Increased outward force of self-expanding BMS in the SFA could be a significant risk factor for restenosis

DIDACTICS
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(COF evaluation of BIOFLEX-I study)

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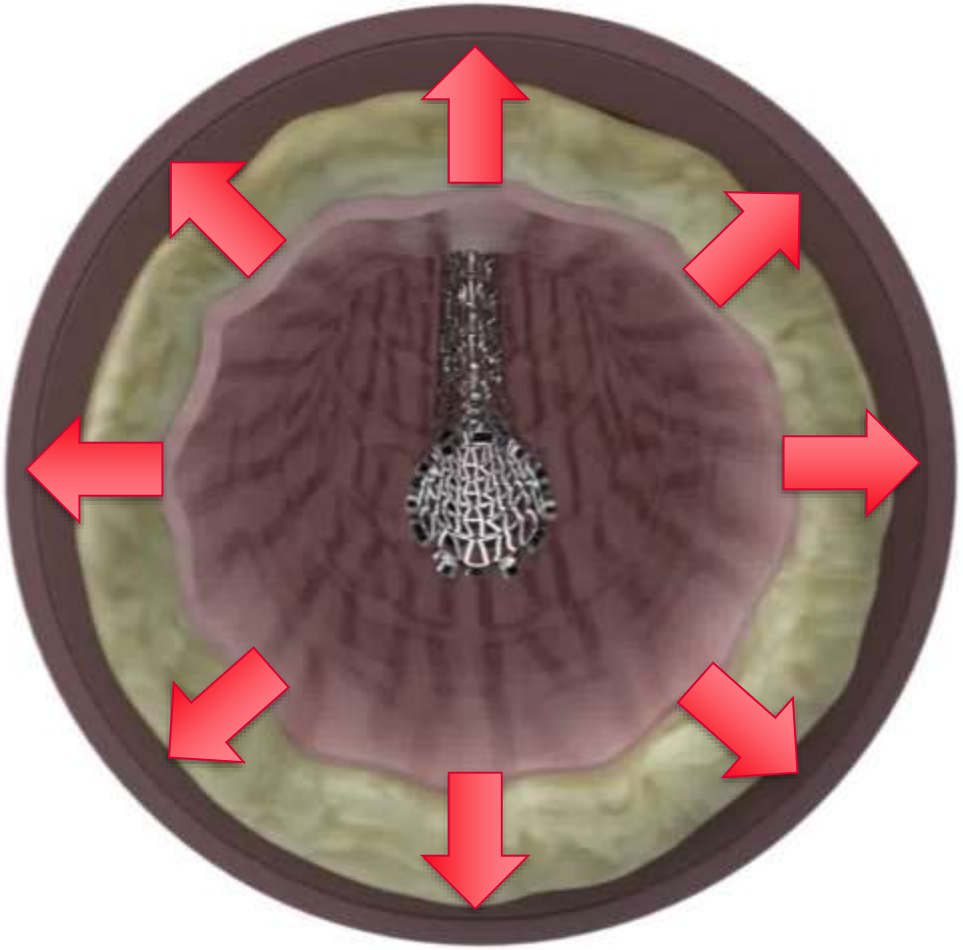
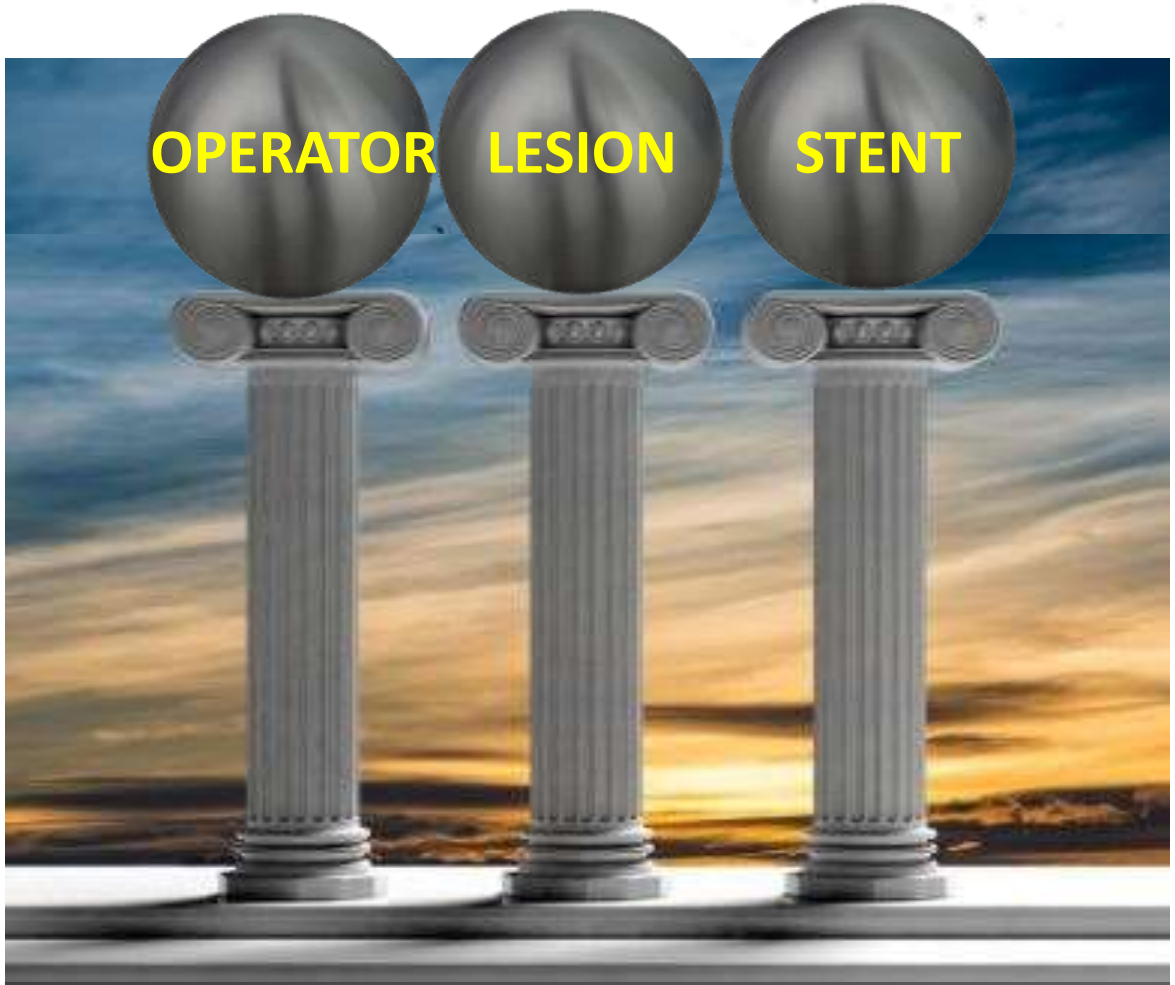
Disclosures Koen Deloose, MD

- ☐ I have the following potential conflicts of interest to report:
  - ☒ Consulting: Abbott, BD, Biotronik, Boston Scientific, Cook, CTI vascular, iVascular, Medtronic, Philips, Terumo, CyndRX, Profusa
  - ☐ Employment in industry
  - ☐ Stockholder of a healthcare company
  - ☐ Owner of a healthcare company
  - ☐ Other(s)
- ☐ I do not have any potential conflict of interest

CHRONIC OUTWARD FORCE



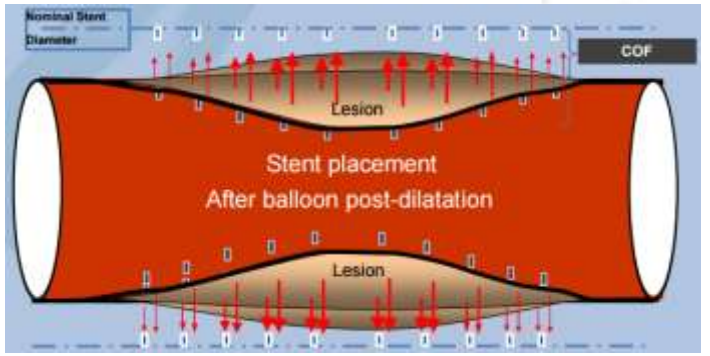


COF : the force exerted on a vessel wall by a self expanding stent

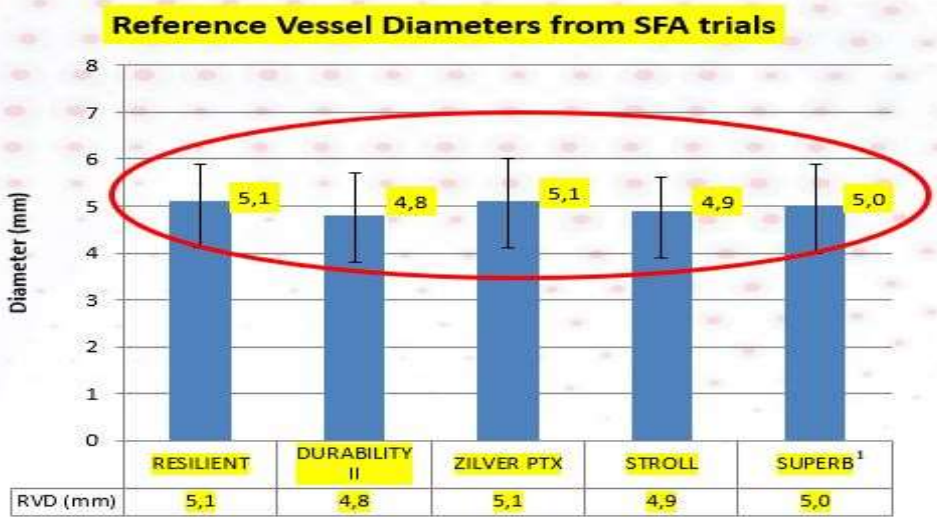
COF DEPENDS ON :

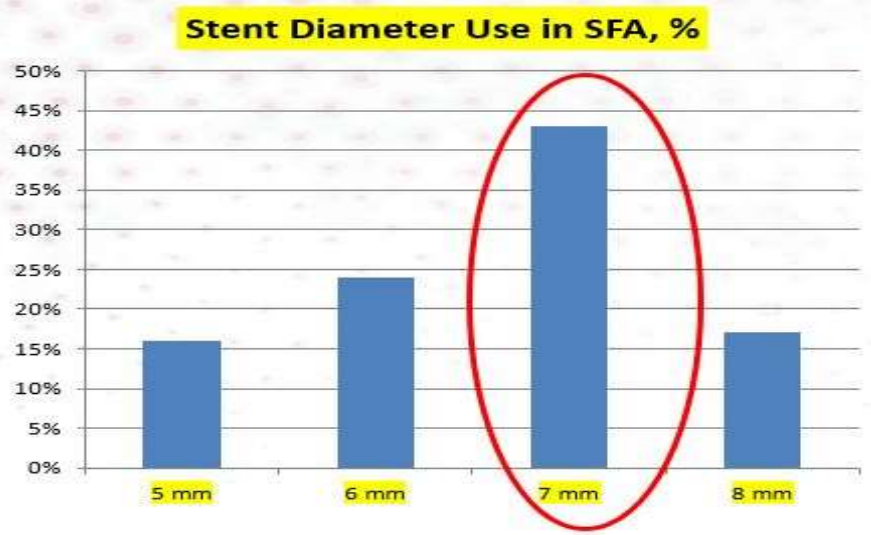
Chronic Outward Force (COF) exerted by a nitinol stent on vessel wall

- Is the lesion sufficiently predilated?



- Average reference vessel diameter of SFA is 5 mm
- Most commonly used stent diameter in SFA is 7 mm

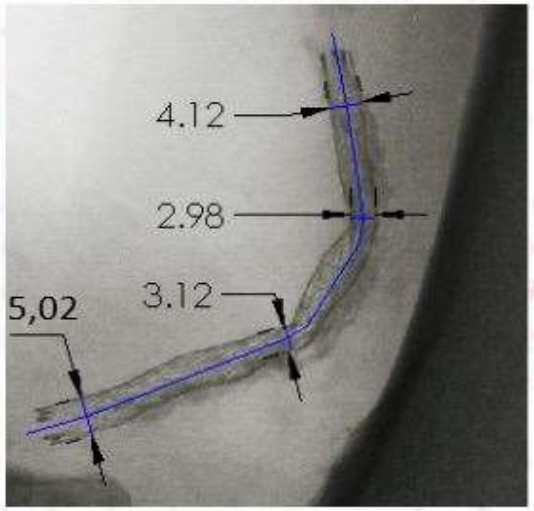




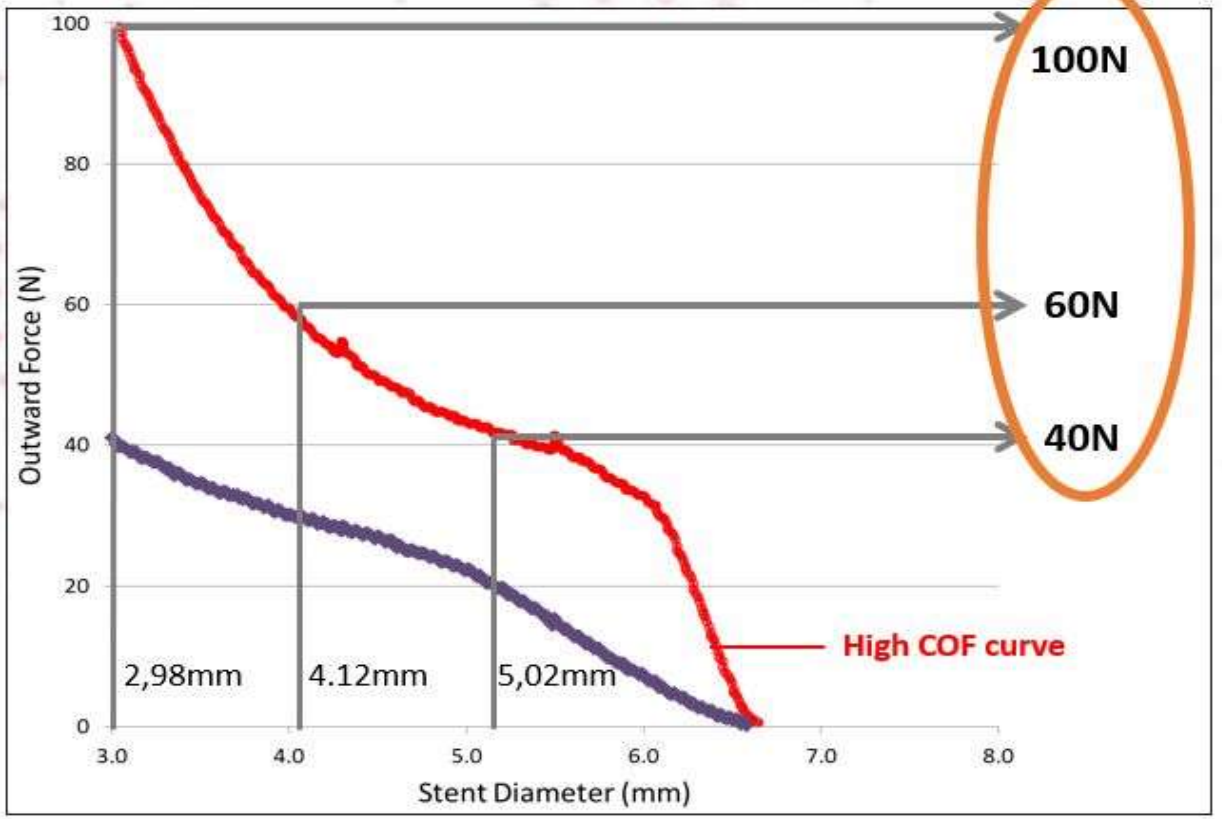
Source: Garcia L. Superb Trial 12 Month Results. Presented at TCT 2012. Miami, FL.

Chronic Outward Force (COF) exerted by a nitinol stent on vessel wall

Bent Leg:vessel diameter range: 5.02 - 2.98 mm : 6mm stent



Expansion force increases with decreasing diameter



Chronic Outward Force (COF) exerted by a nitinol stent on vessel wall

High COF shows increase of neointimal proliferation

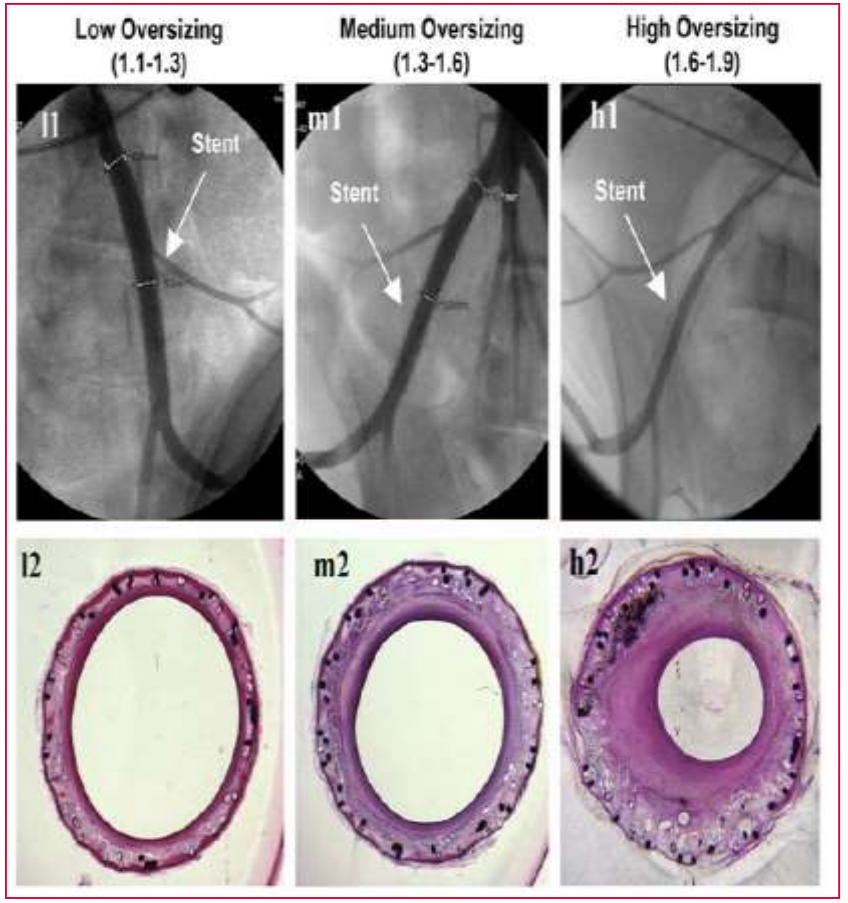
Pre-clinical study on stent oversizing by Zhao

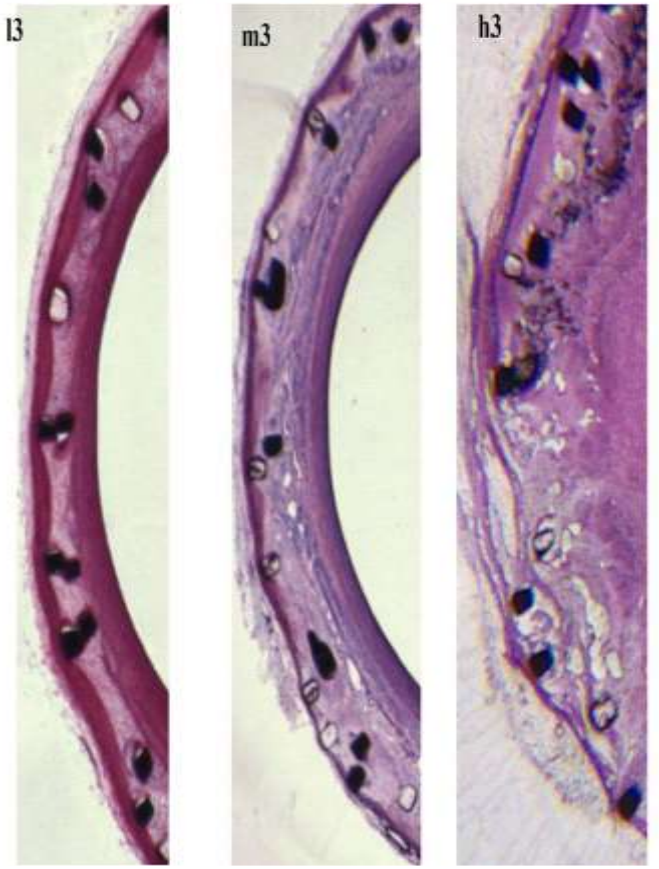
Late Stent Expansion and Neointimal Proliferation of Oversized Nitinol Stents in Peripheral Arteries

Hugh Q. Zhao · Alexander Nikanorov · Renu Virmani · Russell Jones · Erica Pacheco · Lewis B. Schwartz

14 Yucatan swine
6 month follow-up

«… Severe oversizing (stent-to-artery ratio[1.4:1]) results in a profound long-term histological response including exuberant neointimal proliferation, medial disruption by stent struts, higher injury scores and luminal stenosis.»

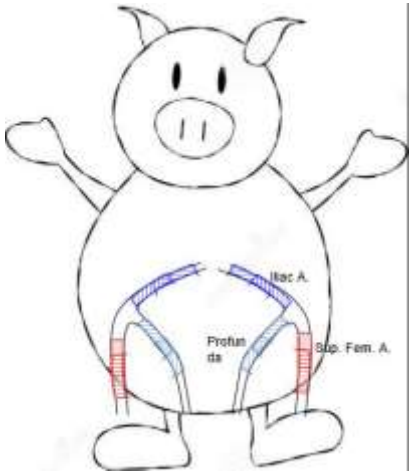




Zhao HQ et al. *Cardiovasc Intervent Radiol*. 2009 Jul;32(4):720-6

High COF shows increase of neointimal proliferation

Pre-clinical study on low vs high COF stents by Vienna University



28 days :

Astron Pulsar (low COF): 10 stents

LifeStent (high COF): 8 stents

90 days:

Astron Pulsar (low COF): 8 stents

LifeStent (high COF): 8 stents

BIOTRONIK

Presented at CIRSE 2017 by Pr Martin Funovic, Medical University of Vienna

High COF shows increase of neointimal proliferation

Pre-clinical study on low vs high COF stents by Vienna University

28 days

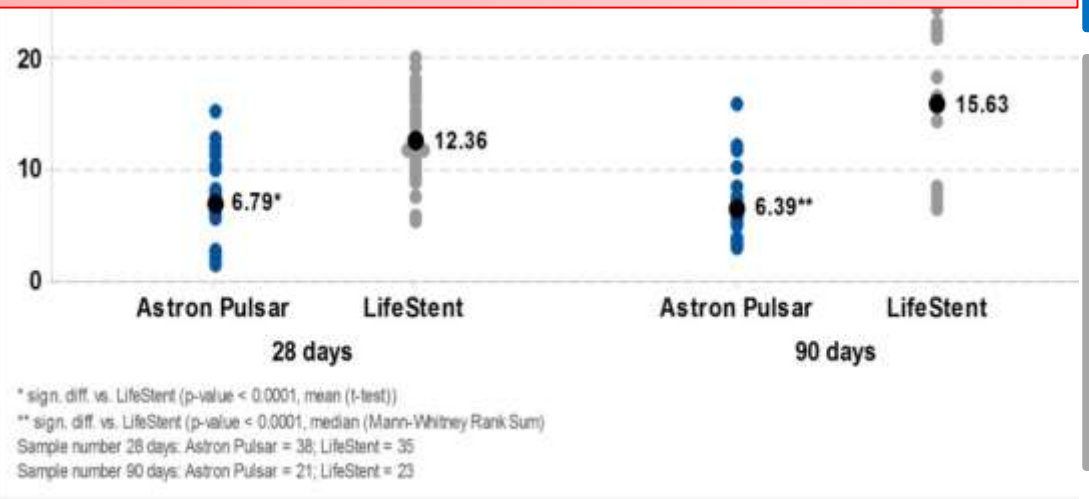
90 days

Astron Pulsar – 6,79

Astron Pulsar – 6,39

Low COF stent shows significantly smaller neointima area than High COF stent

Lifestent – 12,36

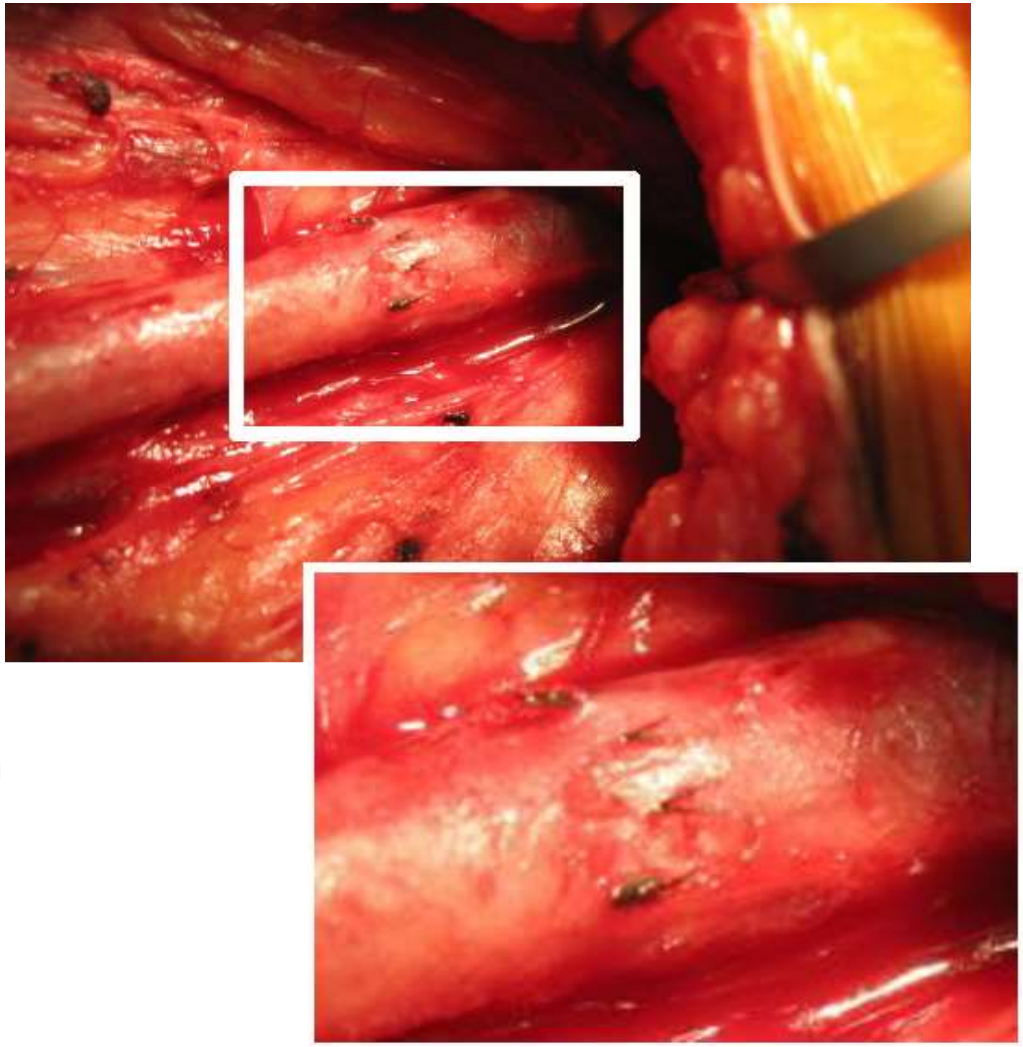


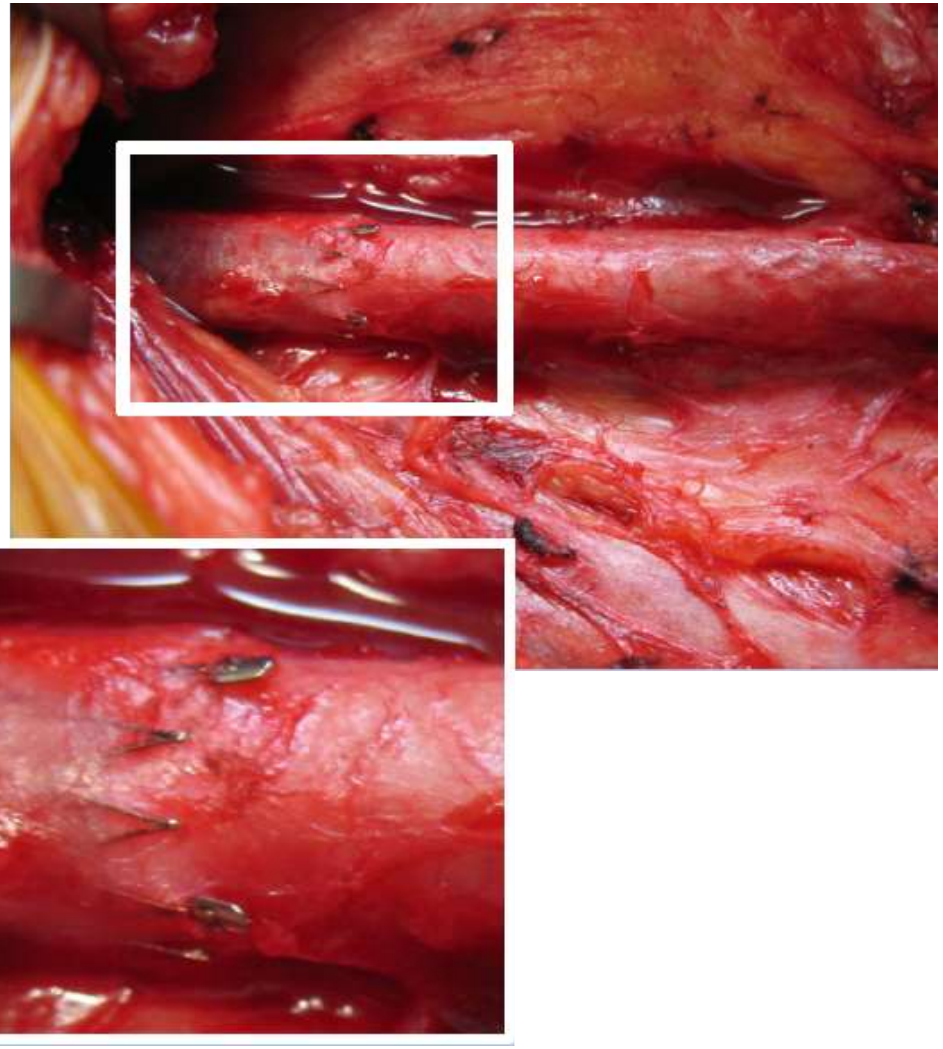
Lifestent – 15,63

Presented at CIRSE 2017 by Pr Martin Funovic, Medical University of Vienna

High COF shows increase of neointimal proliferation

Case experiences with high COF stents





Source: Goverde P, Presented at LINC 2015 - Consequences of SFA stenting and how to overcome them

High COF shows increase of neointimal proliferation

-> Supporting clinical data

Zilver PTX global clinical program, Cox proportional hazards model

Factors with Moderate Impact on TLR from Classification Tree	p-value[1]	Interpretation
Stent oversizing	0.043	• Oversizing (>30%) may impact TLR
Smoking status	0.64	• No significant impact on TLR
Patent runoff vessels	0.91	
Stent diameter	0.12	

[1] joint p-value; not univariate

* Data presented at LINC 2019: "Insights from Global Zilver PTX Experience: What are the Predictors for Clinical Failure and TLR" by Michael D. Dake, MD

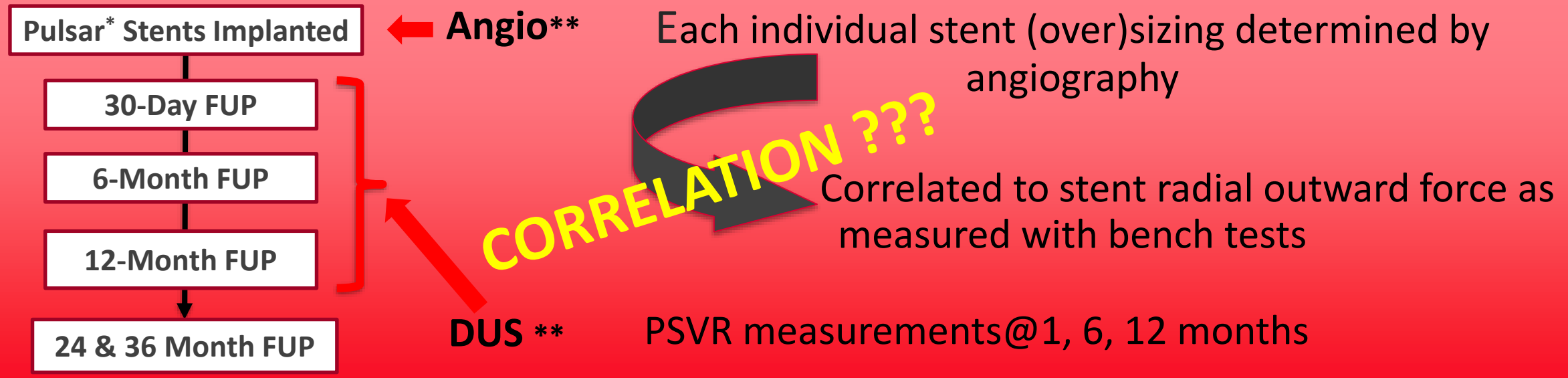
TLR: Target Lesion Resvascularization

High COF shows increase of neointimal proliferation

Are there clinical data available to support this statement?

BIOFLEX-I study

- Prospective, international, multicenter, IDE trial investigating 302 subjects in 38 clinical sites in US (29), Canada (2) and Europe (7)
- PI's : MW. Burket (US/Canada) & M. Brodmann (EU)



* Pulsar stents: Astron Pulsar and Pulsar-18 stents

** independent core lab adjudicated – independent CEC

High COF shows increase of neointimal proliferation

Are there clinical data available to support this statement?

BIOFLEX-I study

		radial outward force	1/PSVR at 1 month	1/PSVR at 6 months	1/PSVR at 12 months	PSVR at 1 month/PSVR at 12 months
radial outward force	Pearson Correlation	1	.129*	-.052	-.161*	-.196**
	Sig. (2-tailed)		.045	.444	.020	.008
	N	456	240	216	208	183
1/PSVR at 1 month	Pearson Correlation	.129*	1	.133	.095	-.428**
	Sig. (2-tailed)	.045		.065	.202	.000
	N	240	240	194	183	183
1/PSVR at 6 months	Pearson Correlation	-.052	.133	1	.584**	.436**
	Sig. (2-tailed)	.444	.065		.000	.000
	N	216	194	217	177	163
1/PSVR at 12 months	Pearson Correlation	-.161*	.095	.584**	1	.819**
	Sig. (2-tailed)	.020	.202	.000		.000
	N	208	183	177	208	183
PSVR at 1 month/PSVR at 12 months	Pearson Correlation	-.196**	-.428**	.436**	.819**	1
	Sig. (2-tailed)	.008	.000	.000	.000	
	N	183	183	163	183	183

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

@ 1 month

Statistically significant
The higher COF -> the lower PSVR

@ 6 month

Statistically not significant
The higher COF -> the higher PSVR

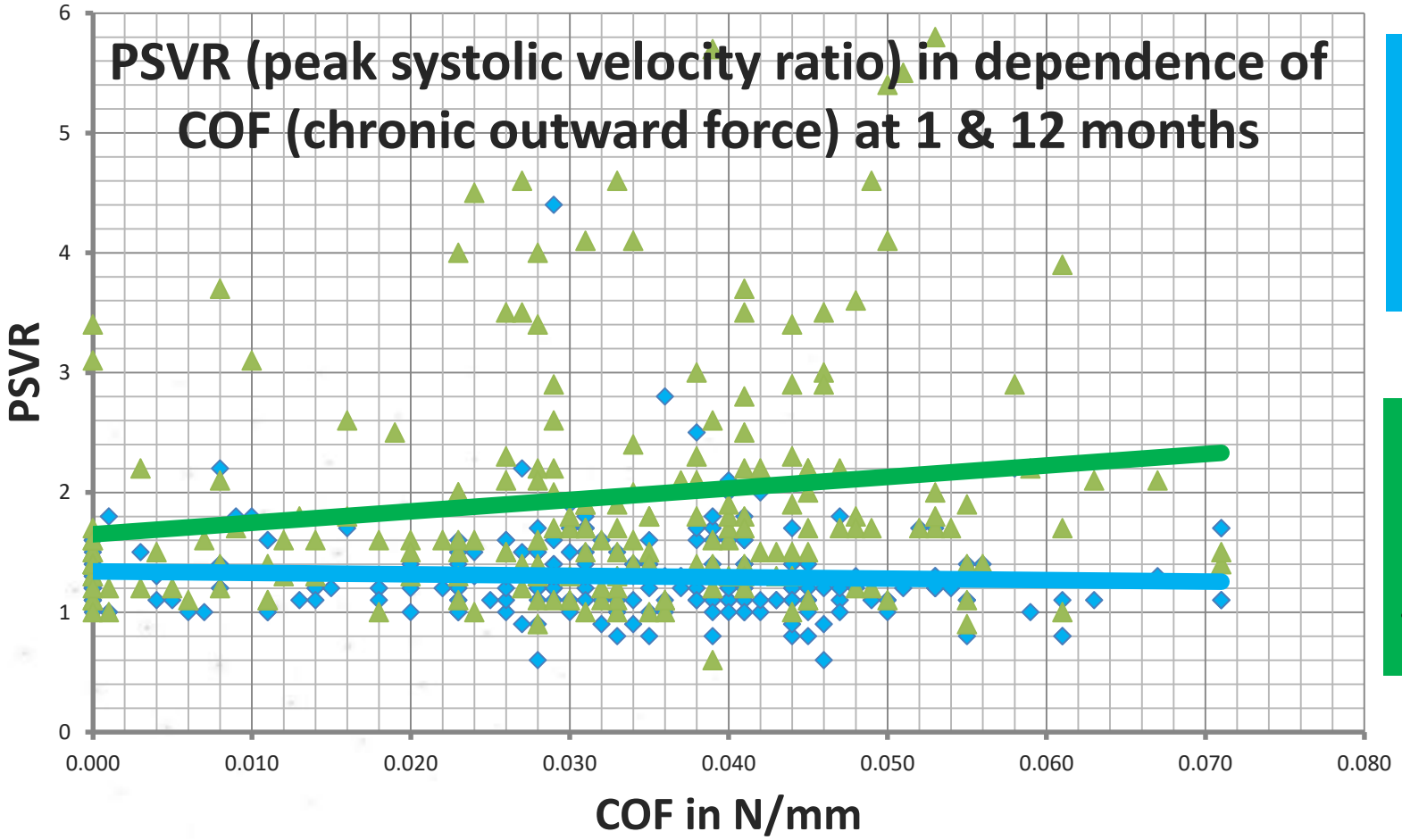
@ 12 month

Statistically significant
The higher COF -> the higher PSVR

High COF shows increase of neointimal proliferation

Are there clinical data available to support this statement?

BIOFLEX-I study



@ 1 month

Statistically significant
The higher COF -> the lower PSVR

@ 12 month

Statistically significant
The higher COF -> the higher PSVR

High COF shows increase of neointimal proliferation

Are there clinical data available to support this statement?

BIOFLEX-I COF as risk factor : linear regression model

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	1.124	.169		6.660	.000	.791	1.457
	radial outward force	-2.970	1.299	-.169	-2.286	.024	-5.536	-.404

Dependent Variable: PSVR at 1 month/PSVR at 12 months

COF is the most significant predictor for worsening of PSVR in the multivariate analysis

Conclusions

Based on the data available (preclinical, cases, BIOFLEX1), we see the following trends:

- At 12 months high COF is a significant risk factor for restenosis (high PSVR), reversing the early (1 month) results
- Long term low COF seems to result in less restenosis and potentially less re-interventions
- Further research is needed to clarify the relation between stent forces and clinical outcome. BIOFLEX COF RCT will provide more insights how COF influences clinical outcome in patients with SFA disease.

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