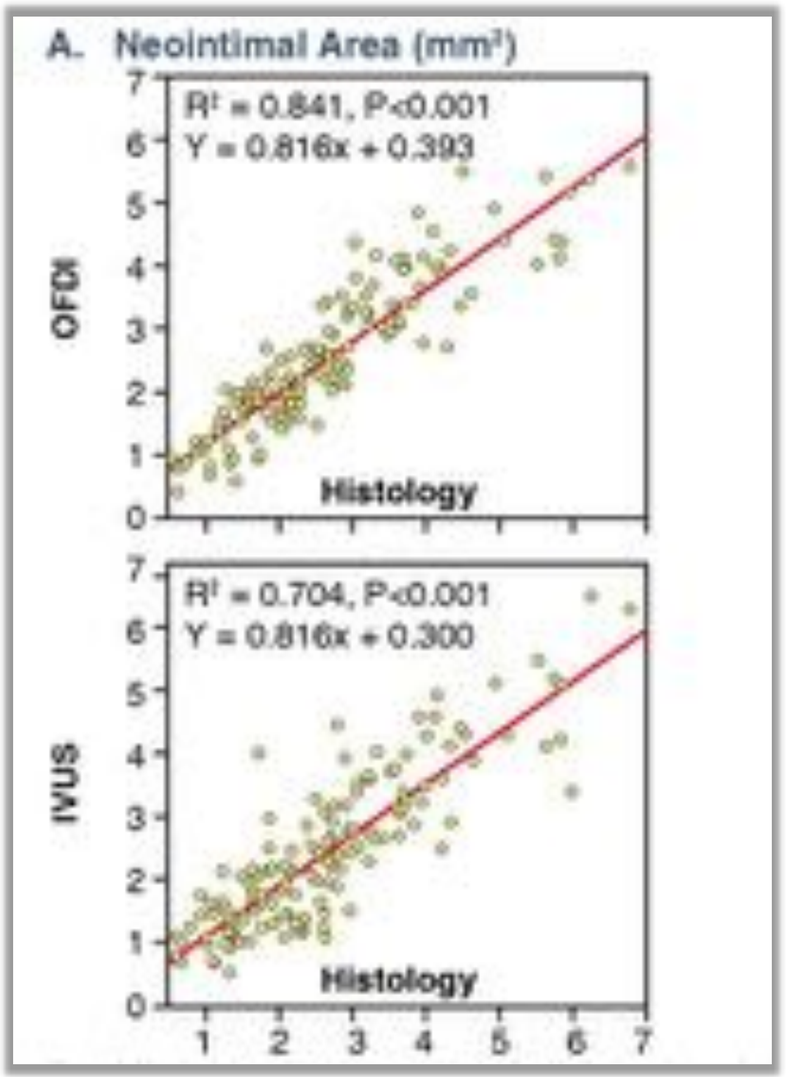
Comparaison mesures, couverture maille et caractérisation néointima

Nakano M. JACC Imaging 2012

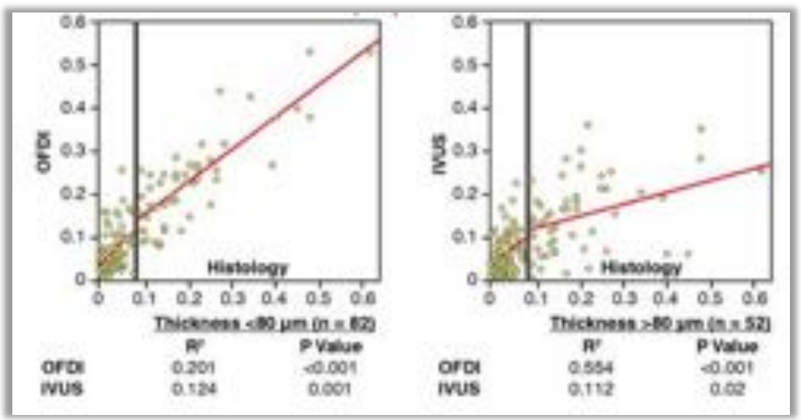
Couverture néointimale

Ex Vivo Assessment of Vascular Response to Coronary Stents by Optical Frequency Domain Imaging





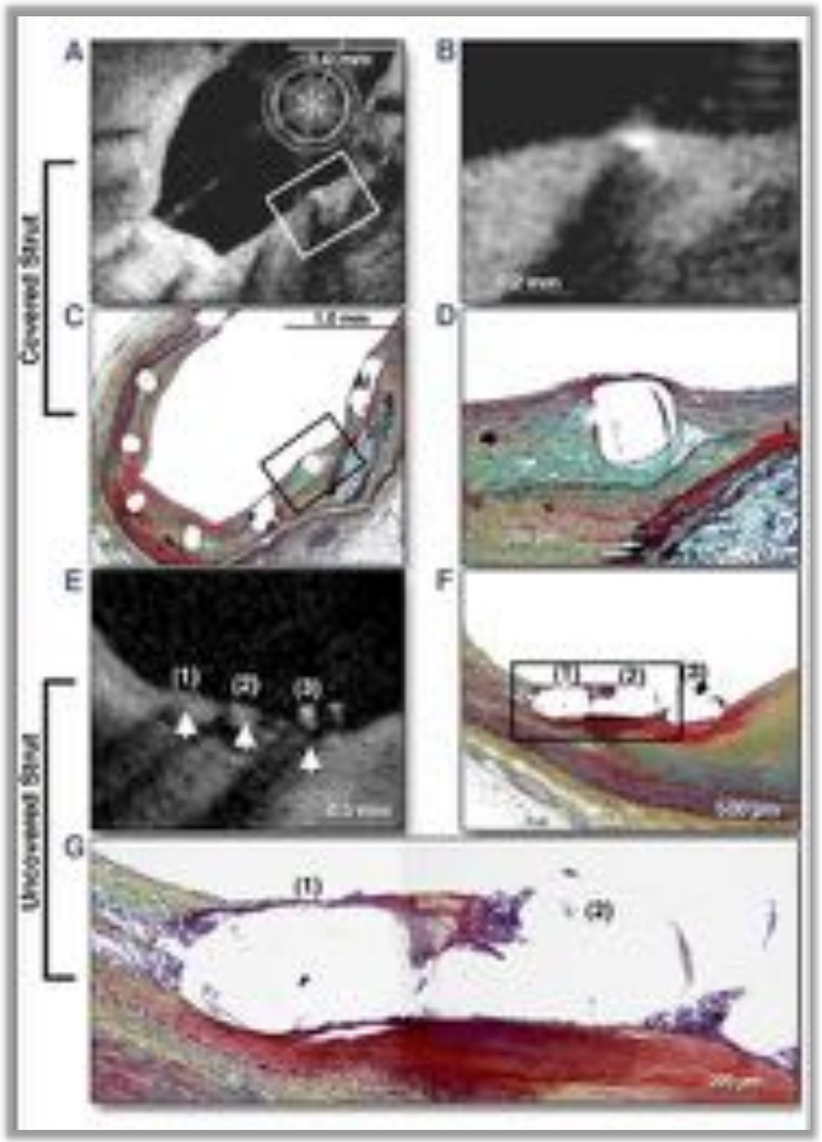
Minimal Neointimal Thickness (mm)



Nakano M. JACC Imaging 2012

Couverture néointimale

Ex Vivo Assessment of Vascular Response to Coronary Stents by Optical Frequency Domain Imaging



Meilleure corrélation OFDI/histologie pour mailles à nu

Nombreux faux positifs en IVUS

	Reviewer 1		Reviewer 2	
	Uncovered Struts	Covered Struts	Uncovered Struts	Covered Struts
Histology				
Uncovered struts n = 43	34	9	33	10
Covered struts n = 97	3	94	4	93
Detection of uncovered struts				
Sensitivity	79.1% [70.3–85.6]		76.7% [67.5–82.0]	
Specificity	96.9% [93.0–98.9]		95.9% [91.8–98.2]	

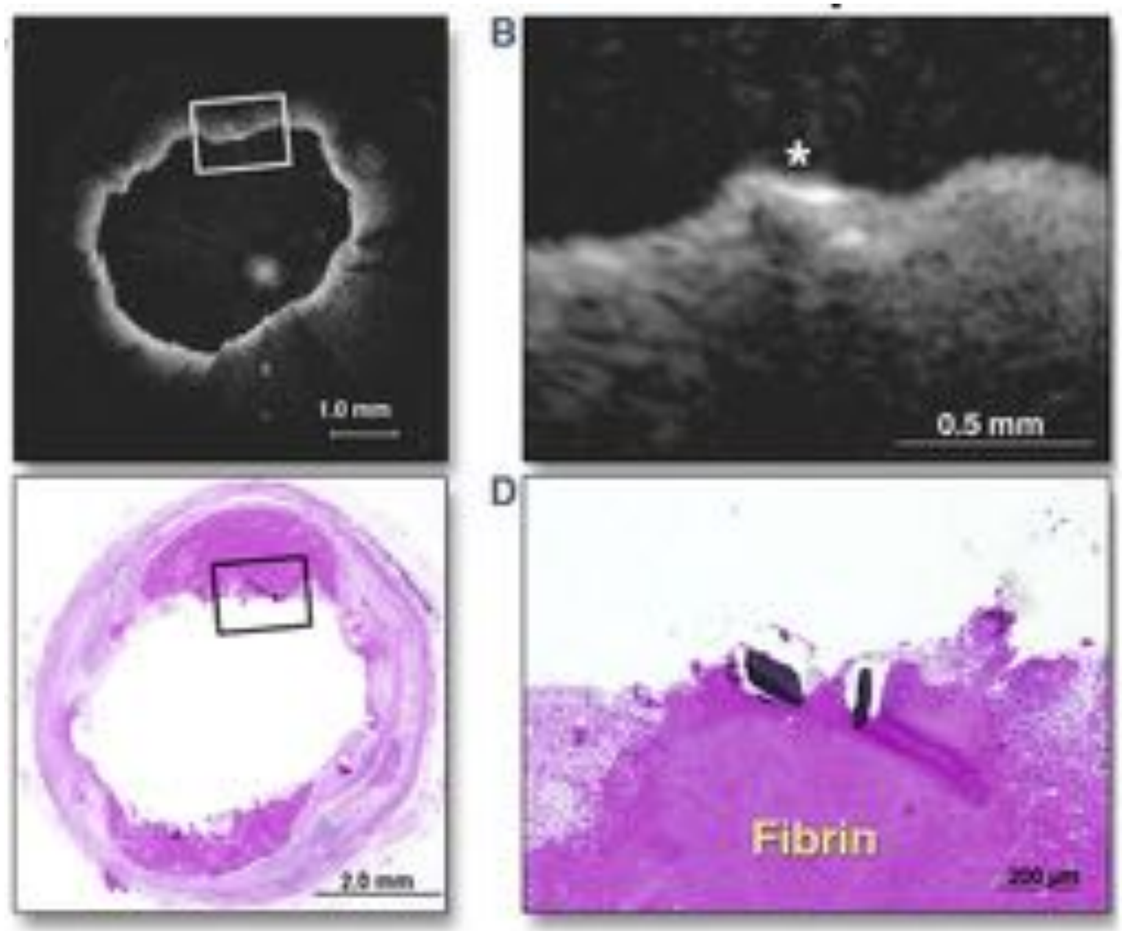
Nakano M. JACC Imaging 2012

Couverture néointimale

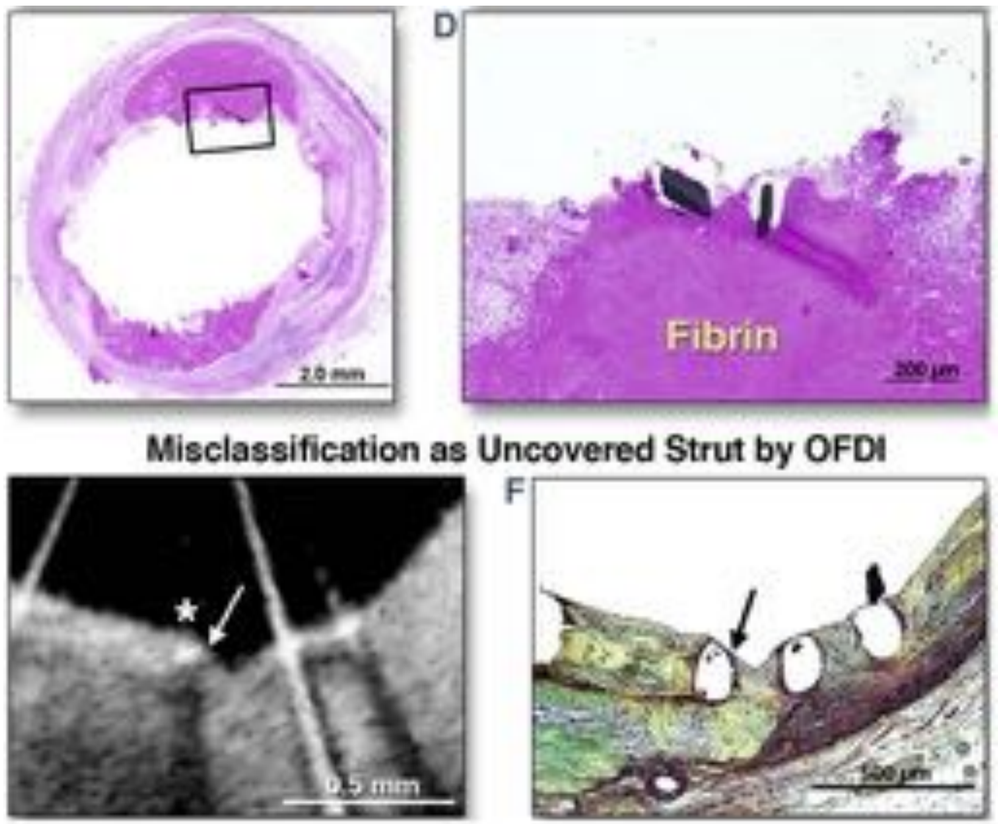
Ex Vivo Assessment of Vascular Response to Coronary Stents by Optical Frequency Domain Imaging

Les Pièges en OCT

Strut couverte?



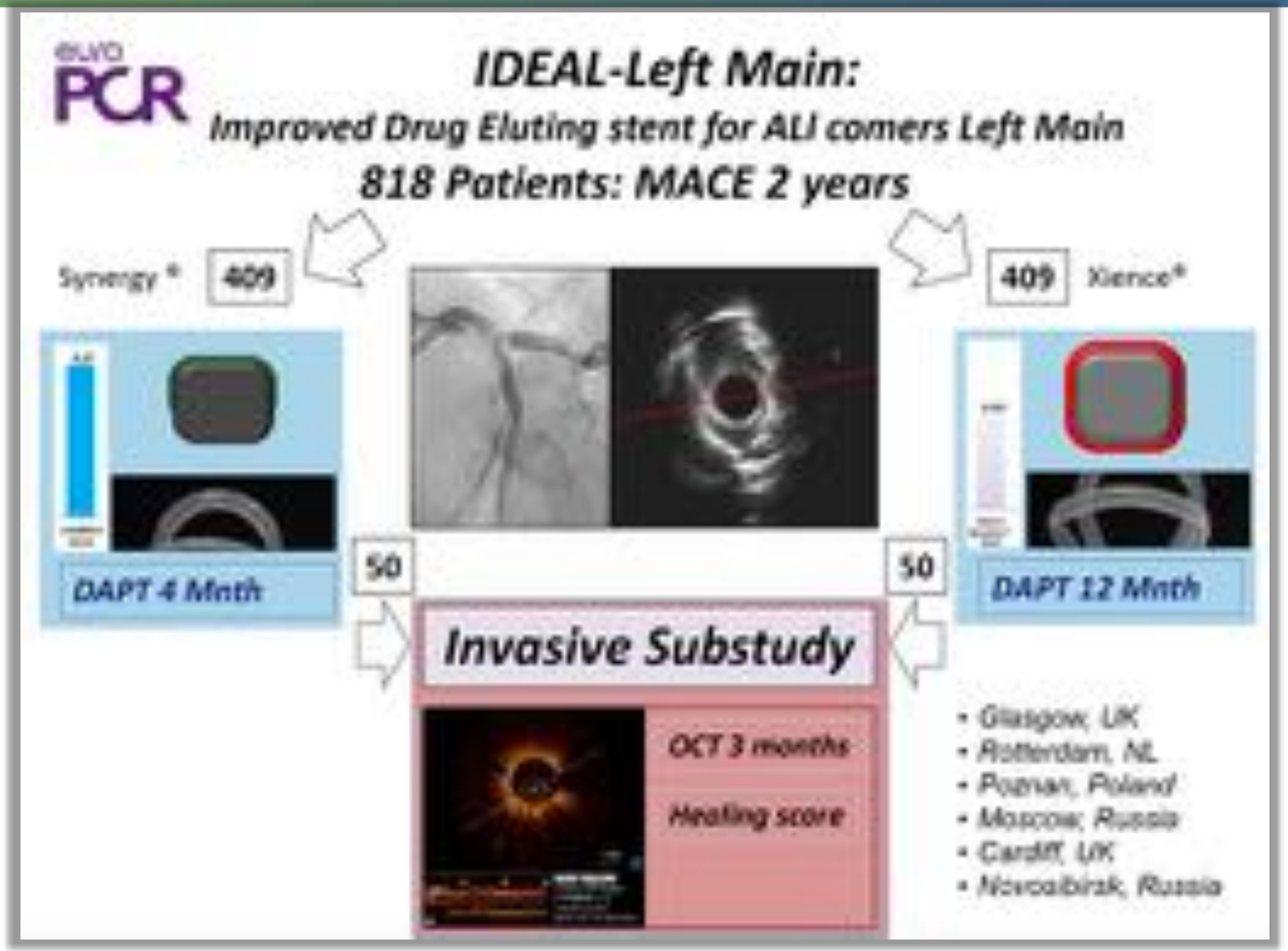
Strut non couverte?



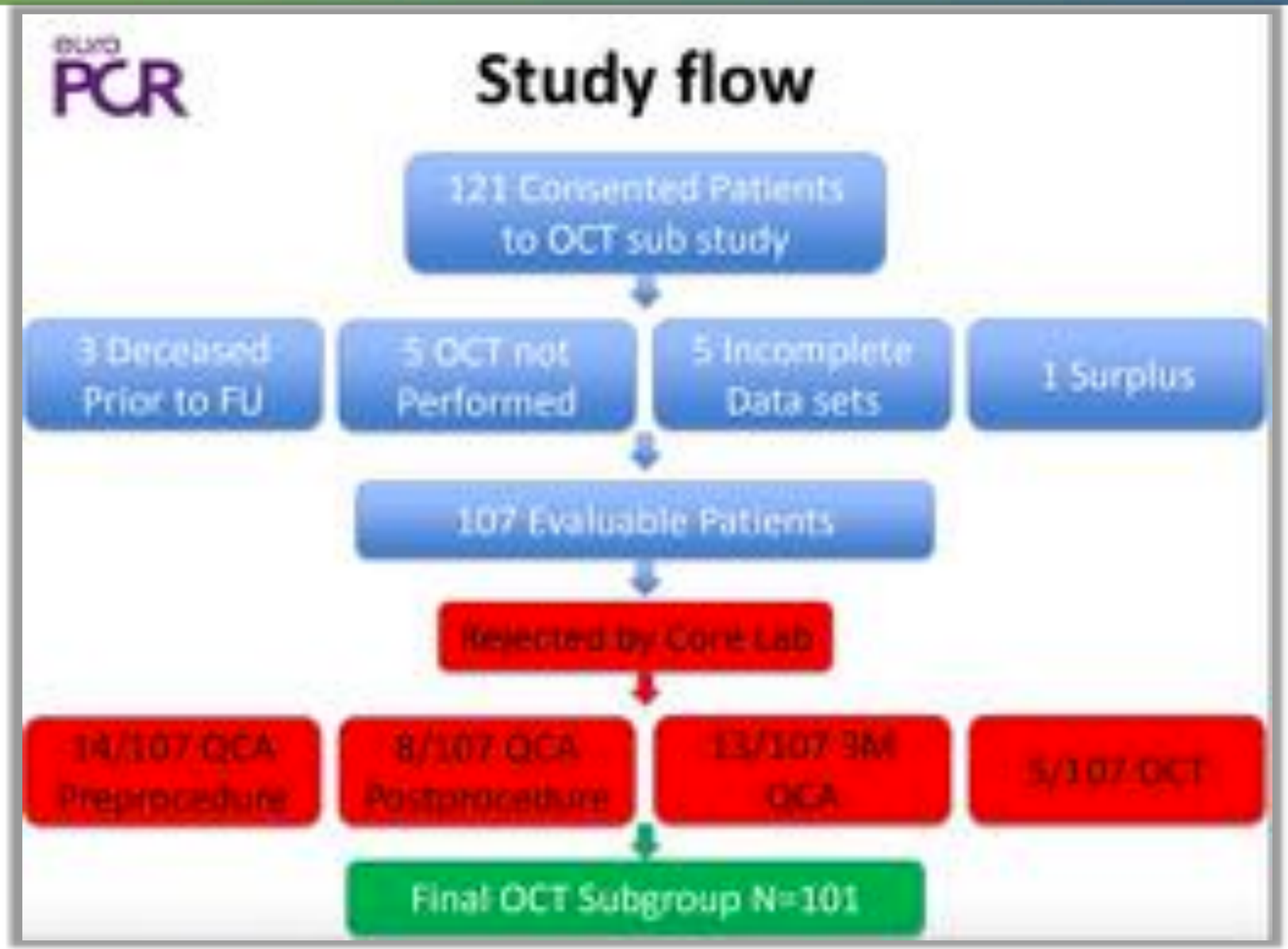
Nakano M. JACC Imaging 2012

Couverture néointimale

Etudes récentes



Couverture néointimale



Couverture néointimale

Analyse OCT à 3 mois

	Malappossed (%)	Uncovered (%)
Proximal main	2.47 ± 4.33	0.00 ± 0.00
Bifurcation Region	2.60 ± 8.25	0.03 ± 0.30
Distal Main	2.39 ± 5.29	0.01 ± 0.11

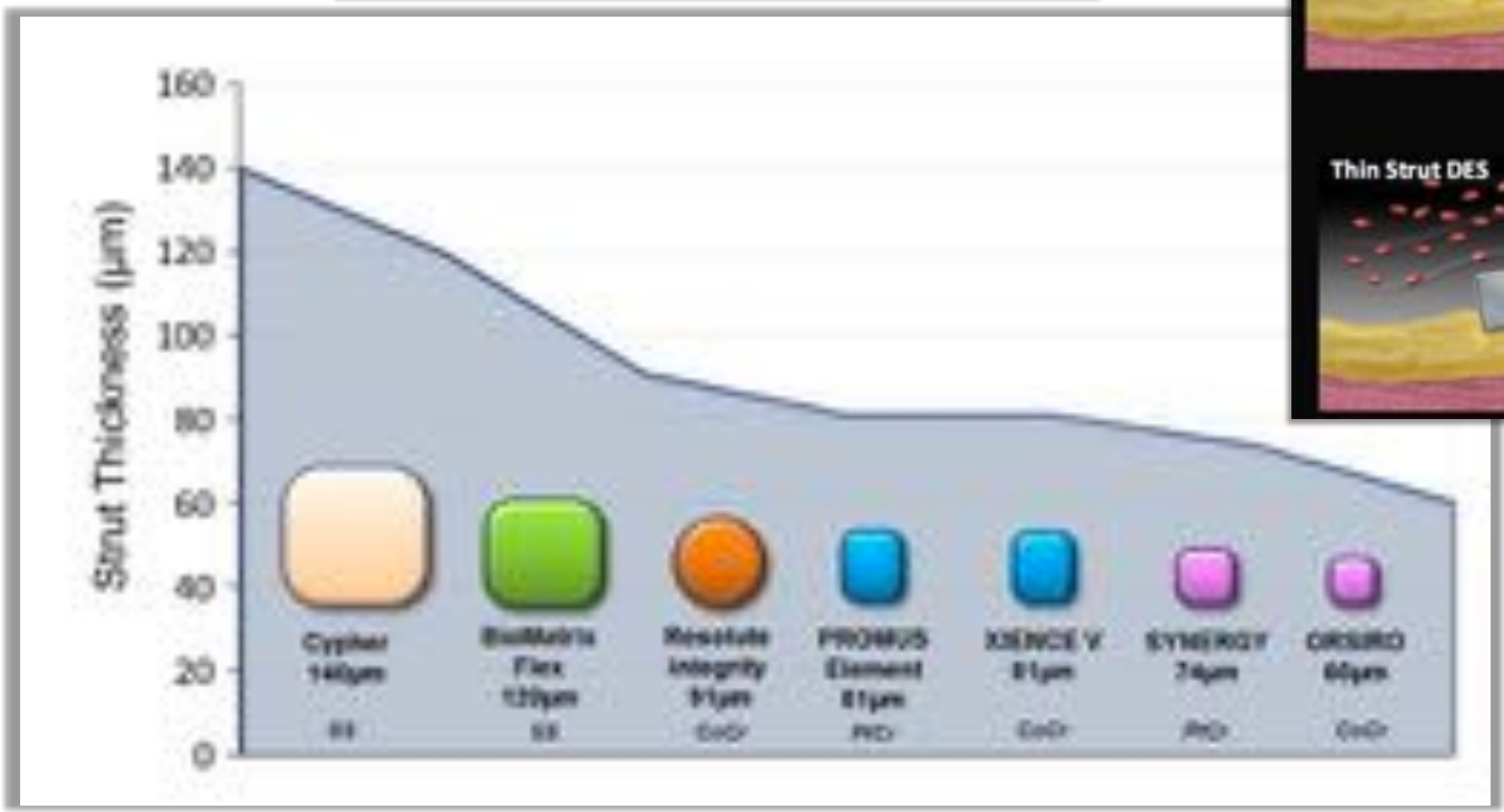
Presque toutes mailles couvertes à 3 mois
2 à 3% malapposition

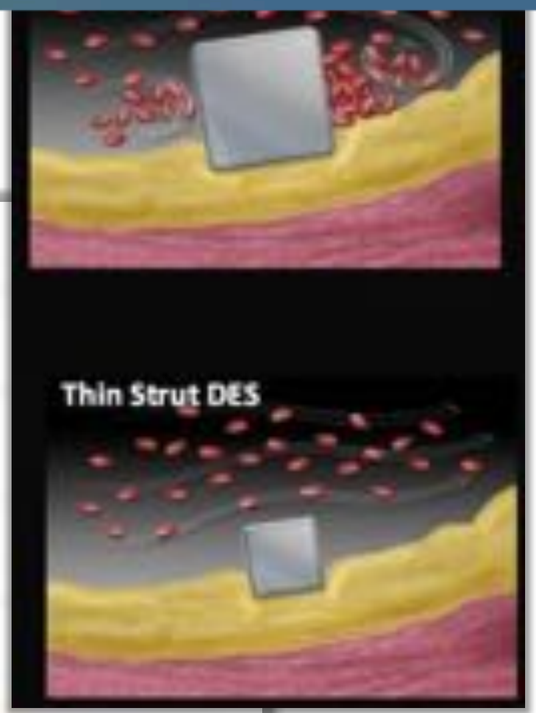
Résultats cliniques 2019

Distal Main	BP-PtCr-EES (N=48)	PP-CoCr-EES (N=43)	p-Value
Mean lumen area	9.51 ± 2.05	8.85 ± 2.59	*0.177*
Minimal lumen area	7.37 ± 2.20	6.74 ± 2.43	*0.198*
Endoluminal: Mean stent area	9.87 ± 1.86	9.35 ± 2.36	*0.251*
Endoluminal: Mean neo-intima areas	0.72 ± 0.31	0.84 ± 0.48	*0.912*
Uncovered struts (%)	0.00 ± 0.00	0.02 ± 0.16	*0.291*
Covered >20 micron (%)	96.29 ± 4.13	97.23 ± 2.42	*0.468*
Malapposed struts (%)	3.07 ± 6.80	1.62 ± 2.69	*0.758*
Endoluminal: Mean ISA area	0.18 ± 0.39	0.11 ± 0.23	*0.758*

Les Progrès

Epaisseur des mailles

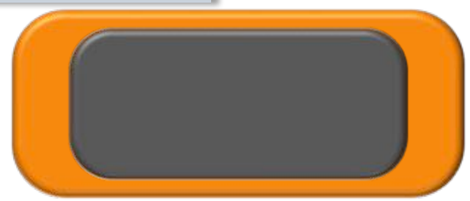




Les Progrès

Polymère :
bio-compatibles, bio-résorbables
Moins épais

Taxus liberté



Acier 316 L

Strut thickness 132 µm

Coating permanent SIBS

Epaisseur coating 16/32 µm

coating circonférentiel

Sirolimus

Synergy

PtCr

Strut thickness 74 µm

Coating résorbable PLGA

Epaisseur coating 4 µm

coating abluminal

Everolimus

Courtesy Levesque S.

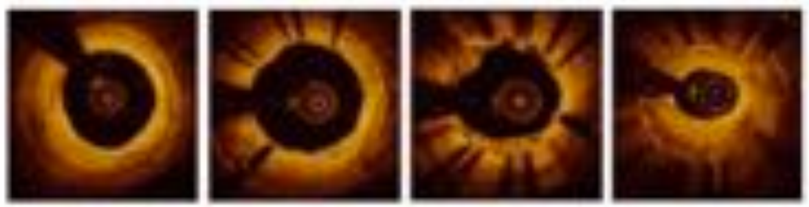
Les Progrès

Polymère :
bio-compatibles
Moins épais

	Xience	Onyx	Synergy	Ultimaster	Orsiro	Biomatrix
Stent material	CoCr	CoNi	PtCr	CoCr	CoCr	316L
Stent strut thickness	81 µm	89 µm	79 µm	80 µm	60 µm	120 µm
Polymer thickness	7-8 µm	4.8 µm	4 µm	15 µm	3.5/7.5 µm	16.6 µm
Drug	Evero-limus	Zotaro-limus	Evero-limus	Siro-limus	Siro-limus	Bio-limus
Polymer type	PVDF-HFP	Biolinx	PLGA	PDLLA-PCL	PLLA	PDLLA
						

Couverture des stents

Etudes récentes



TRANSFORM-OCT*: A Prospective, Randomized Trial Using OCT Imaging to Evaluate Strut Coverage at 3 Months and Neoatherosclerosis at 18 Months in Bioresorbable Polymer-Based and Durable Polymer-Based Drug-Eluting Stents

*TRiple Assessment of Neointima Stent FOrmation to Reabsorbable polyMer with OCT

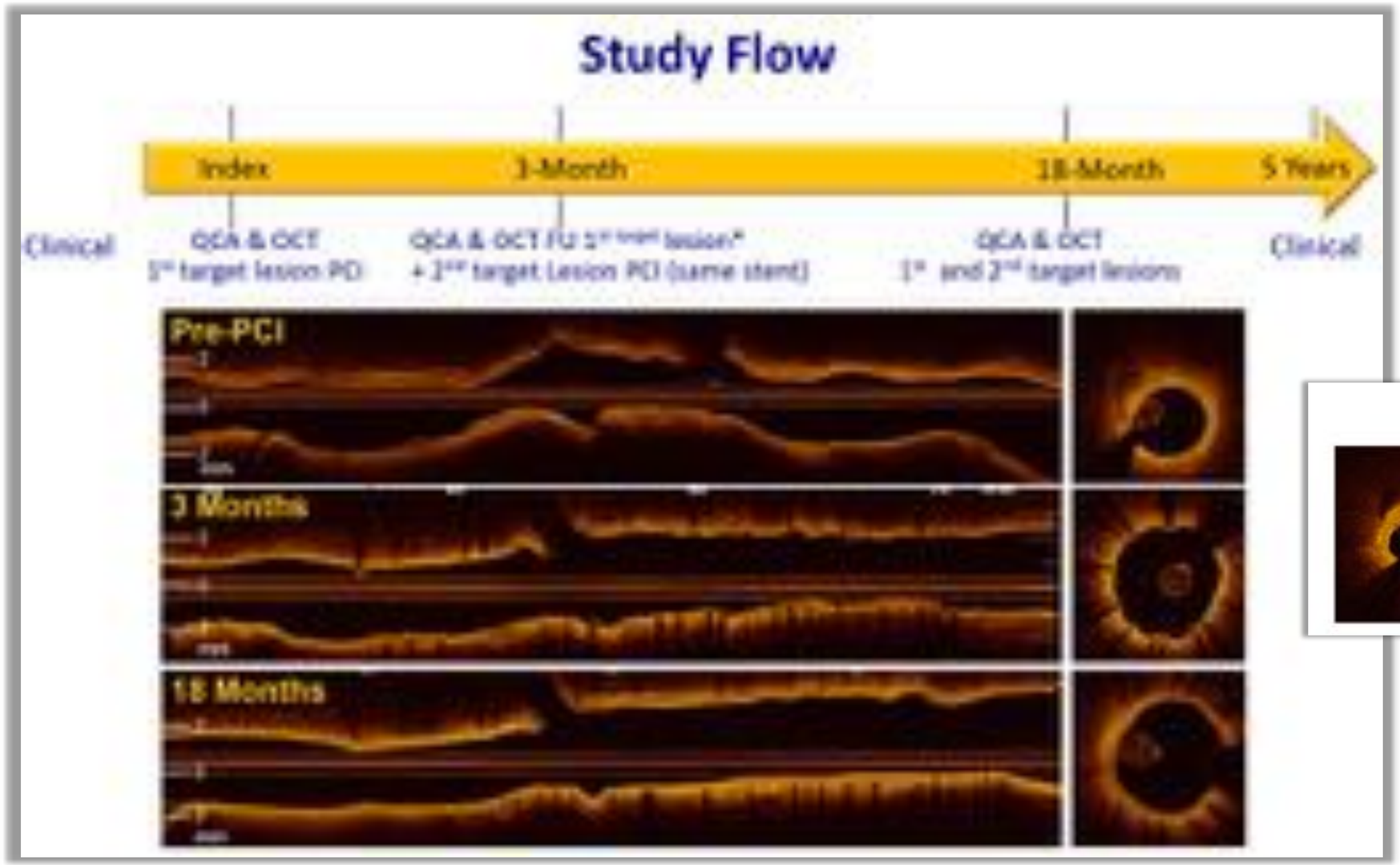
Etude prospective, 2 centres italiens

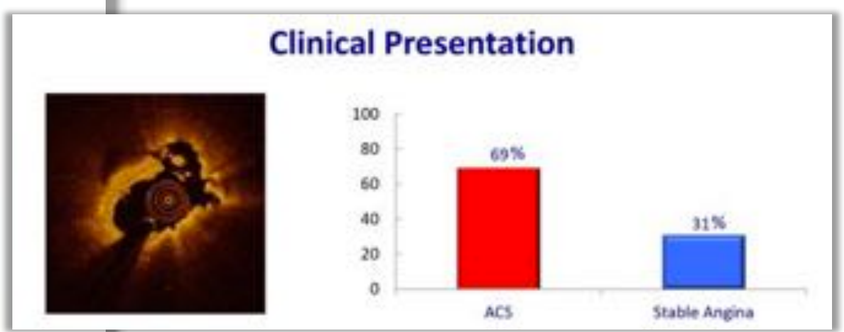
90 patients nécessitant au moins 2 angioplasties
Randomisés entre stent Synergy™ ou resolute Integrity™

OCT à l'implantation, 3 mois et 18 mois

Guagliumi G. TCT 2016

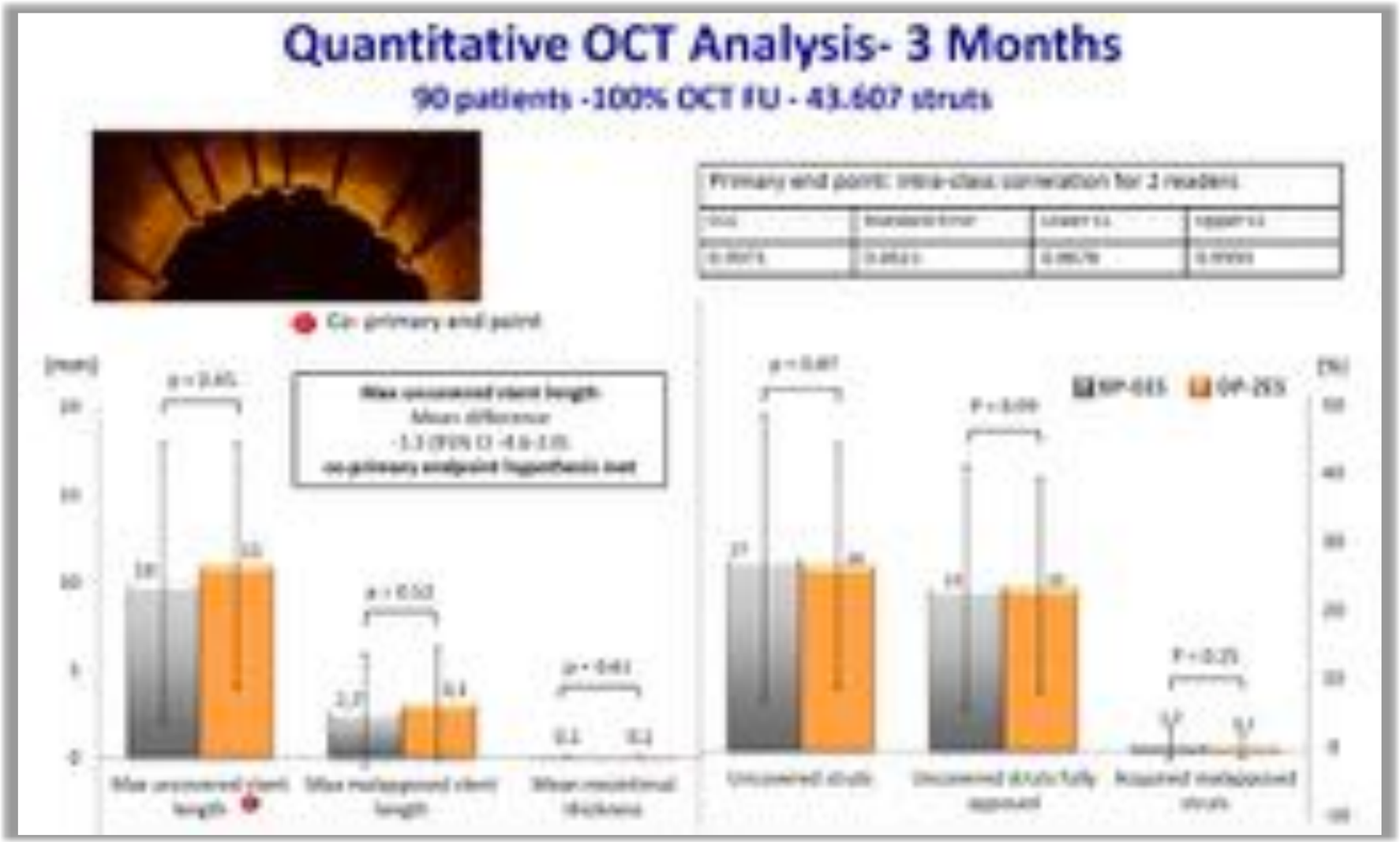
Couverture des stents





Guagliumi G. TCT 2016

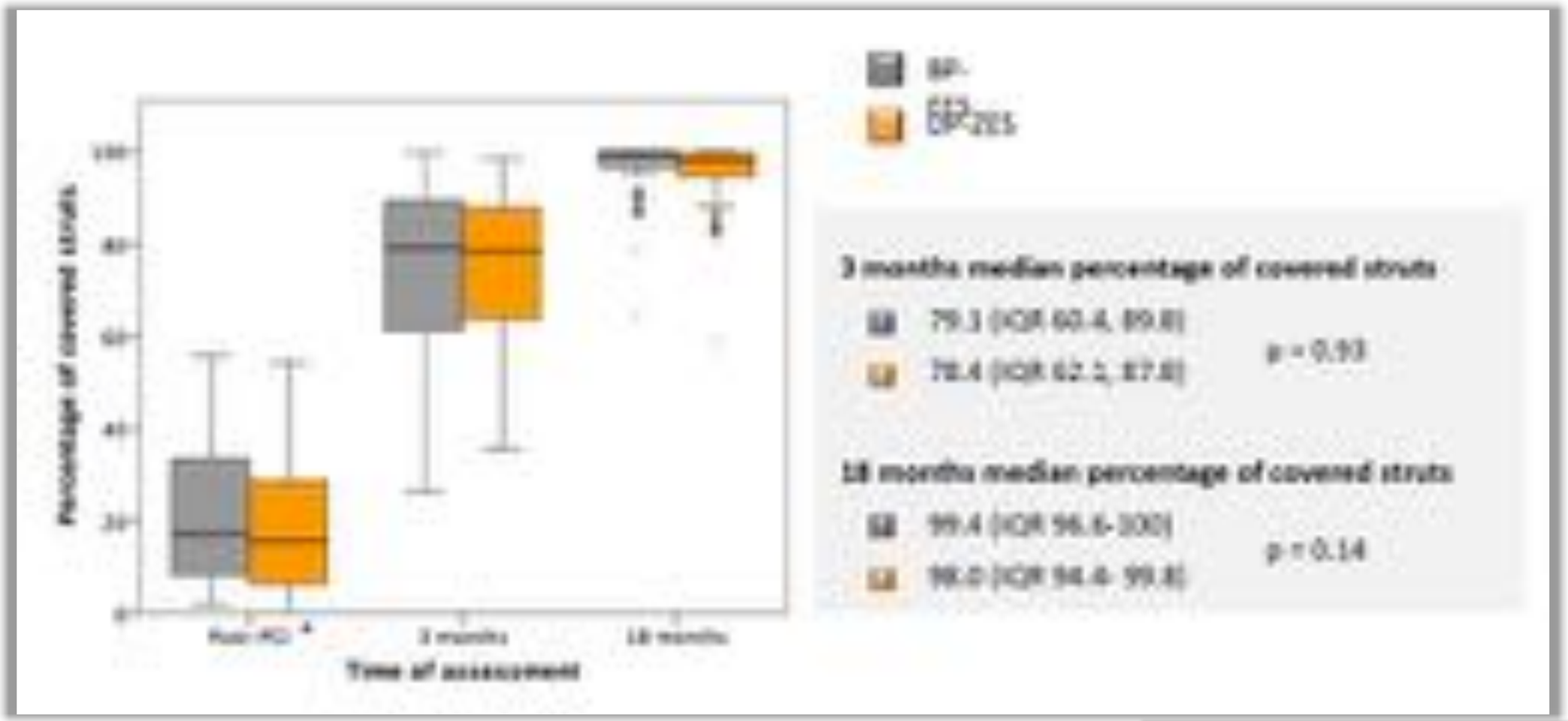
Couverture des stents



Guagliumi G. TCT 2016

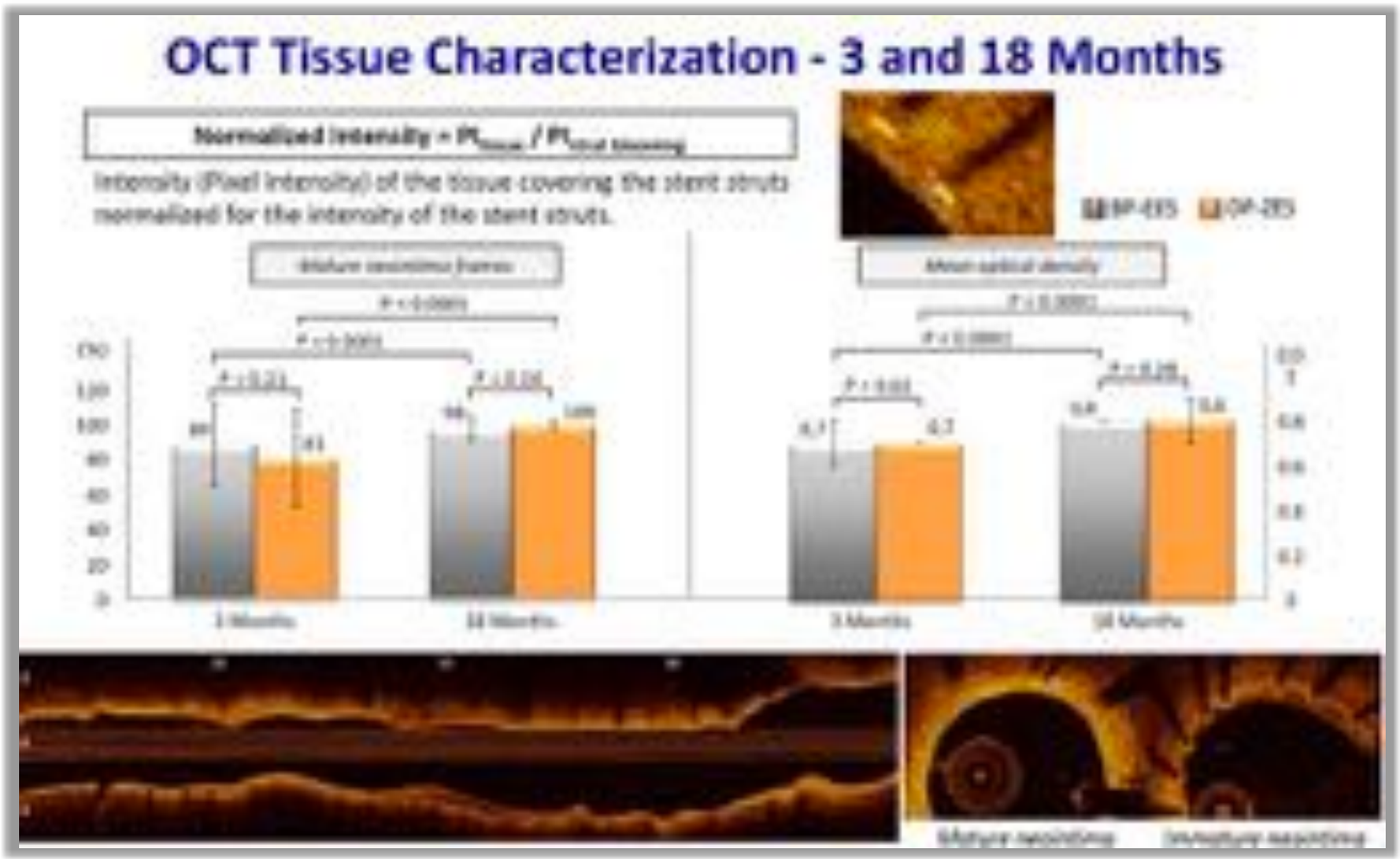
Couverture des stents

Evolution couverture des mailles



Guagliumi G. TCT 2016

Couverture des stents



Guagliumi G. TCT 2016

Couverture des stents

Analyse quantitative OCT à 18 mois

	BP-EES (N=43)	DP-ZES (N=44)	P value
Frames with uncovered struts, %	0.7 (0.0-3.4)	2.1 (0.0-5.6)	0.14
Frames with uncovered and apposed struts, %	0.7 (0.0-3.1)	1.8 (0.2-5.5)	0.09
Frames with malapposed struts, %	0.0 (0.0-0.3)	0.0 (0.0-0.4)	0.26
Mean malapposition area, mm^2	0.0 ± 0.0	0.0 ± 0.1	0.22
Net volume obstruction, %	18.3 (13.9-25.6)	15.1 (11.0-19.7)	0.03

Guagliumi G. TCT 2016

Thrombose de stent

Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial

ORSIRO
SYNERGY
RESOLUTE INTEGRITY

BIO-RESORT

Comparaison de 3 types DES 2ème génération

3514 patients randomisés (70% SCA)
Non infériorité entre les 3 types de stents

Suivi à 12 mois :

- **5% MACE** (cardiac death, MI, TVR)
- **0,3% Stent thrombosis**

Von Birgelen C. Lancet 2016

Thrombose de stent

Safety and Efficacy of Everolimus-Versus Sirolimus-Eluting Stents

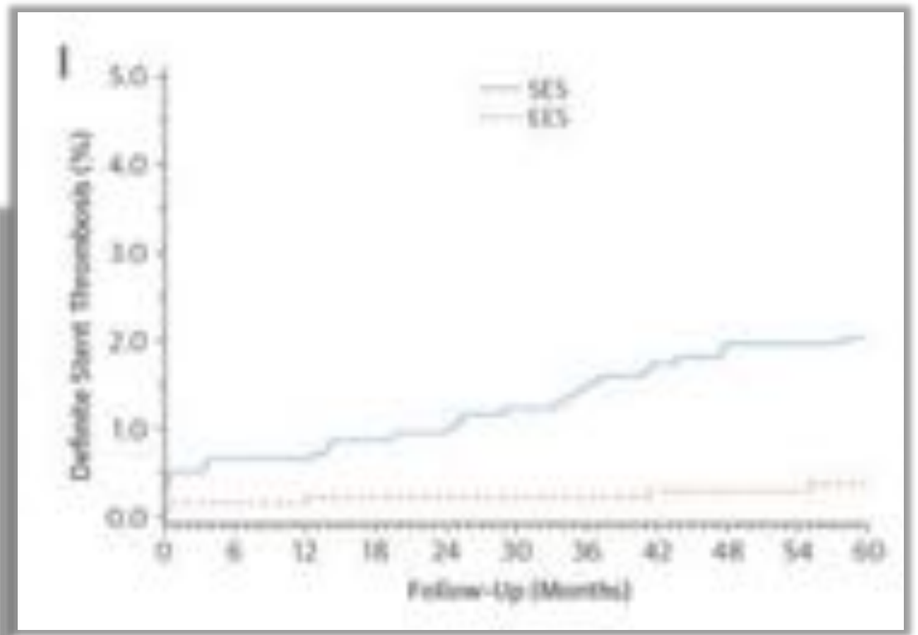
5-Year Results From SORT OUT IV

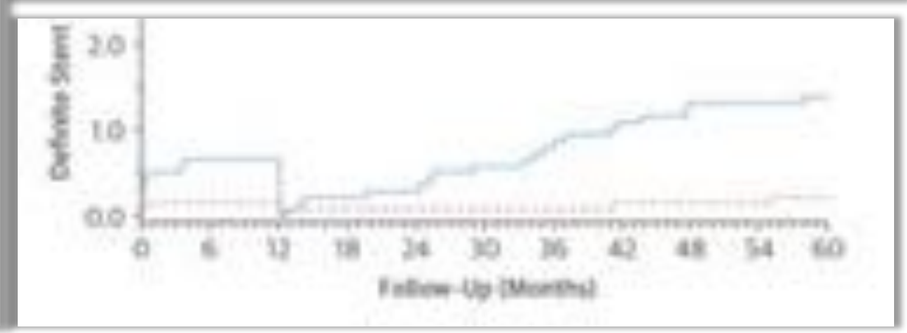
2771 patients randomisés stents EES vs SES
Suivi 3 ans

Suivi 5 ans

Thrombose avérée : 0,4% groupe EES vs 2% à 5 ans

<1mois : 0.1% vs 0.5%





L.O. Jensen. JACC 2016

Endothélialisation

Couverture des mailles :

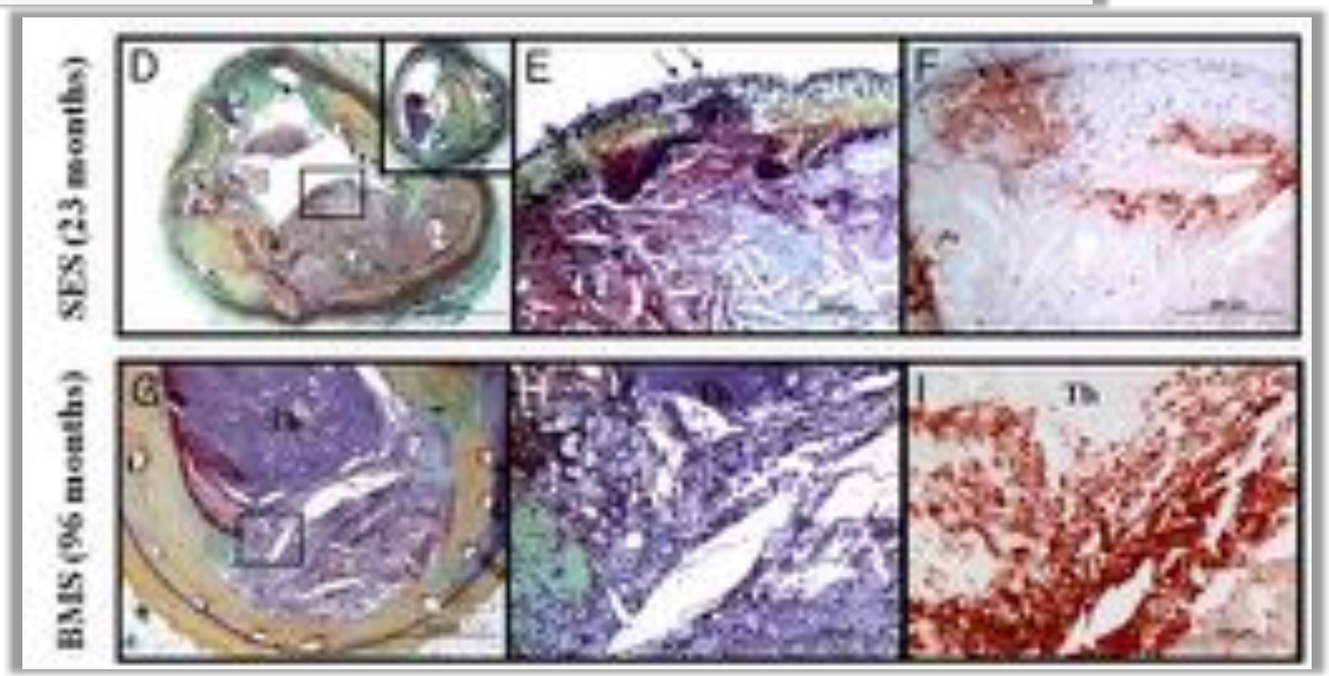
Toujours la même?

Néoathérosclérose

The Pathology of Neoatherosclerosis in Human Coronary Implants

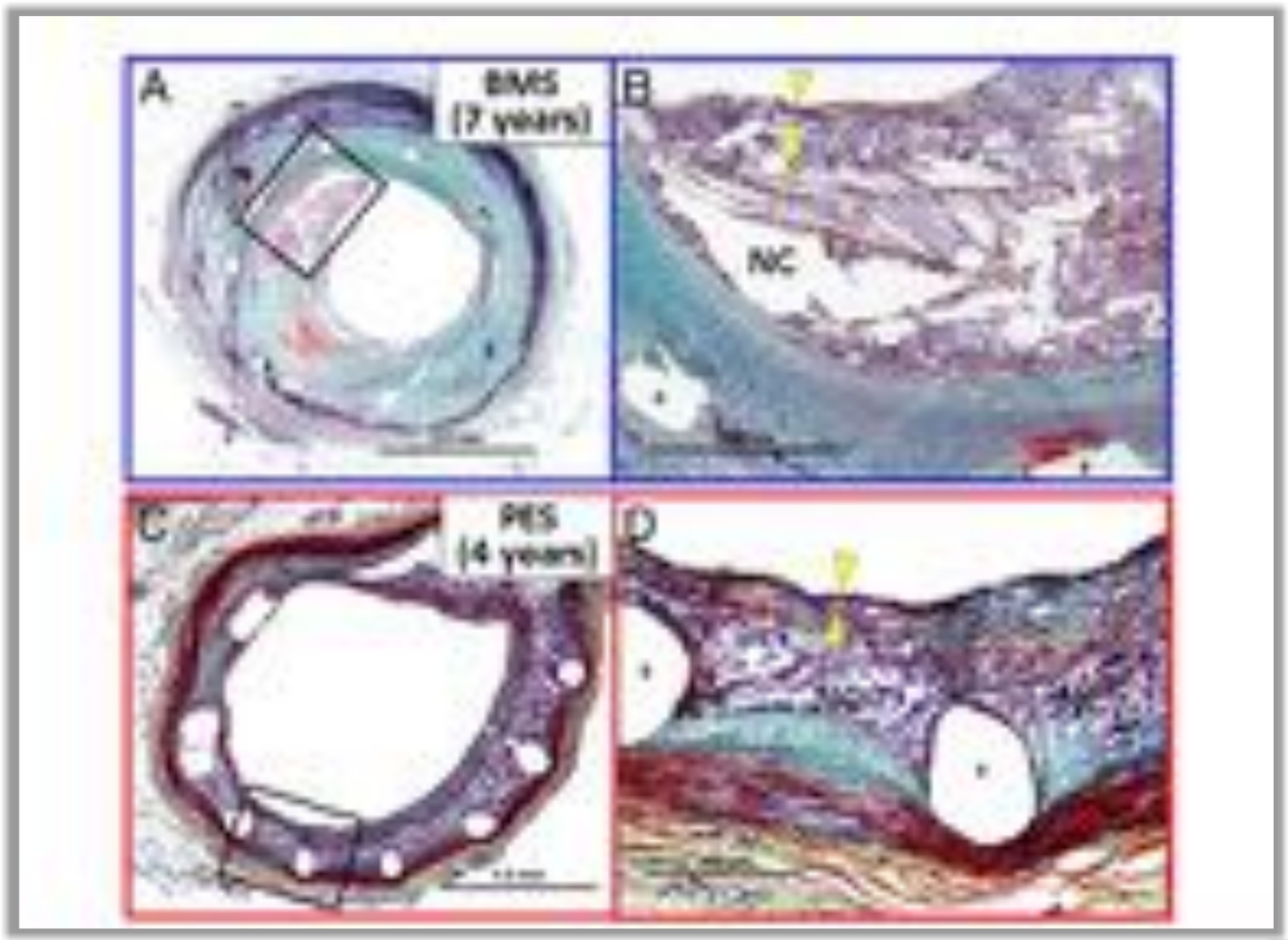
Bare-Metal and Drug-Eluting Stents

406 stents évalués en anapath
209 stents actifs (103 SES, 106 PES) (médiane 361 jours)
197 stents nus (médiane 721 jours)



Nakazawa, JACC 2011

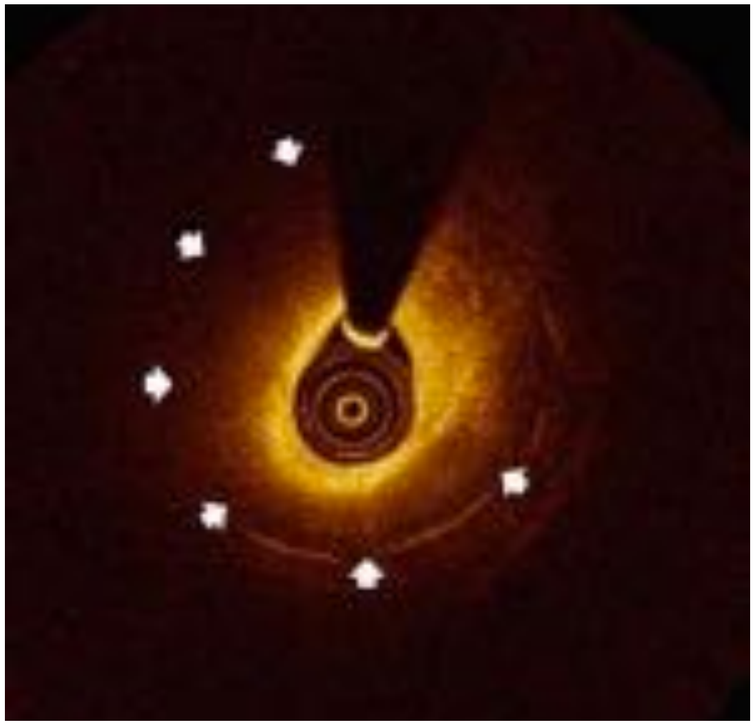
Néoathérosclérose

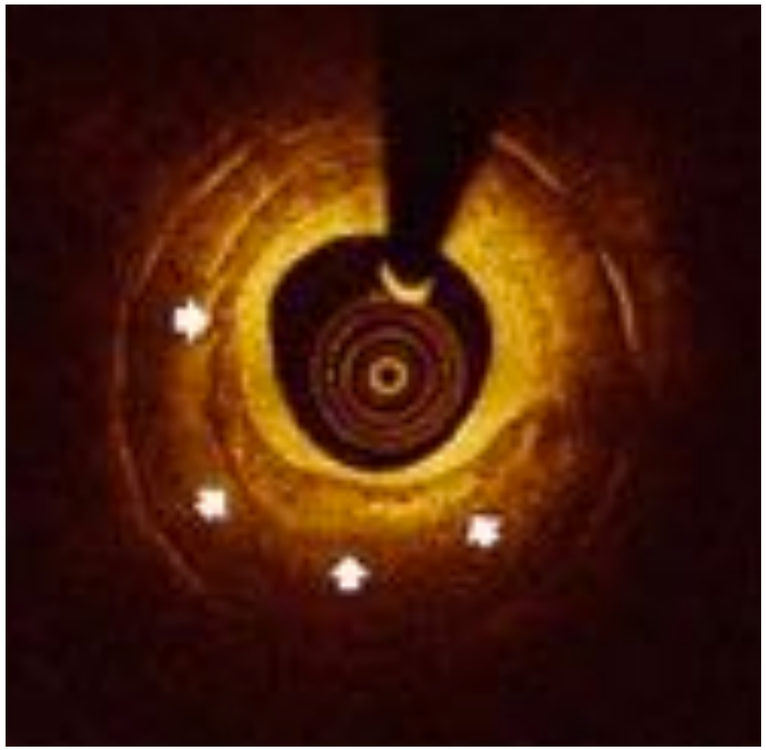


PARK SJ. JACC 2012

Néoathérosclérose

OCT et néoathérosclérose



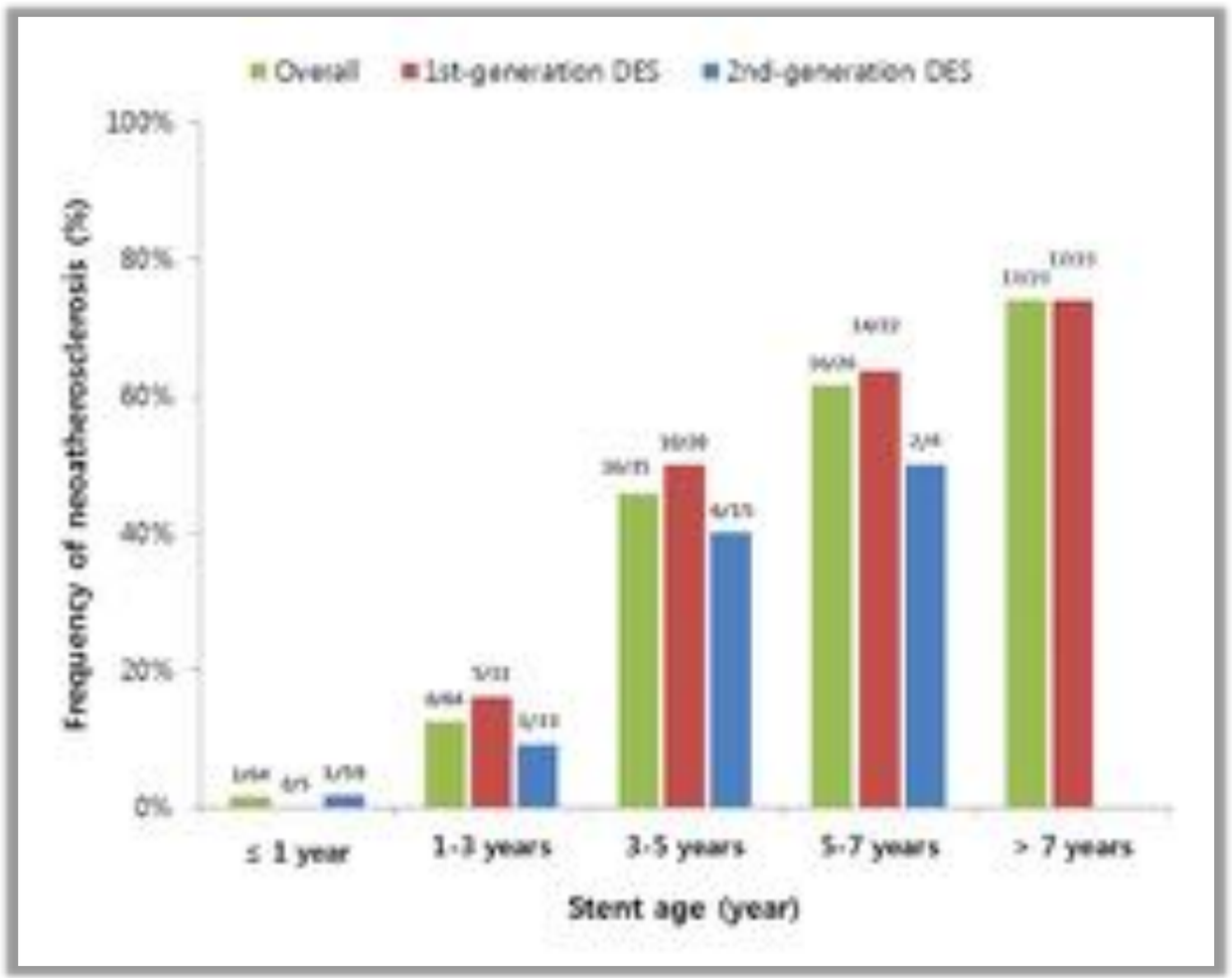


Définition néoathérosclérose présence plaque lipidique ou plaque calcifiée

Lee SY Circ interv 2015

Néoathérosclérose

OCT et néoathérosclérose



Prédicteurs Néoathérosclérose :

- **Insuffisance rénale (OR 4)**
- **LDL > 0.7g/l (OR 2.5)**
- **Age du stent (OR 1.7)**

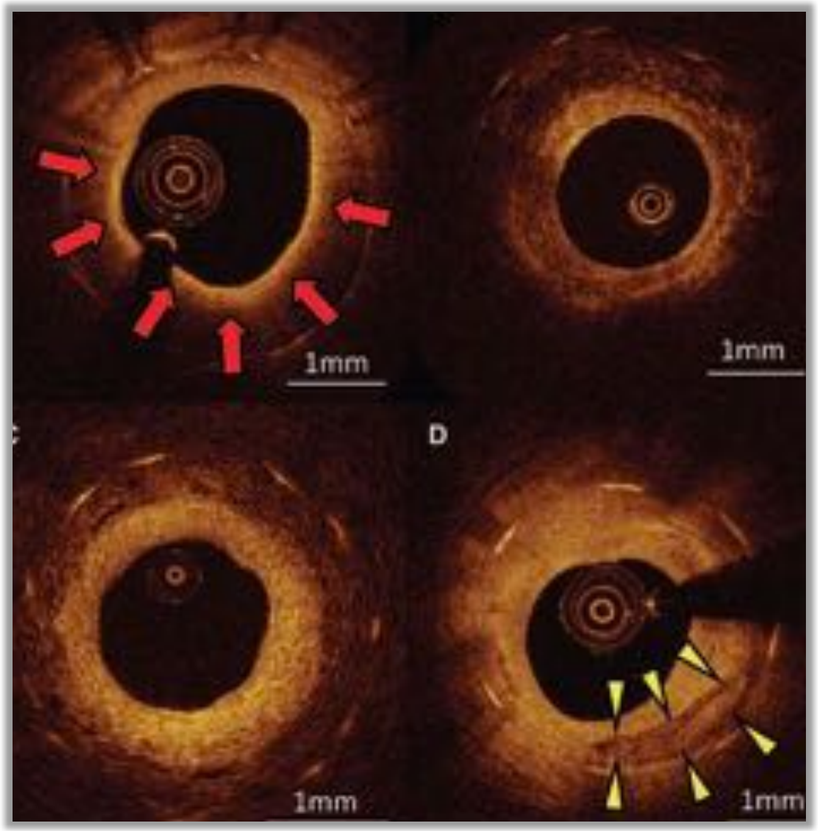
Patients avec néaothérosclérose
19% SCA au suivi vs 3.9%

Lee Circ SY interv 2015

Néoathérosclérose

OCT et néoathérosclérose

Predictors for Neoatherosclerosis
A Retrospective Observational Study From the Optical Coherence Tomography Registry



1080 patients ayant eu 0CT
179 stents analysés

Prédicteurs néoathérosclérose :

- **Stent âge > 48 mois (OR 4.48)**
- **Insuffisance rénale (OR 4.42)**
- **DES (OR 2.66)**
- **Tabagisme actif (OR 2.3)**
- **Âge > 65ans (1.91)**

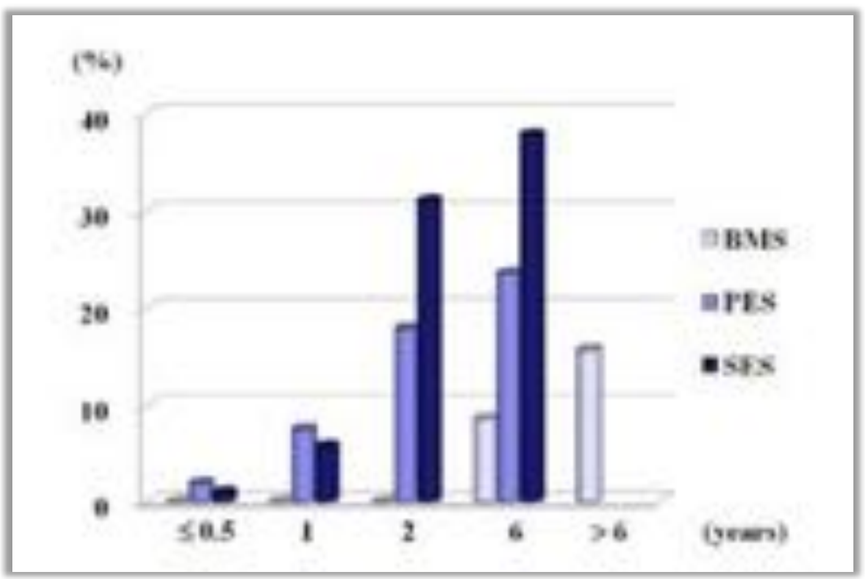
Yonetsu T. Circ Cardiov Imaging 2012

Néoathérosclérose

Incidence Néoathérosclérose en fonction délai implantation

	BMS (197 Lesions)	DES All (SES + PES) (209 Lesions)	DES SES (103 Lesions)	DES PES (106 Lesions)	p Value BMS vs. DES (SES + PES)
Duration with any neoatherosclerosis, days	2,160 (1,800–2,880)	420 (361–683)	450 (361–660)	383 (270–721)	< 0.001
Incidence of any neoatherosclerosis					
≤2 yrs	0/88 (0)	51/177 (29)	32/87 (37)	19/90 (21)*	< 0.001
>2 yrs, ≤6 yrs	17/76 (22)	13/32 (41)	7/16 (44)	6/16 (38)	0.053
>6 yrs	14/33 (42)	—	—	—	—
All	31/197 (16)	64/209 (31)	39/103 (38)	25/106 (24)†	< 0.001

Néoathérosclérose plus précoce après DES
Et plus fréquente : <u>31 vs 16%</u>

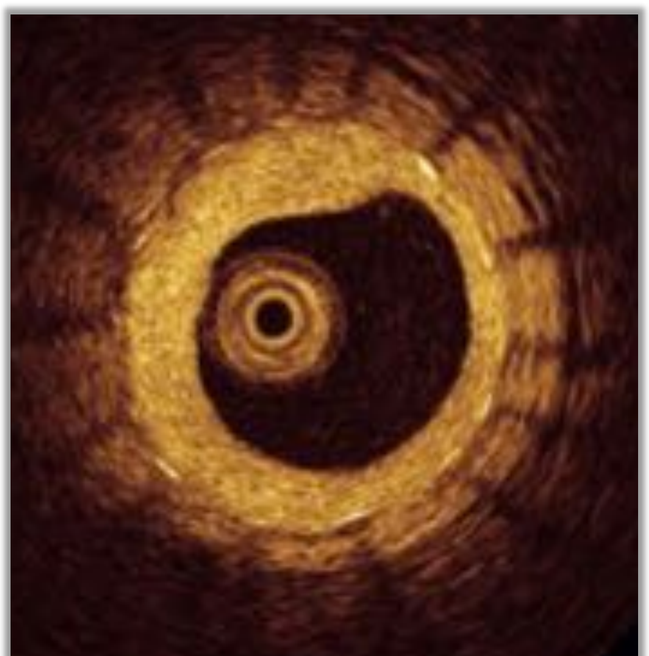


Nakazawa, J Am Coll Cardiol 2011

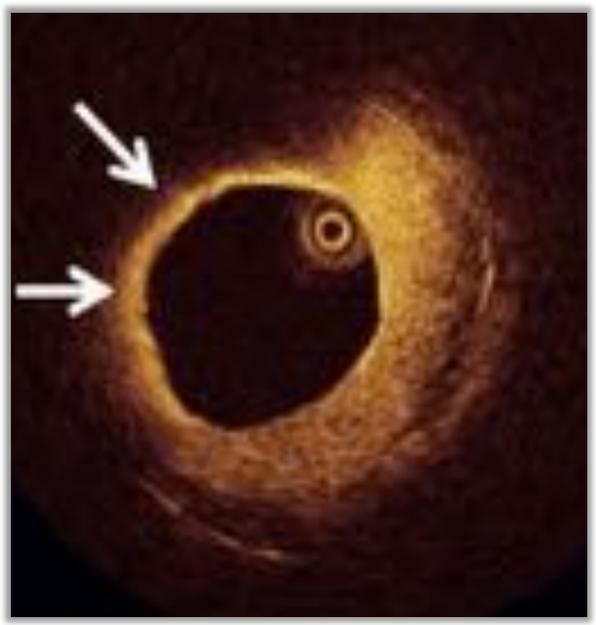
Néoathérosclérose

Analyse néointima 152 stents avec >50% sténose
128 DES
24 BMS

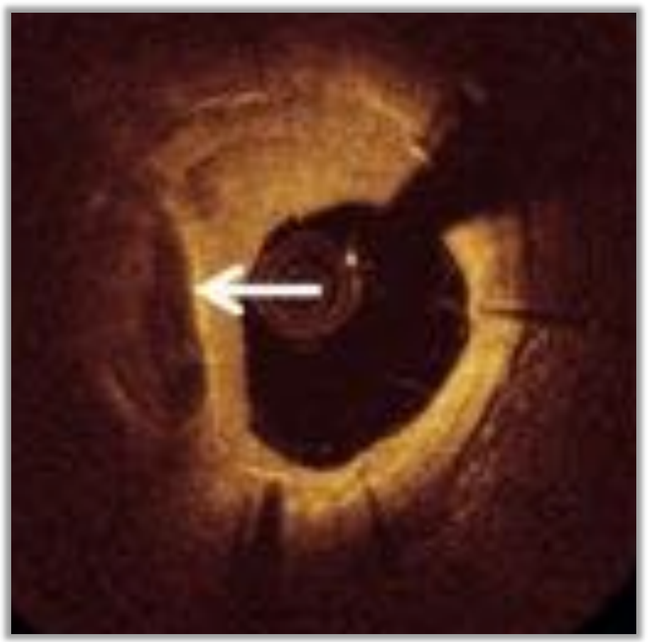
Néoathérosclérose



Néointima homogène



Plaque lipidique



Plaque calcifiée

Lee SY. Eurointervention 2013

Néoathérosclérose

35% diagnostic néoathérosclérose

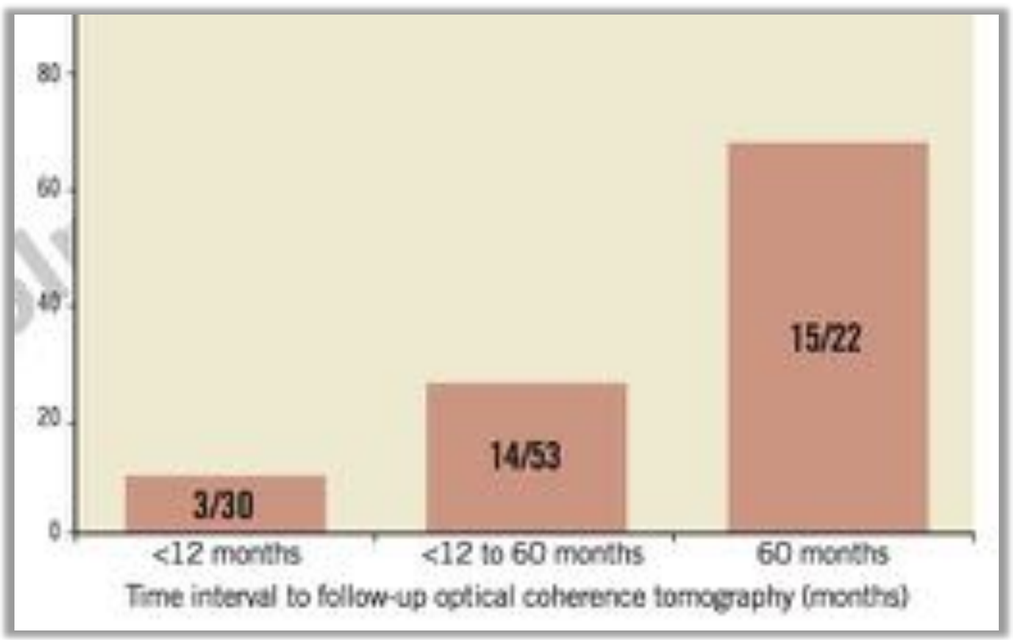
Délai médian suivi :

- **70 mois néoathérosclérose**
- **13 mois sans**

58 mois DES et 129 mois BMS

14% thrombose vs 0%

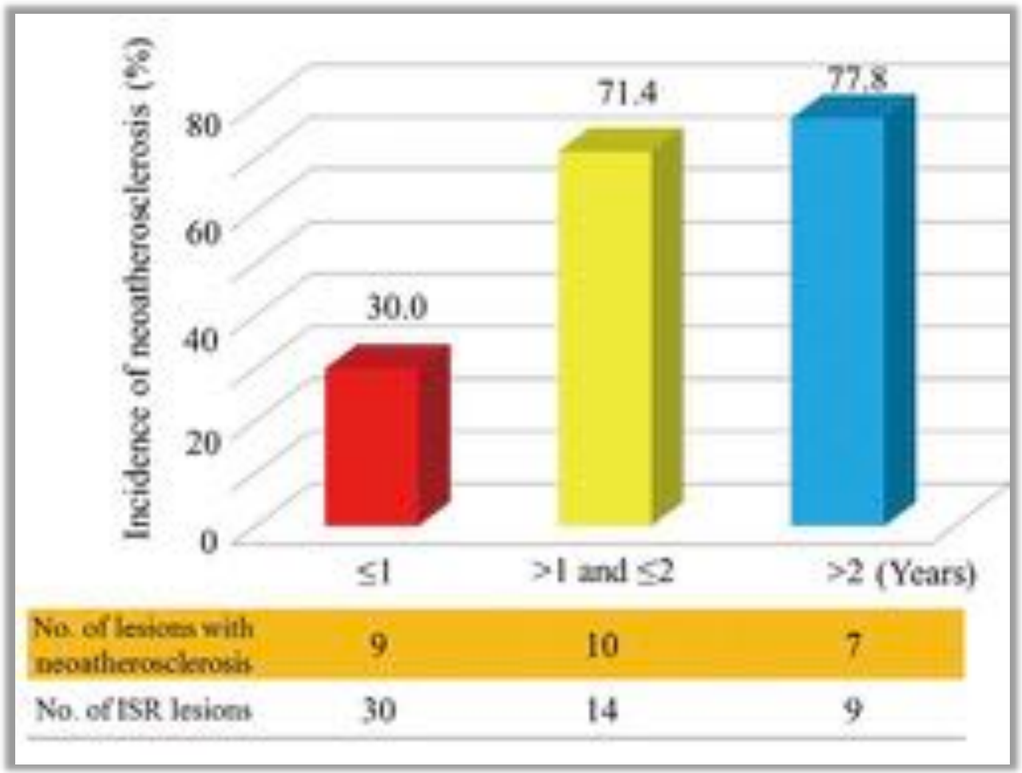
Fréquence néoathérosclérose DES



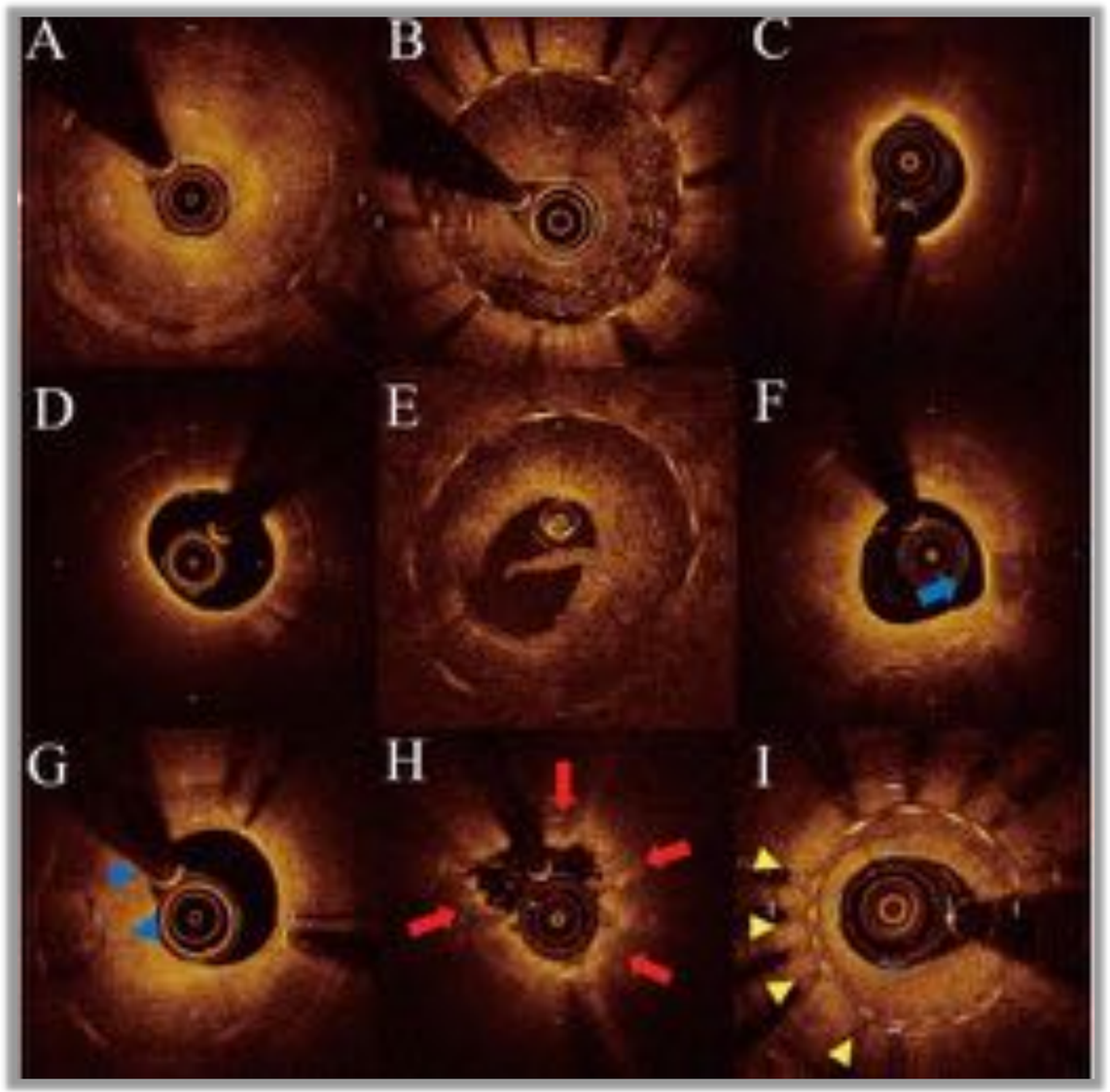
Lee SY. Eurointervention 2013

Néoathérosclérose

53 patients avec resténose intrastent stent de 2ème génération



No. of lesions with neoatherosclerosis	9	10	7
No. of ISR lesions	30	14	9



Jinnouchi H Circ J 2017

Néoathérosclérose

- N=65 patients with ISR (n=14 BMS ; n=51 DES)
- OCT +NIRS analysis
- PCI-ISR median duration: 33 months

Table 3. LCBI and OCT Findings in BMS and DES

	BMS (n=14)	DES (n=51)	*P* Value
Neoatherosclerosis, n (%)	5 (36)	35 (68)	0.02
Minimal cap thickness, μm (IQR)	141 (112–158)	61 (53–80)	0.03
TCNA, n (%)	1 (7)	24 (47)	0.01
Multiple TCNA, n (%)	1 (7)	10 (19)	0.27
Neovascularization, n (%)	5 (36)	15 (29)	0.65
Calcium, n (%)	8 (57)	17 (33)	0.10
Thrombi, n (%)	0	5 (10)	0.22
Red thrombi, n (%)	0	1 (2)	0.59
Intimal rupture, n (%)	0	6 (12)	0.17

Table 4. Incidence of Neoatherosclerosis by Duration Since Implant

	BMS (n=5)	DES (n=35)	*P* Value
Months (IQR)	36 (15–113)	33 (16–60)	0.45
<2 y	3 (60)	13 (37)	
2–6 y	0	21 (60)*	
>6 y	2 (40)	1 (3)*	0.01

BMS indicates bare-metal stent; DES, drug-eluting stent; IQR, interquartile range; and ISR, in-stent restenosis.

**P* vs intragroup comparison. χ^2 test.

Ali ZA et al , Circ Cardiovasc Interv 2013

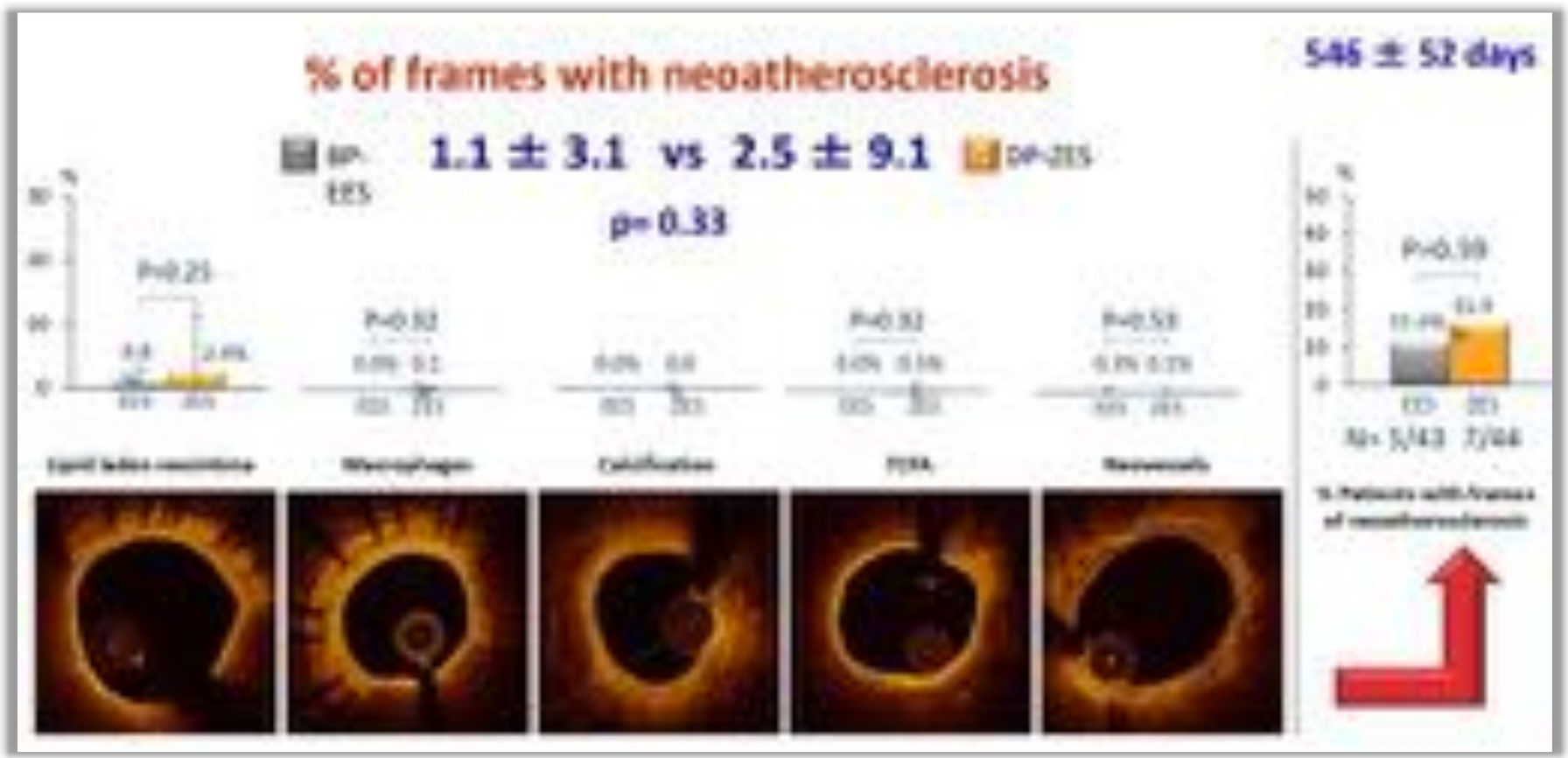
Couverture des stents

	BP-EES SYNERGY™ (N=45)	DP-ZES RESOLUTE™ (N=45)	P value
3-months follow-up, n (%)			
Death	0	0	-
Myocardial infarction	0	1 (2.2)	1.0
Stent thrombosis	0	0	-
TLR	0	0	-
Stroke	0	0	-
18-months follow-up, n (%)			
Death	1 (2.2)	1 (2.2)	1.0
Cardiac	0	0	-
Non cardiac	1 (2.2)	1 (2.2)	1.0
Myocardial infarction	2 (4.4)	1 (2.2)	1.0
Stent thrombosis	0	0	-
TLR	2 (4.4)	2 (4.4)	1.0
TVR	1 (2.2)	1 (2.2)	1.0
Stroke	1 (2.2)	1 (2.2)	1.0

Guagliumi G. TCT 2016

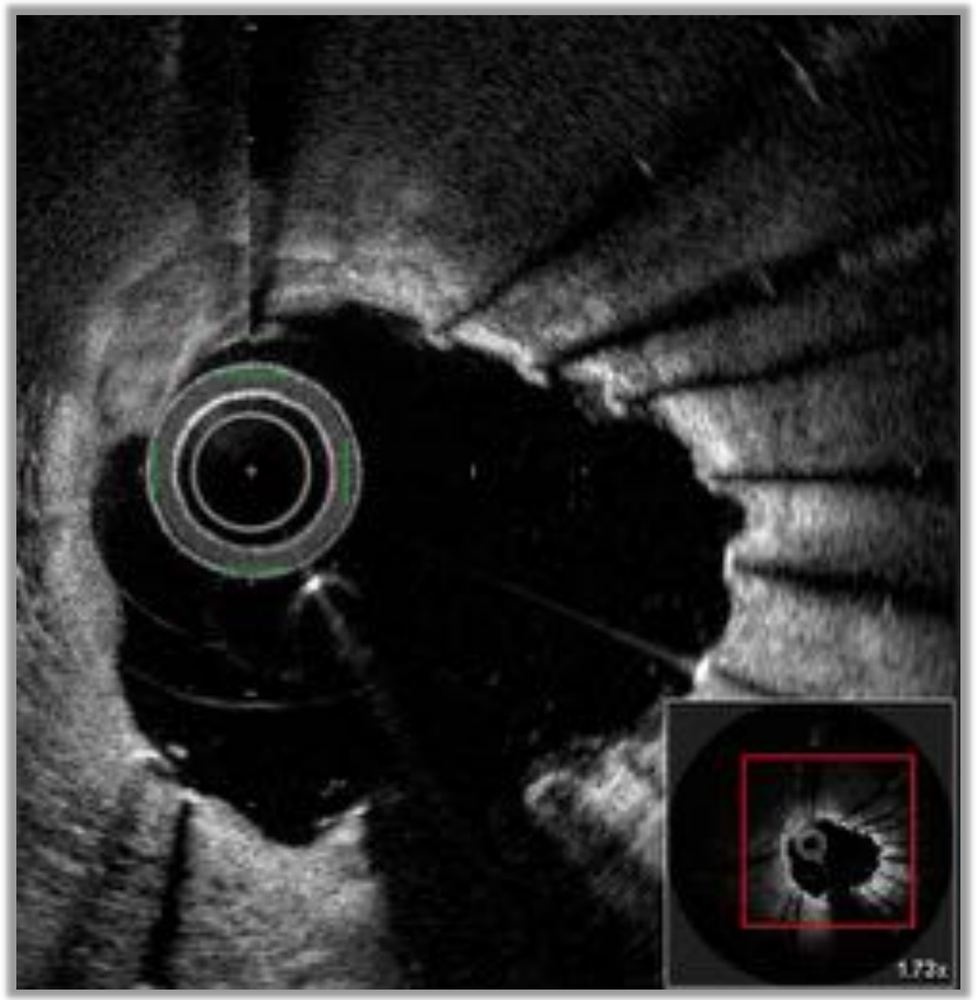
Couverture des stents

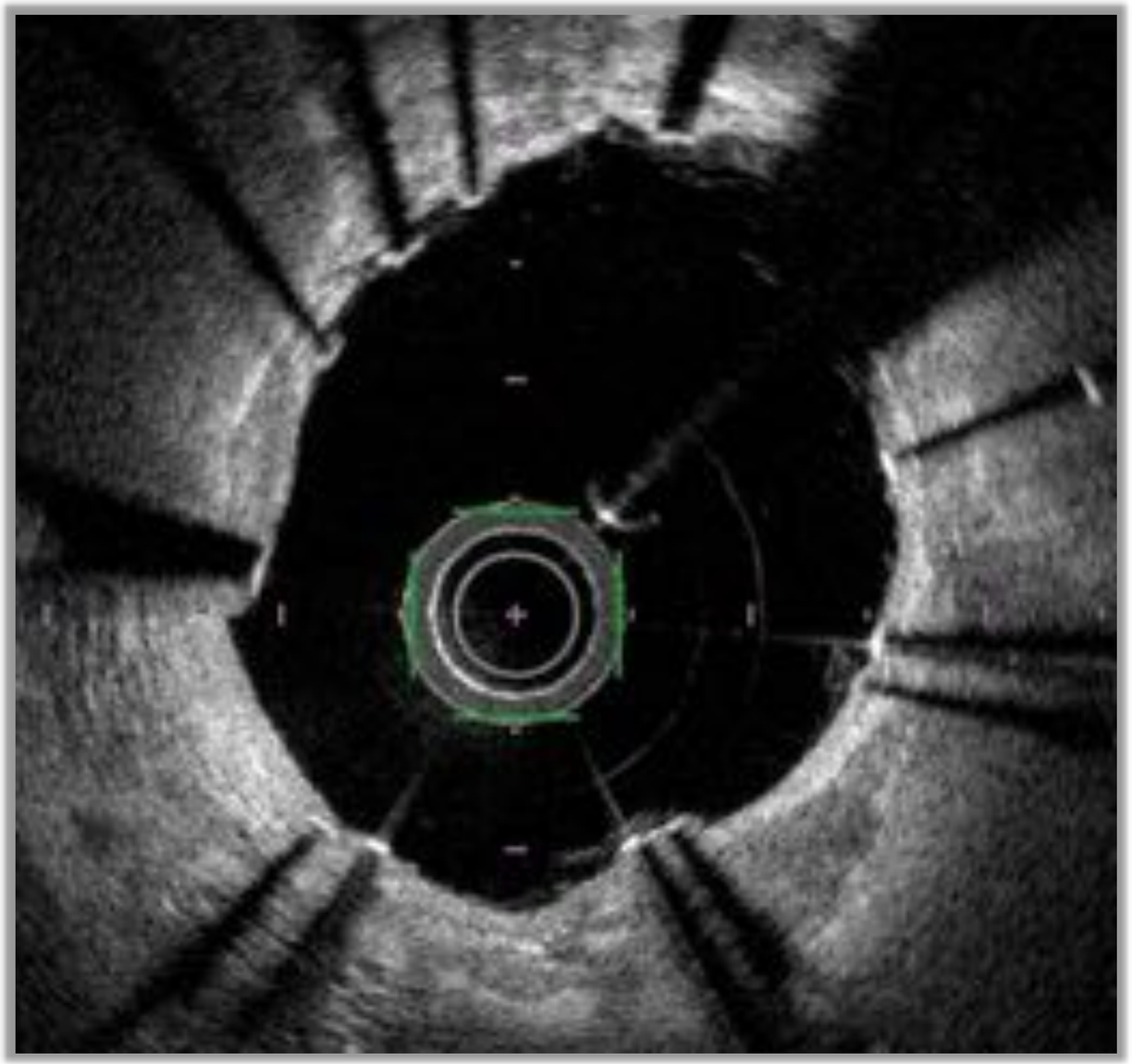
Néoathérosclérose en OCT à 18 mois
87/88 patients, 42262 struts



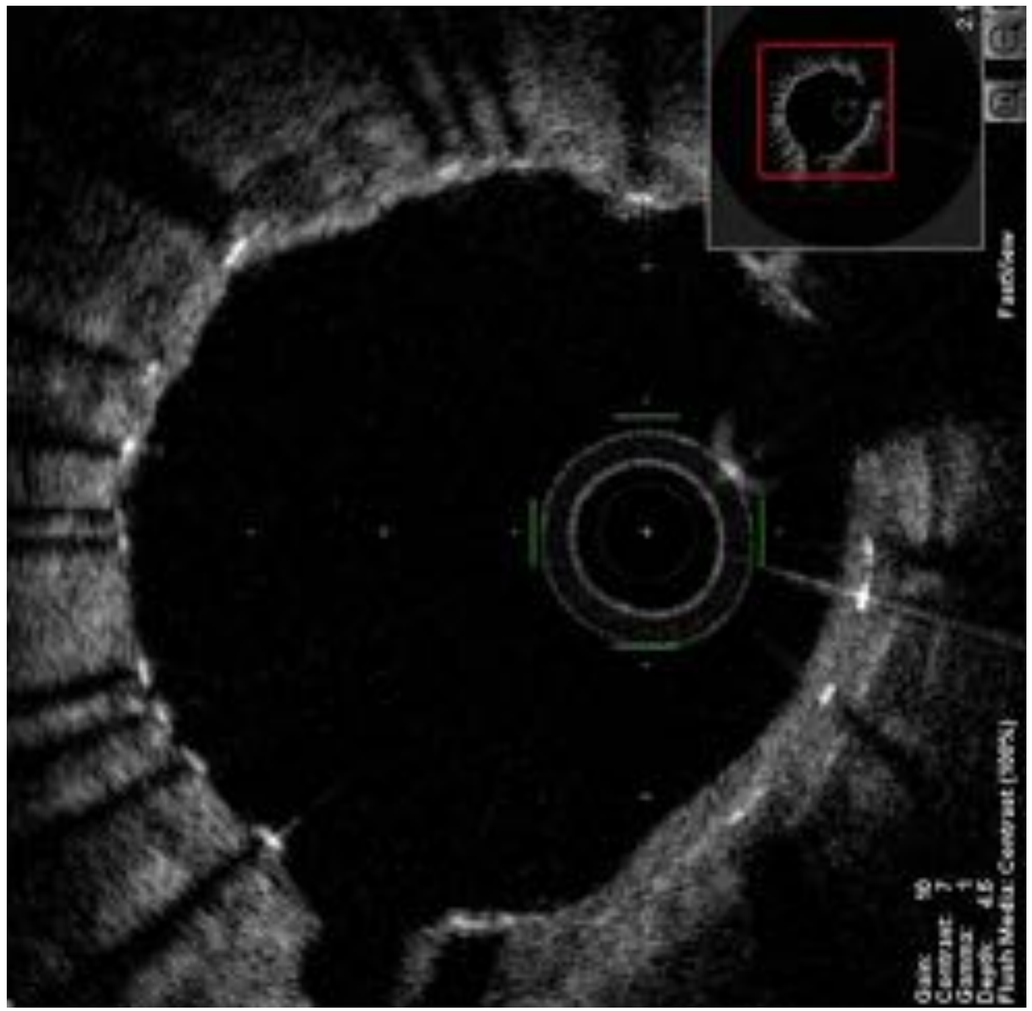
Guagliumi G. TCT 2016

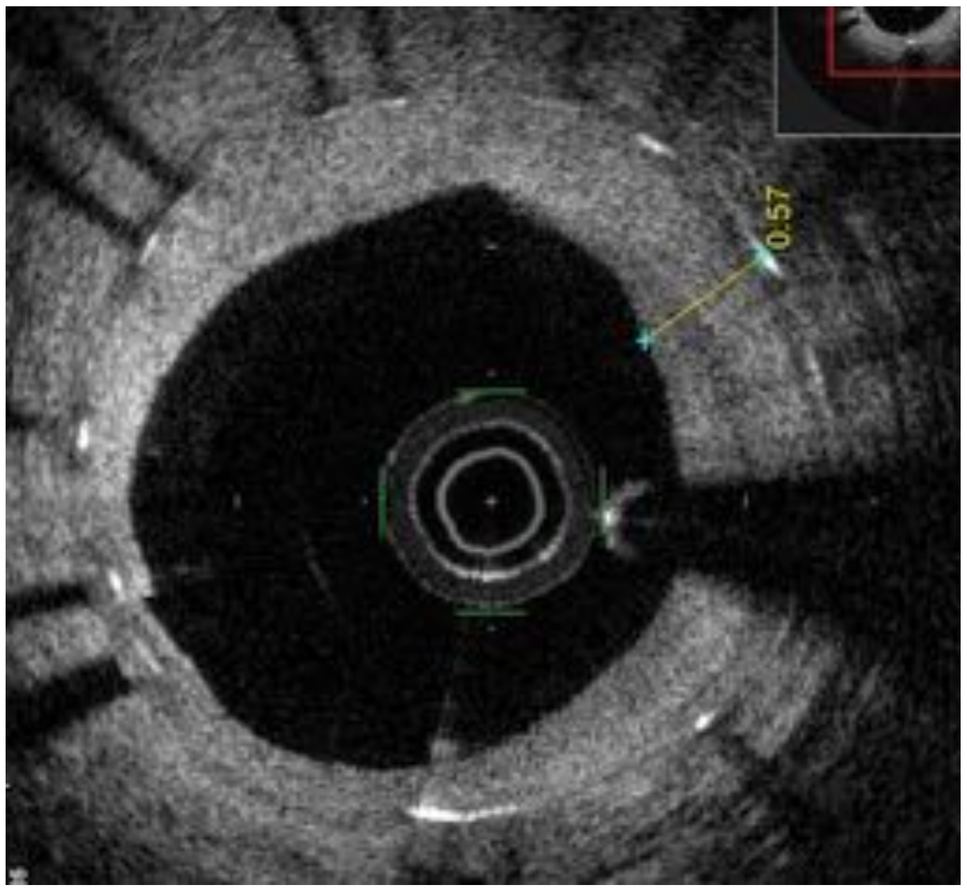
Couverture des stents



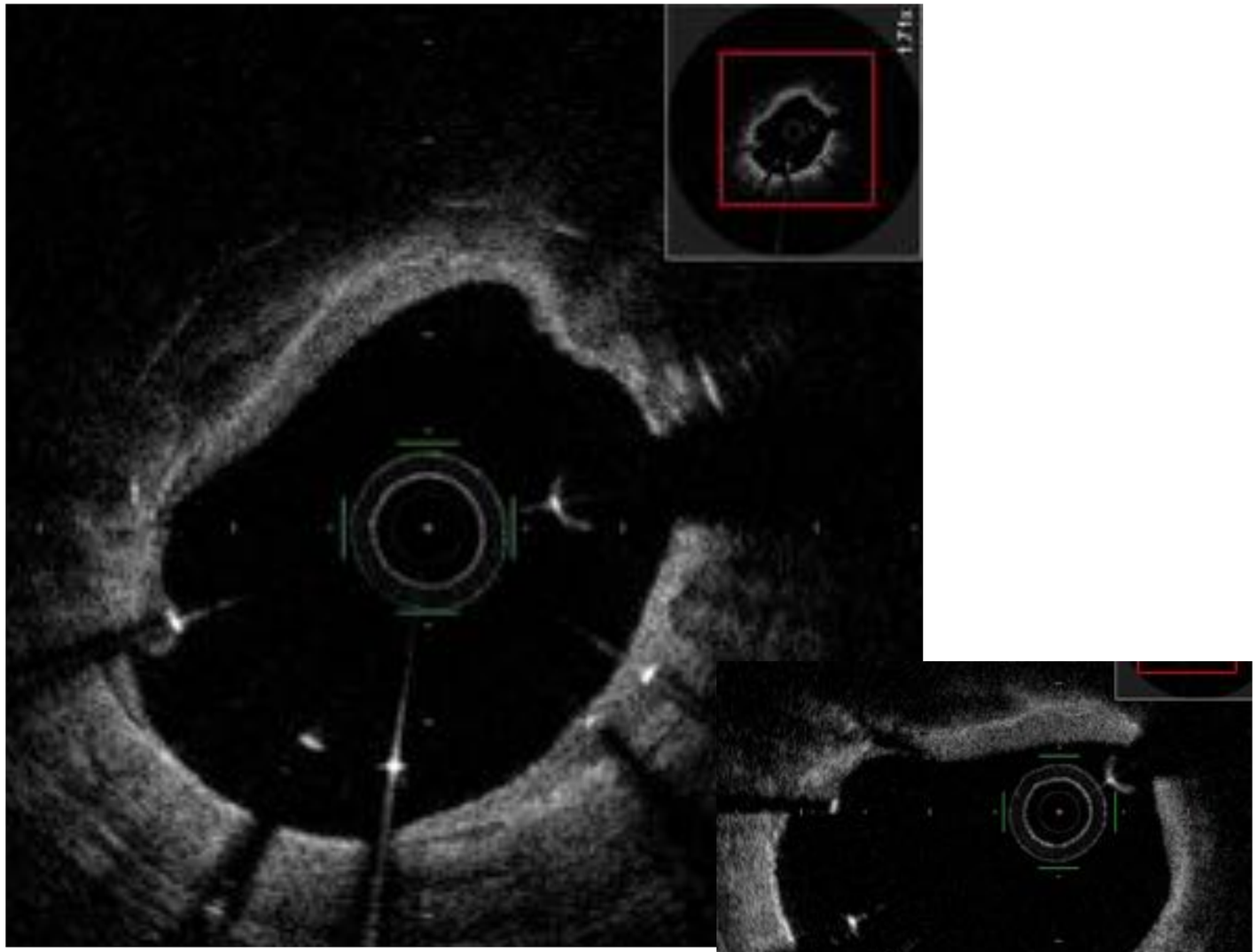


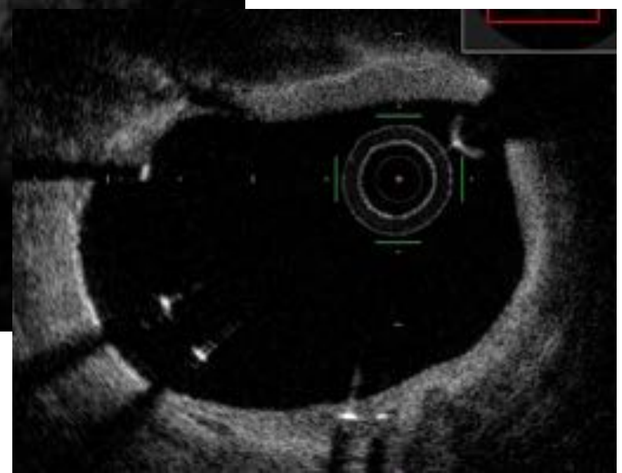
Couverture des stents

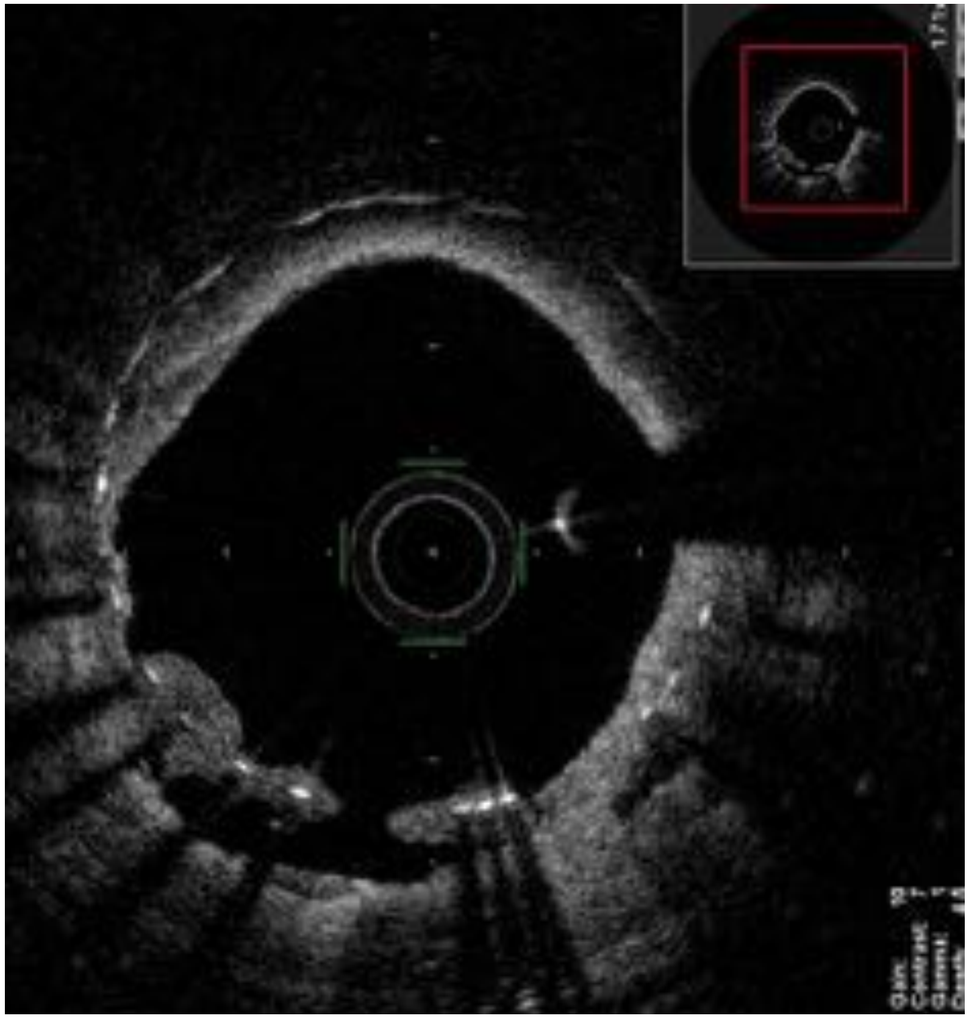




Couverture des stents



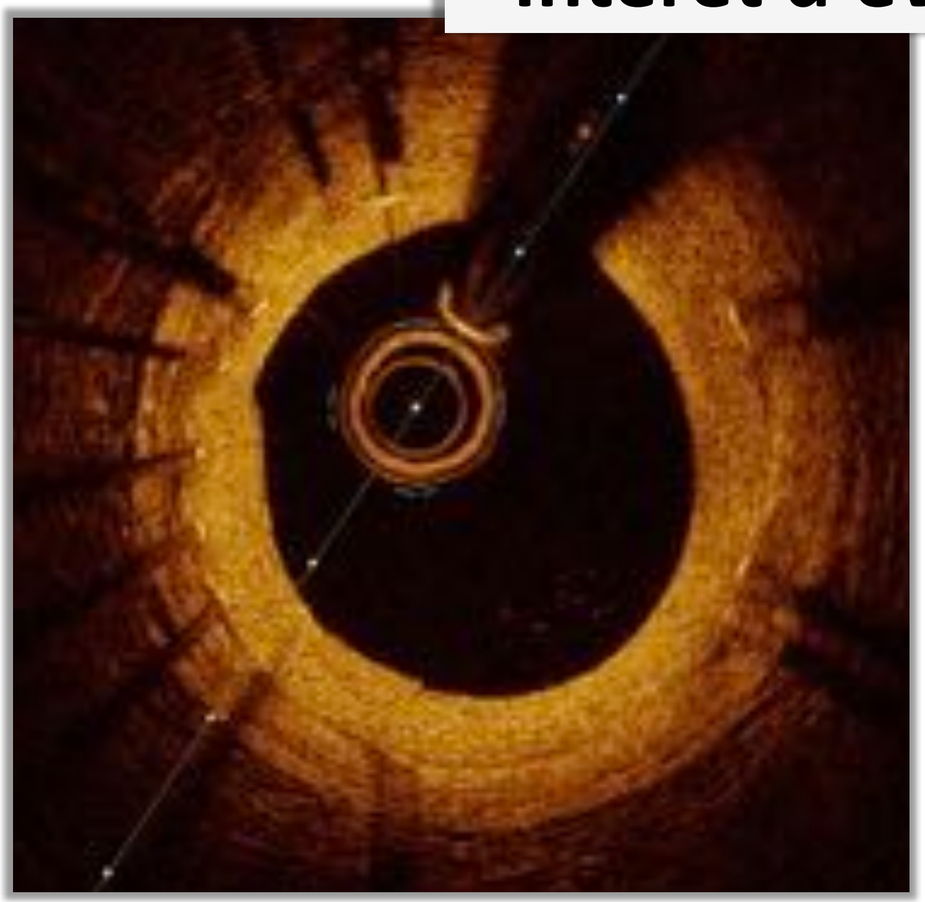


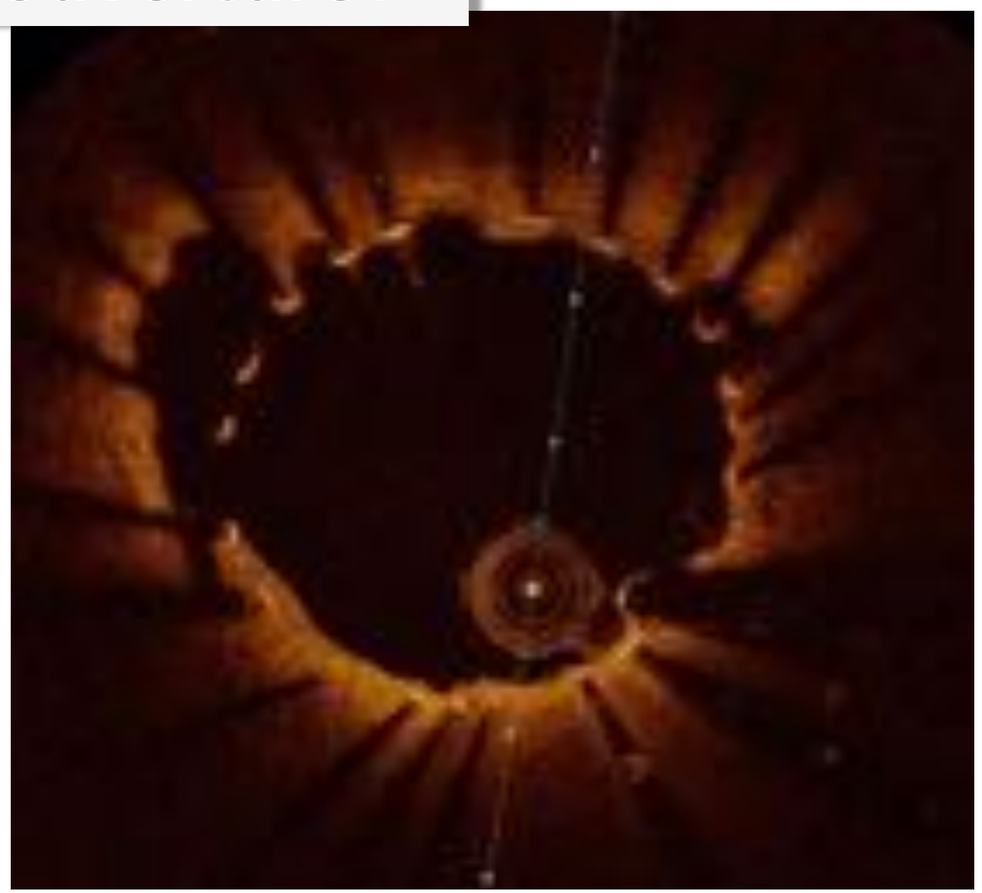


Mailles couvertes?

Couverture des stents

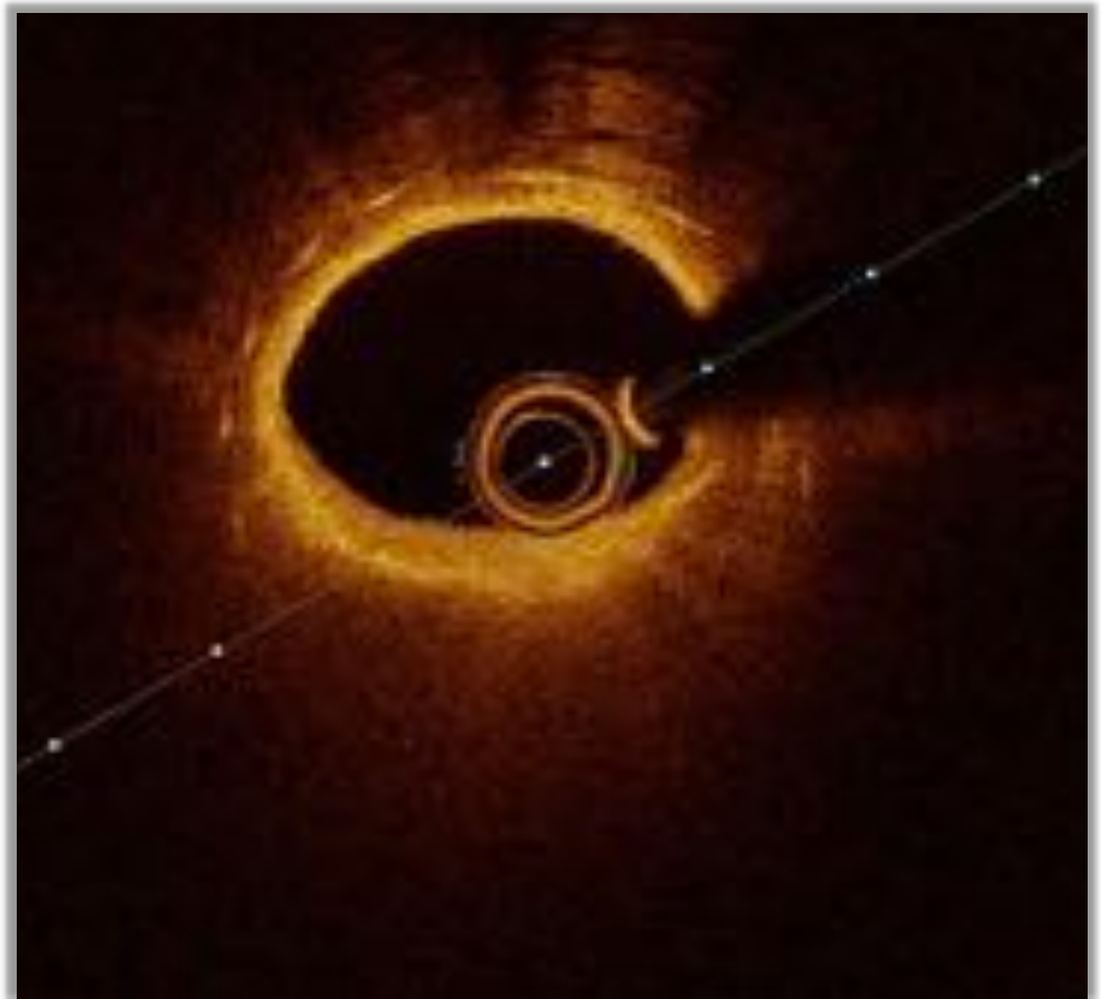
OCT avant chirurgie?
Intérêt d'évaluer la couverture?

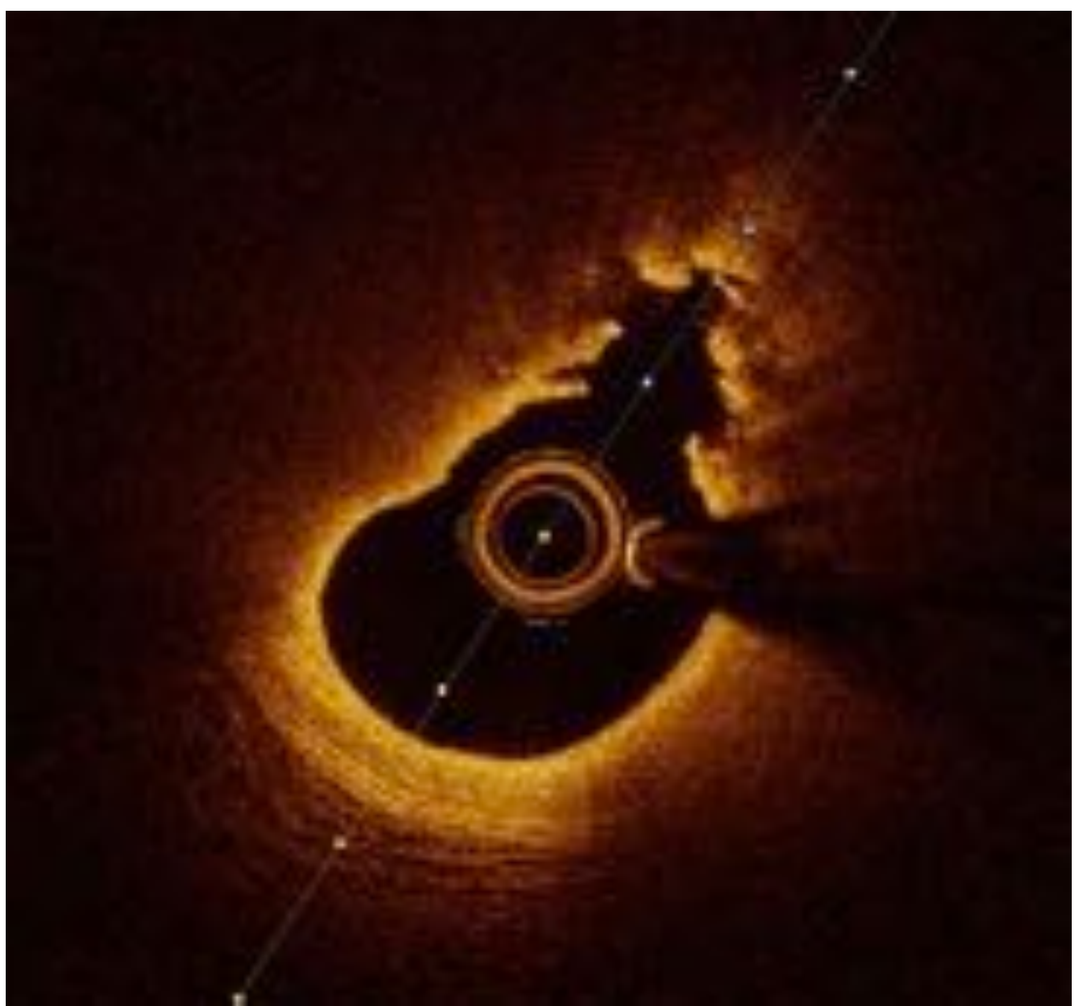




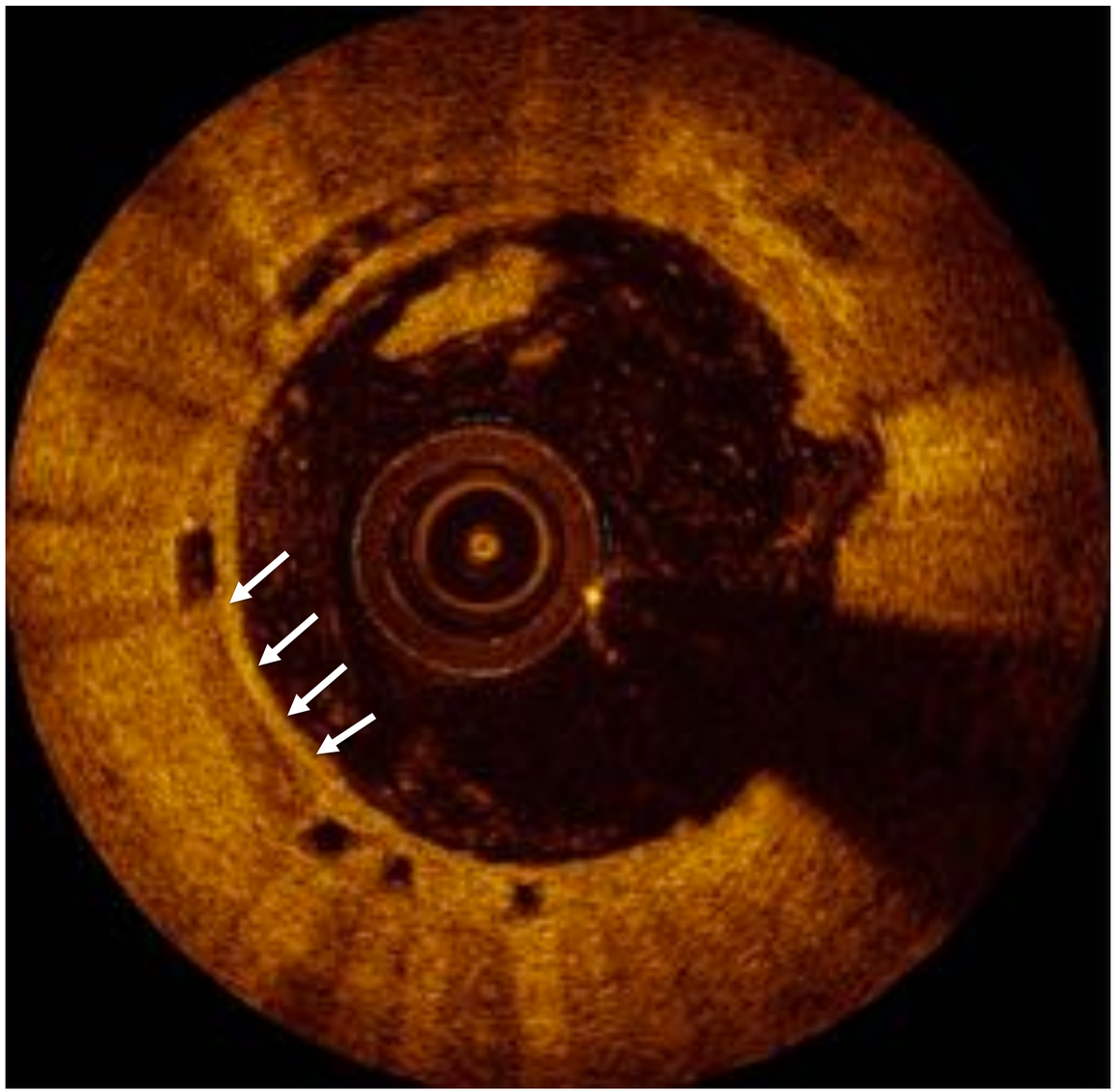
Couverture des stents

Thrombose intrastent actif à 8 ans





Thrombose de stent



<u>Thrombose de BVS</u>

Zones de faible intensité du signal autour des struts

En corrélation avec inflammation sur études histologiques

Rapportés dans les thomboses tardives et très tardives de BVS

CONCLUSION

- **OCT outil évaluation endothélialisation**
- **Stents actifs dernière génération : meilleurs résultats cliniques**
- **Différents types endothélialisation**
- **Néoathérosclérose facteur de risque thrombose**