

For DES: Time-honored Treatment, The Older One is Better

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Cardiovascular Research Foundation



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- Eight different DCB products are currently available for human use
- While all 8 products deliver paclitxel, there is no good data comparing pharmacokinetics among them (and in some cases no data at all); and major differences are probable.
- It is hard to transfer data from one product to another
- A class-effect cannot be presumed.
- There is randomized data for only 2 of 8 products.

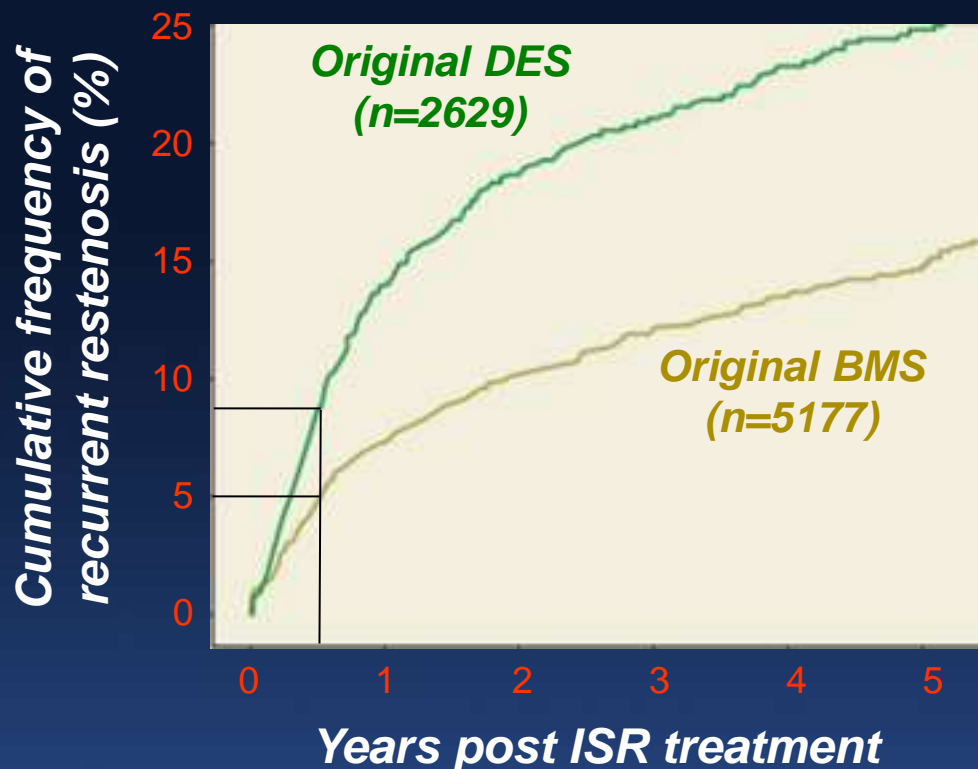
Trial	#	BMS or DES	Device	Control	1° endpoint	Winner ?
Paccocath ISR-I	52	?	Paccocath	Balloon	6 mo LLL	DCB
Paccocath ISR-II	108*	?	Paccocath	Balloon	6 mo LLL	DCB
PEPCAD-II	131	BMS	SeQuent Please	TAXUS	6 mo LLL	DCB
Habara et al	50	SES	SeQuent Please	Balloon	6 mo LLL	DCB
PEPCAD-DES	110	DES	SeQuent Please	Balloon	6 mo LLL	DCB
ISAR DESIRE-III	402	Limus-ES	SeQuent Please	Balloon or PES	6-8 mo DS	DCB or DES
PEPCAD China ISR	220	DES	SeQuent Please	TAXUS	9 mo LLL	-
Habara et al	208**	Both	SeQuent Please	Balloon	6 mo TVR	DCB

**included pts in Paccocath ISR-I*

***?included pts in previous publication*

- There is modest data on 1 product (SeQuent Please), minimal data on a 2nd product (Paccocath), and no data on 6 other products.
- The most common primary endpoint was LLL, typically at 6 months. The only study with a clinical endpoint measured TVR, but also only at 6 months. We know from experience that catheter-based treatment of ISR is rarely durable; and 6 months does not tell the whole story (especially the whole clinical story!) and is, quite frankly, misleading.
- In 6 of 8 studies, “controls” were treated with balloon angioplasty. We know from experience that balloon angioplasty is the least durable of catheter-based treatments of ISR.
- We have no *long-term* data.

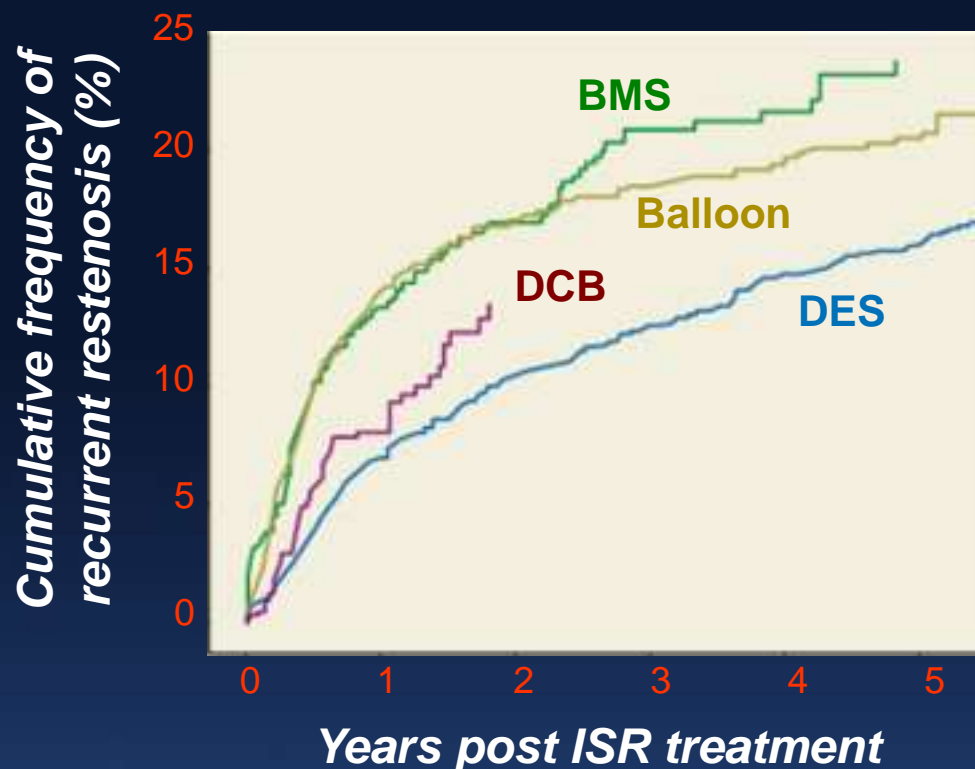
Cumulative crude incidence of recurrent restenosis independent of ISR treatment modality in 7806 ISR patients from SCAAR



at risk

DES	5177	3988	3137	2284	1539	897
BMS	2629	1757	1284	938	652	423

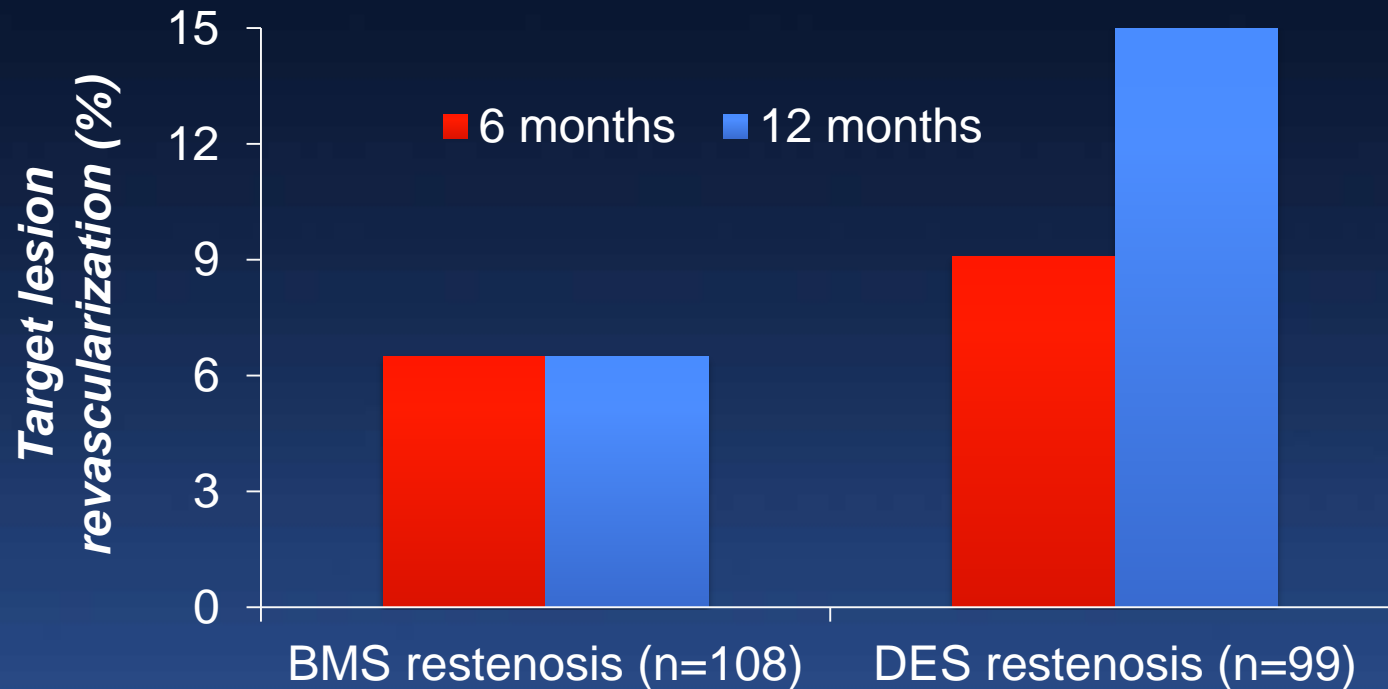
Cumulative crude incidence of recurrent restenosis relative to treatment modality in 7806 ISR patients from SCAAR



at risk

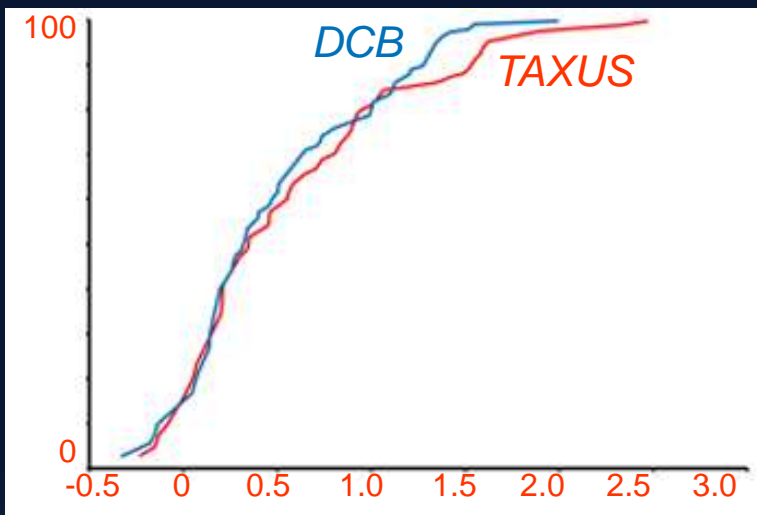
DES	4335	3436	2714	1832	1389	870
BMS	647	456	359	261	174	101
Balloon	2160	1536	1253	948	629	351
DCB	664	317	95	0	0	0

Two PCB registries (Spanish DIOR and PEPPER [Paclitaxel REleasing Balloon in Patients PresEnting with In-Stent Restenosis]) reported both 6-month and 12-month results after DCB treatment of ISR



PEPCAD China ISR

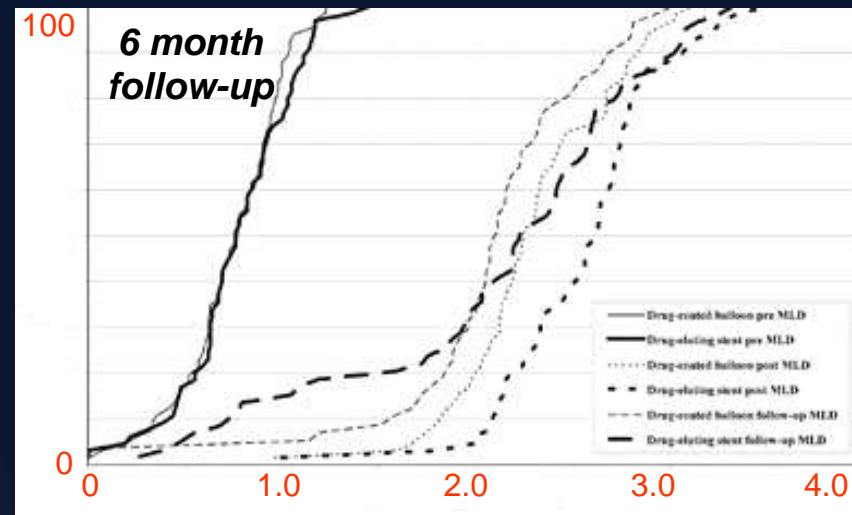
Cumulative frequency (%)



6 month late lumen loss (mm)

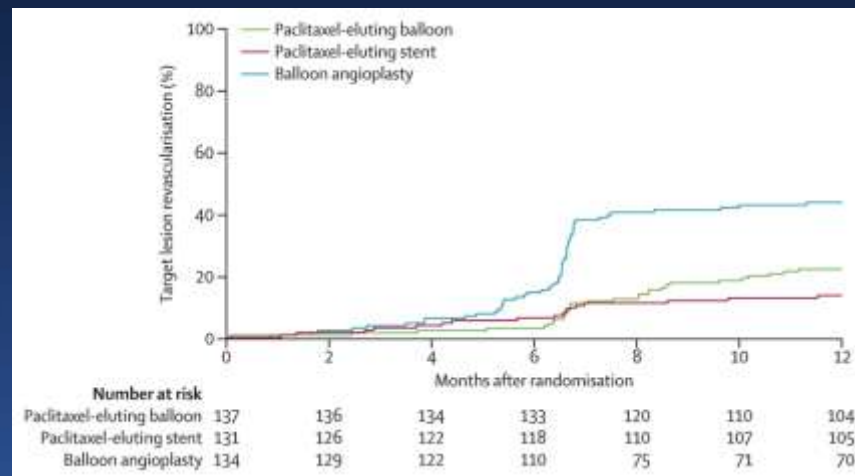
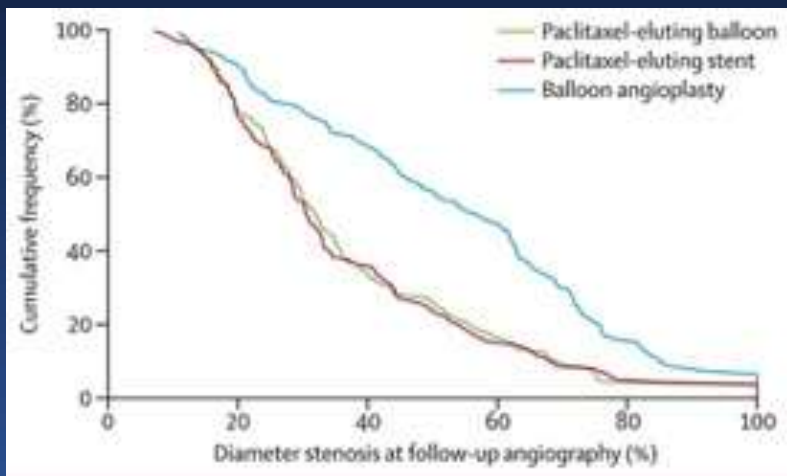
PEPCAD - II

Cumulative frequency (%)



Minimum lumen diameter (mm)

ISAR DESIRE III

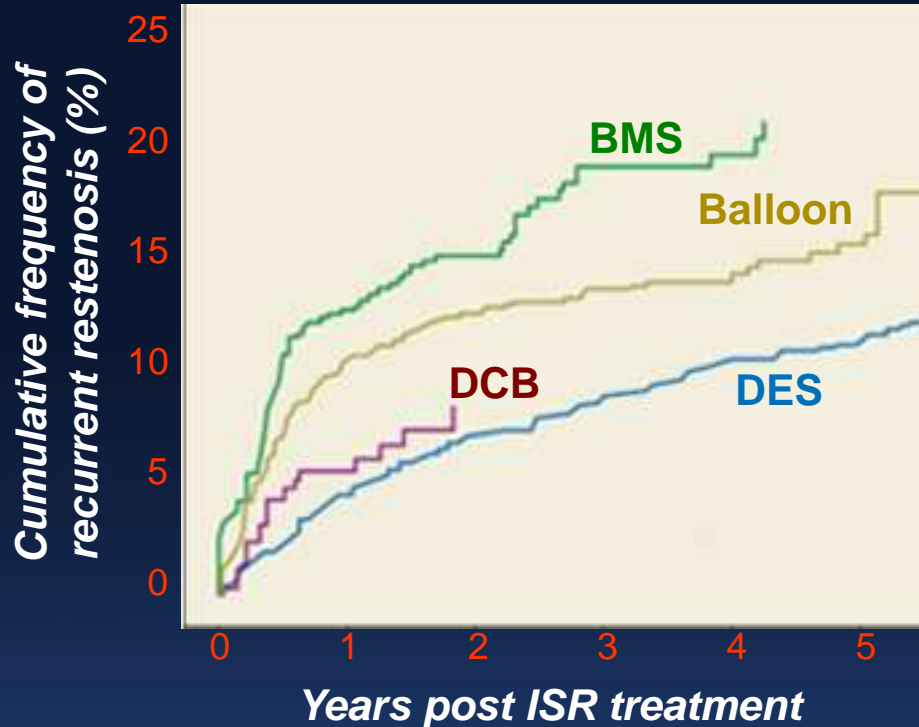


ISAR-DESIRE-III

(DCB vs DES vs POBA in Limus/DES Restenosis
in 402 pts)

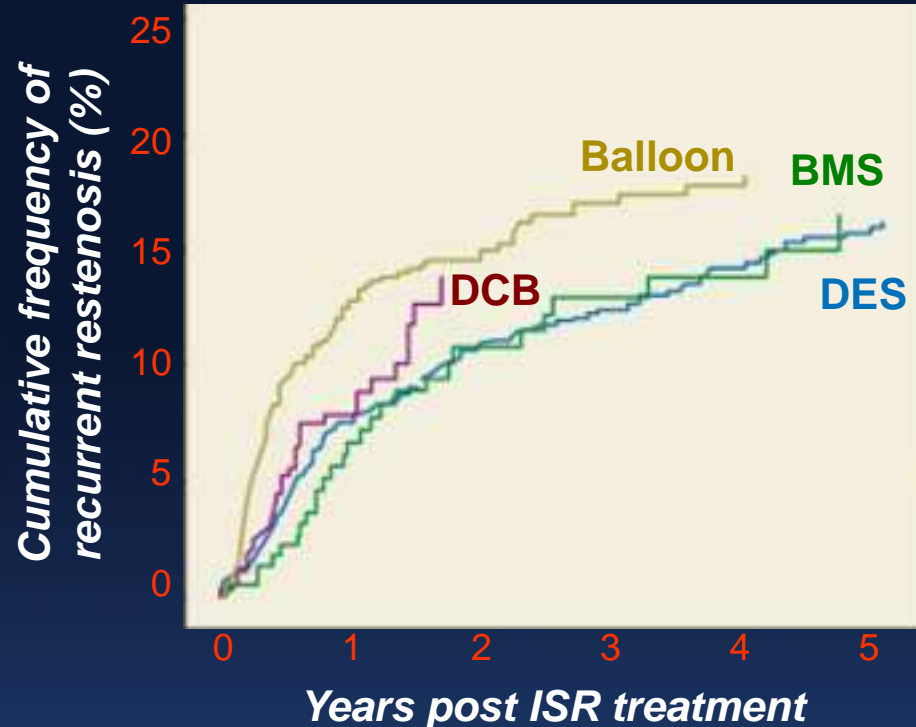
	DCB	PES	POBA	P-values		
				DCB vs PES	DCB vs POBA	PES vs POBA
Death	2.2%	4.6%	5.3%	0.3	0.2	0.8
MI	2.1%	2.4%	1.5%	0.9	0.7	0.6
QMI	0.7%	0.8%	0	1.0	0.3	0.3
TLR	22.1%	13.5%	43.5%	0.09	<0.0001	<0.0001
TVR	24.2%	16.6%	45.1%	0.18	0.0001	<0.0001
Death/MI	4.4%	6.9%	6.8%	0.4	0.4	1.0
Death/MI/ TLR	23.5%	19.3%	46.2%	0.5	<0.0001	<0.0001

SCAAR Registry - BMS



# at risk	0	1	2	3	4	5
DES	3214	2641	2138	1583	1091	682
BMS	492	341	269	190	125	74
Balloon	1098	808	671	511	324	142
DCB	374	197	59	0	0	0

SCAAR Registry - DES

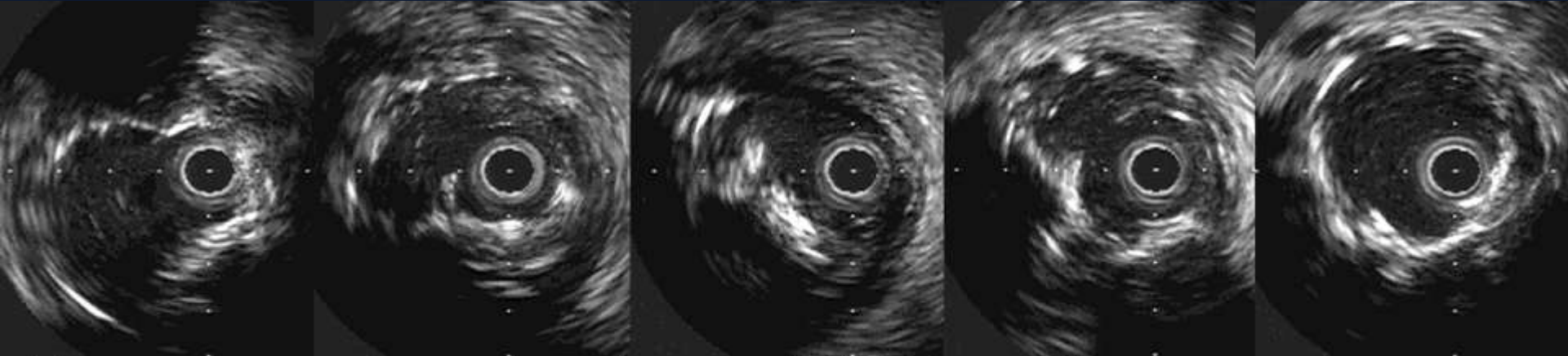


# at risk	0	1	2	3	4	5
DES	1121	794	576	429	298	188
BMS	155	115	90	71	49	27
Balloon	1062	728	584	437	305	209
DCB	290	119	36	0	0	0

Not all causes of stent failure are the same

	Bare Metal Stents				Drug-eluting Stents				
	Stent Thrombosis		Restenosis		Stent Thrombosis			Restenosis	
	<30d	>1y	<5y	>5y	<30d	30d - 1y	>1y	<18m	>18m
Procedure-related complications incl. underexpansion	X		X		X			X	
Intimal hyperplasia			X					X	
Neoatherosclerosis		X		X			X		X
Late malapposition or aneurysm							X		
Stent fracture	X	X			X		X		X
Delayed healing						X			
Uncovered stent struts/fibrin deposition						X	X		
Vessel wall inflammation							X		

Proximal



0 —————> 2.5mm —————> 10.0mm

Neoatherosclerosis (lipidic atherosclerosis developing within the neointima of a stent). . .

- Occurs earlier in DES (≈18-24 months) than in BMS (≈4-5 years)
- Occurs with greater frequency in all types of DES than in BMS although most of the data comes from first generation DES
- Can present as either late ISR or VLST and may be responsible for the majority of very late (beyond 1 year) DES thrombosis and/or restenosis
- Presentation and treatment are associated with greater clinical instability
 - ACS vs stable angina (or sxs vs no sxs) in patients with ISR
 - STEMI vs non-STEMI in patients with stent thrombosis
 - Post-procedural myonecrosis in patients treated for ISR
- Does not appear to respond to DCB

Takano et al. J Am Coll Cardiol 2009;55:26-33

Lee et al. J Am Coll Cardiol. 2010;55:1936-42

Hou et al. Heart. 2010;96:1187-90

Kang et al. Circulation 2011;123:2954-2963

Habara et al. Circ Cardiovasc Interv 2011;4:232-8

Park et al. J Am Coll Cardiol 2012;59:2051-7

Yonetsu et al. Am J Cardiol 2012;110:933-9

Yonetsu et al. Circ Cardiovasc Imaging 2012;5:660-6

Habara et al. Eur Heart J Cardiovasc Imaging. 2013;14:276-84

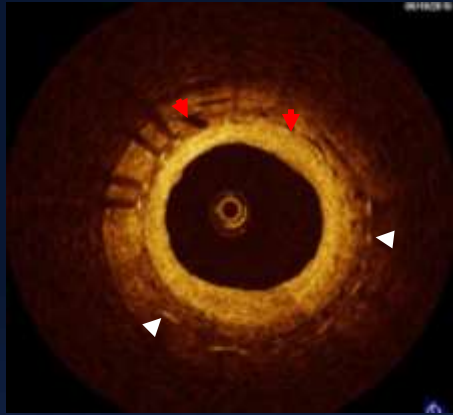
Ali et al. Circ Cardiovasc Interv, in press

Yamabili, et al. Eur Heart J Cardiovasc Imaging 2013, in press

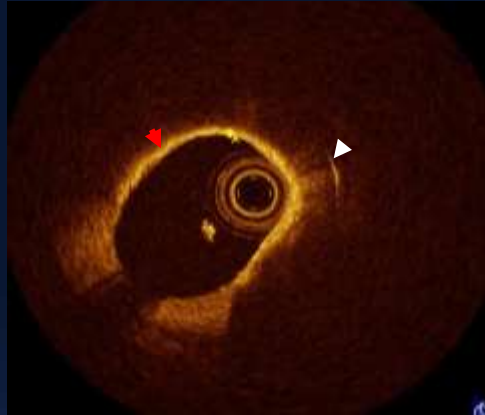
Tada, et al. Eur Heart J Cardiovasc Imaging 2013, in press

In-stent neoatherosclerosis in DES

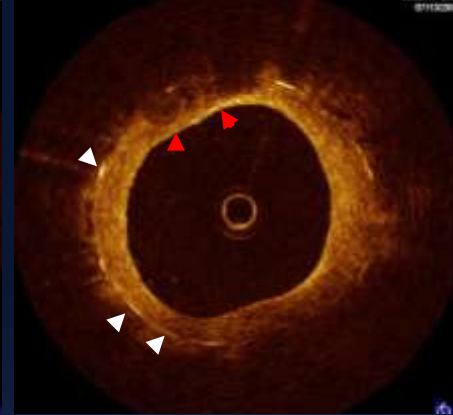
Microvessel



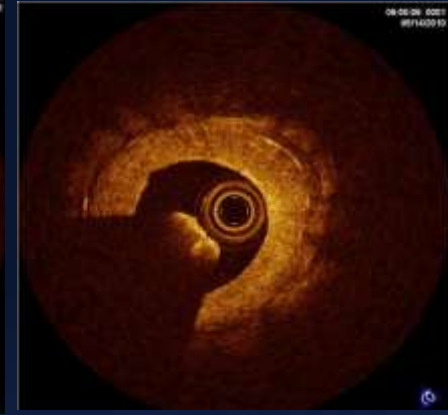
TCFA-like neointima



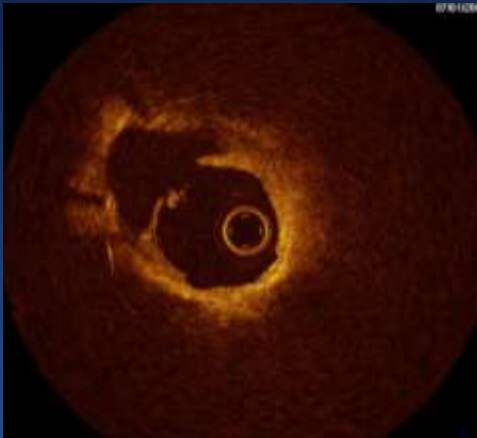
Calcium



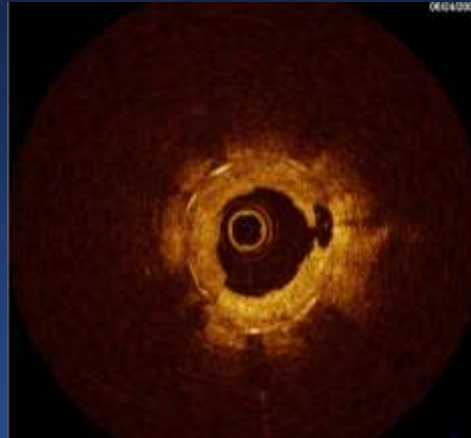
Red thrombus



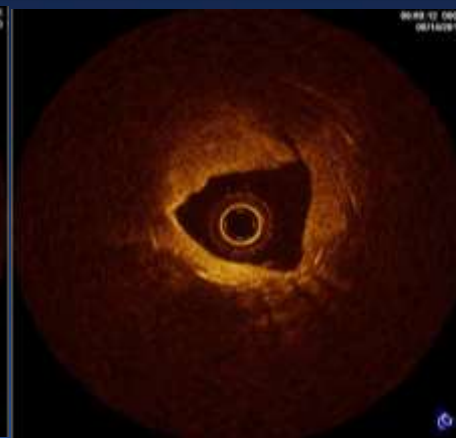
Neointimal rupture



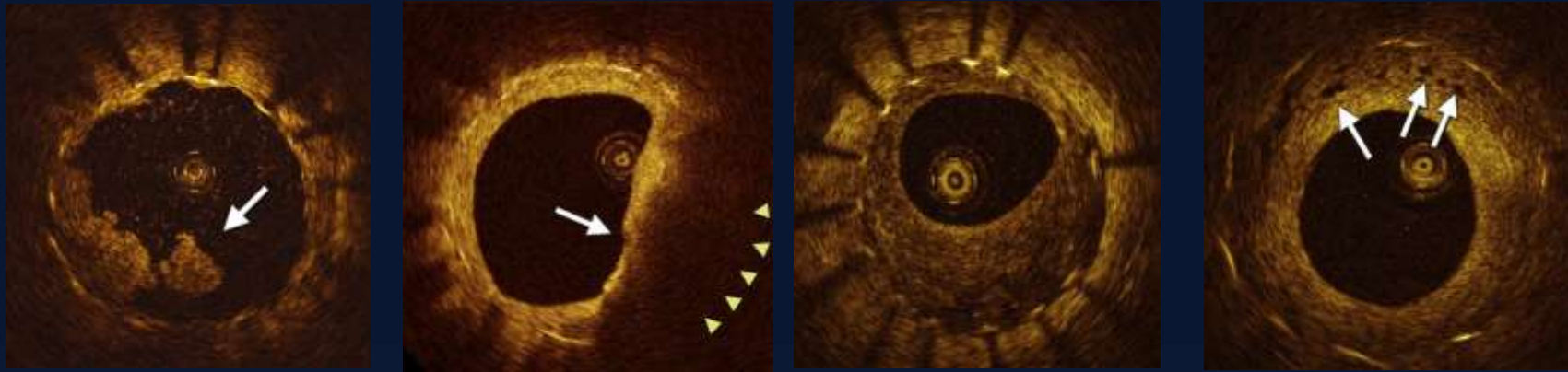
Mixed thrombus



White thrombus



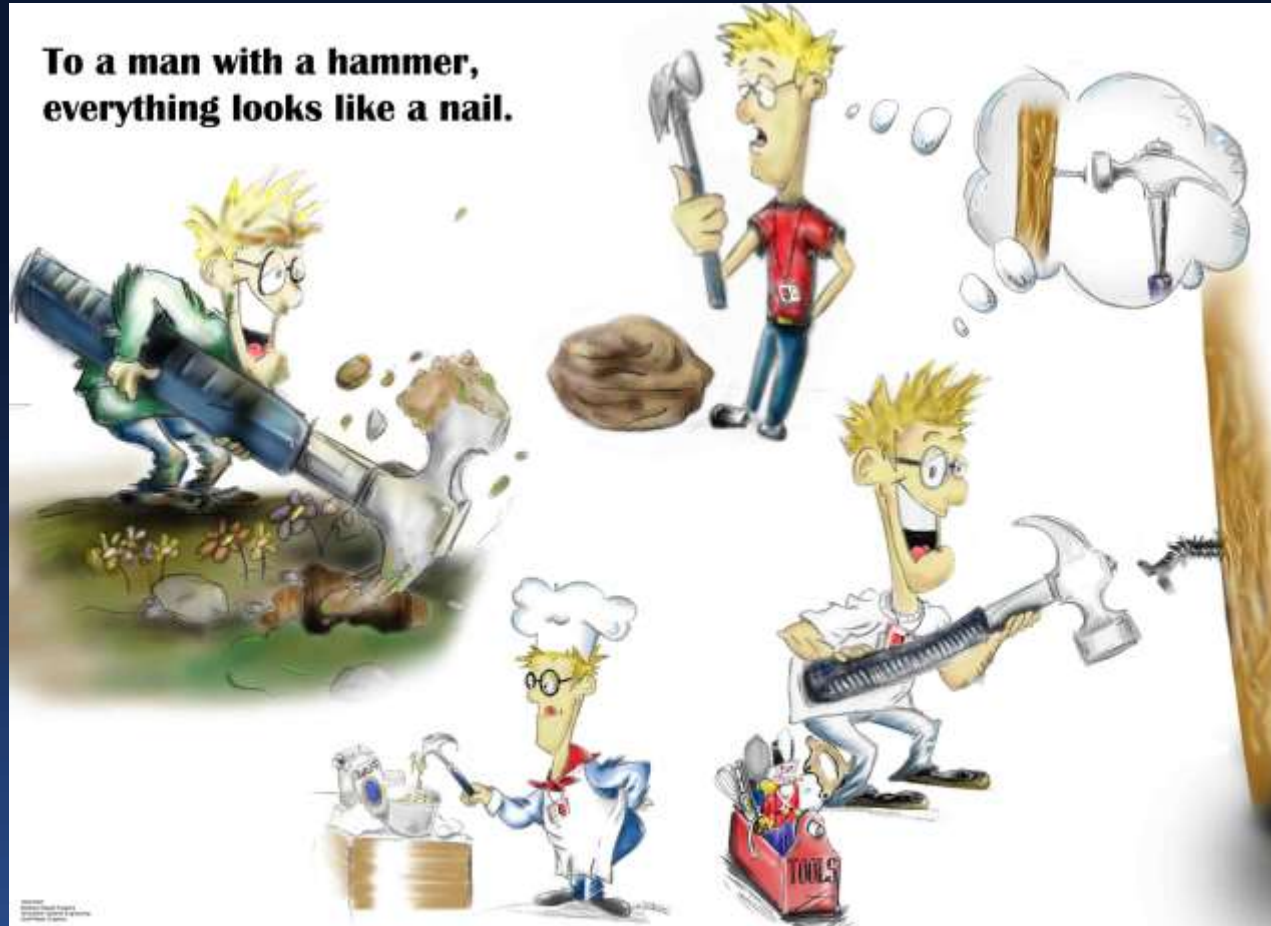
Serial OCT in 76 DES-treated lesions



	Thrombus	Lipidic neointima	TCFA	Heterogeneous	Neovascularization
9 mos	10.5%	14.5%	3.9%	64.5%	44.7%
2 yrs	9.2%	27.6%	13.2%	61.8%	73.7%
P-value	1.0	0.0009	0.07	1.0	<0.001

Percentage of uncovered struts significantly decreased from 4.4% at 9 mos to 2.3% at 2 yrs ($p < 0.001$). Completely covered lesions were more frequently observed at 2 yrs (44.7% vs. 59.2%, $p = 0.07$), but approximately one-half of the stented lesions were still not completely covered at 2 yrs.

To a man with a DCB, everything looks like “garden variety” in-stent restenosis



Conclusions

- The best that can be said for DCB is that it avoids putting in more metal which may or may not be bad.
 - **SCAAR Registry:** “ISR in BMS should be treated with DES or DEB while the optimal treatment of ISR in DES remains to be proven.”
 - **PEPCAD China ISR:** “Treatment with PEB [DCB] should be a better alternative for DES restenosis than repeat implantation of a PES by avoiding additional stent layers.
 - **ISAR-DESIRE-III:** By obviating the need for additional stent implantation, PEB could be a useful treatment for patients with restenosis after implantation of a drug-eluting stent.
 - **Italian Society of Interventional Cardiology:** DCB for DES Restenosis Management: Class IIa (Level of Evidence B)