ACTUALISATIONS ET PERSPECTIVES EN PATHOLOGIE CARDIOVASCULAIRE

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Stents de nouvelle génération :
Pour quelles indications ?

APPAC

14ème EDITION

ACTUALISATIONS ET PERSPECTIVES EN PATHOLOGIE CARDIOVASCULAIRE

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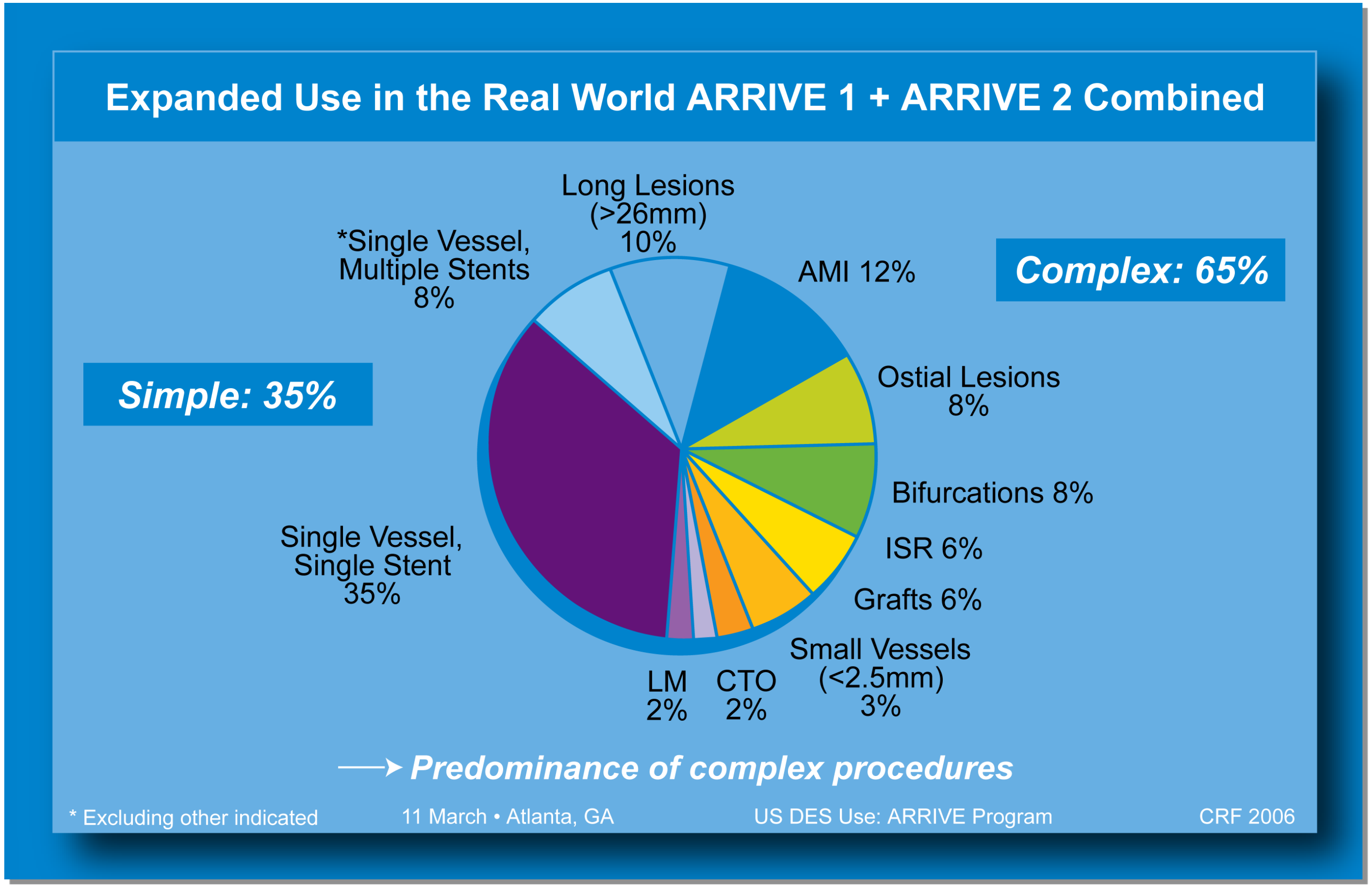
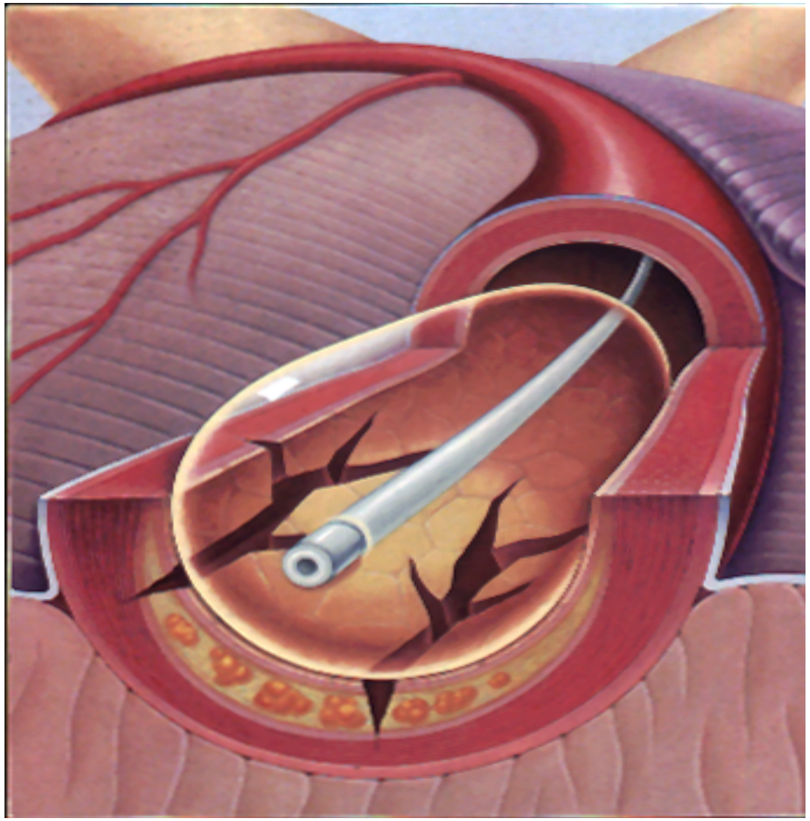
déclare n'avoir aucun conflit d'intérêt concernant les données de sa communication

Reality: 65% of Procedures Are Complex!



What is the Physiologic Mechanism of Dilatation?

- Plaque fracture
  - Inflation fractures intima & media
- Arterial wall stretch
  - Stretches media & adventitia
- Lumen enlargement
  - Inner & outer diameters increase

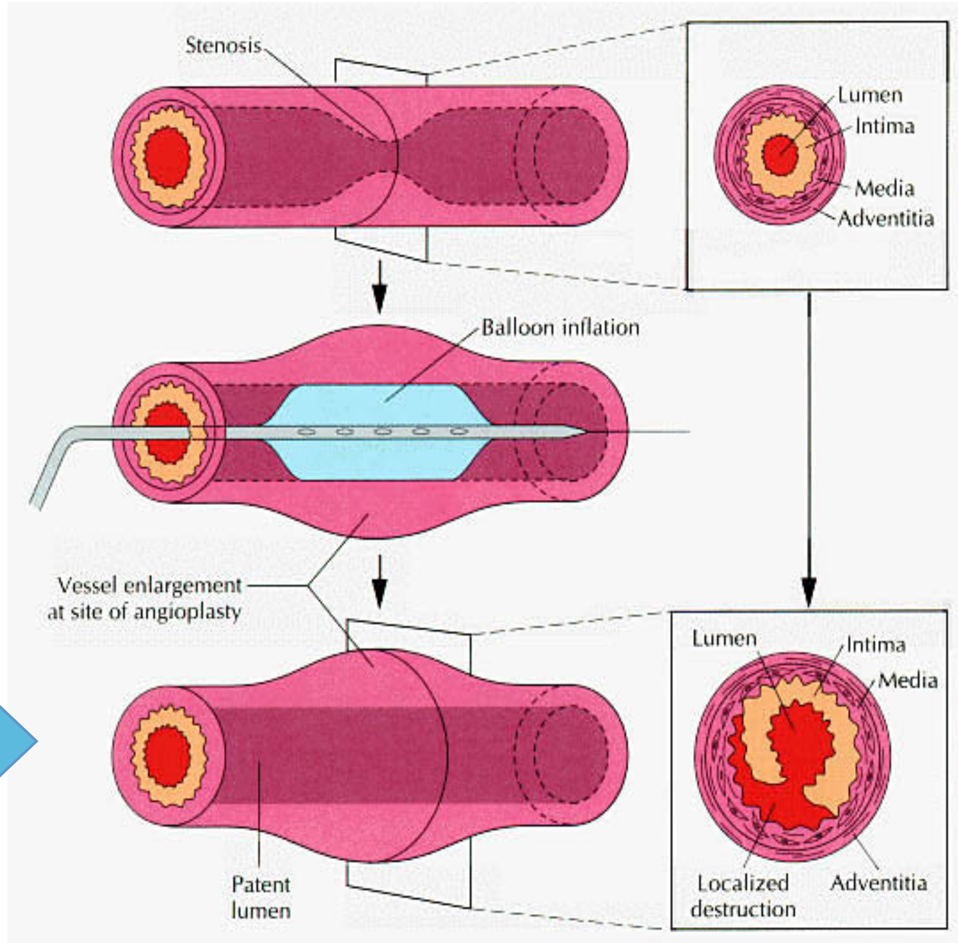


Dilatation – Anatomical Results

Stenosis

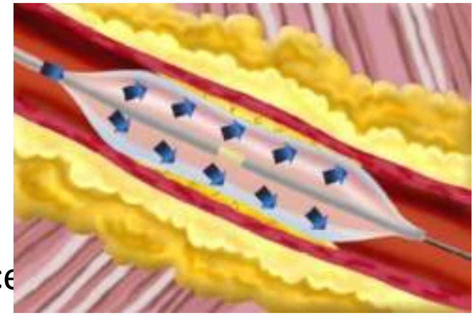
Inflation

Plaque fracture, lumen enlargement

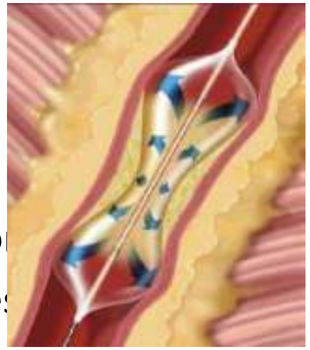


Source: Angioplasty.org – PTCA Devices and Procedures

Balloon Inflation Considerations



- Dilatation Force
    - Force/pressure exerted on the lesion and vessel wall by an inflated dilatation balloon
    - Dilatation force is dependent on 2 factors: Inflation Pressure & Balloon Material i.e. thickness & proce
- Dog-boning > in resistant lesions or within a stent
    - Stretching of a dilatation balloon along the path of least resistance, outside the lesion or stent margins
- Watermelon Seeding
    - Retrograde or antegrade movement when inflated within a lesio
    - Concern is related to resistant lesions, especially with in-stent re

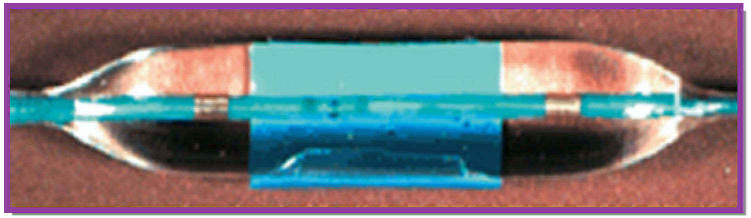


There is the potential for **unwanted trauma** and/or **dissection of the healthy vessel** adjacent to the lesion or outside the margins of the stent

Inflation Characteristics

Bench test showing the different profiles during high-pressure (>14 atm) inflation.

Non-compliant



Little change in volume even at high pressures, concentrating dilatation force at the lesion site.

Semi-compliant

“Dog bone” effect at the edge of the cylinder that can damage the vessel wall in vivo.

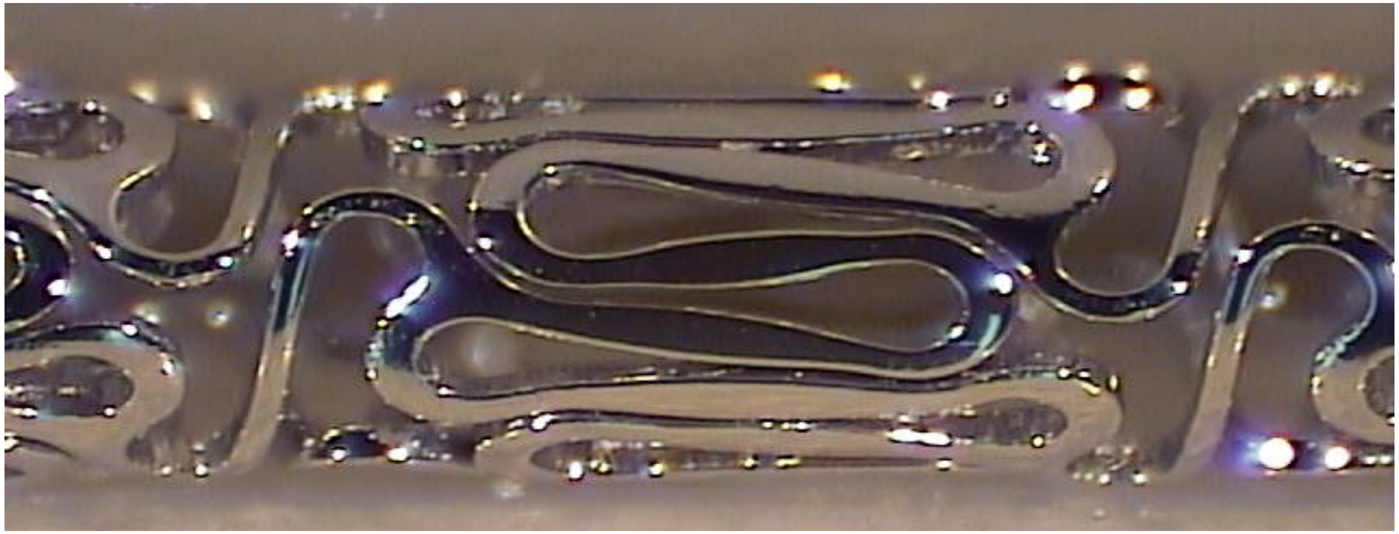
Romagnoli, Enrico et al., “Drug Eluting Stenting The Case for Post Dilatation,” JACC, 2008.

Technical Aspect:

- **System**
  - Crossing profiles (no cross risk) → Lowest Crossing profile
  - Stent retention (stent loss risk) → Proprietary crimping
  - Temporary occlusion (no distal visualization) → Lowest crossing profile
  - Vessel trauma during advancement → Lowest crossing profile
  - Trackability/Flexibility (not getting to the lesion) → Superior trackability

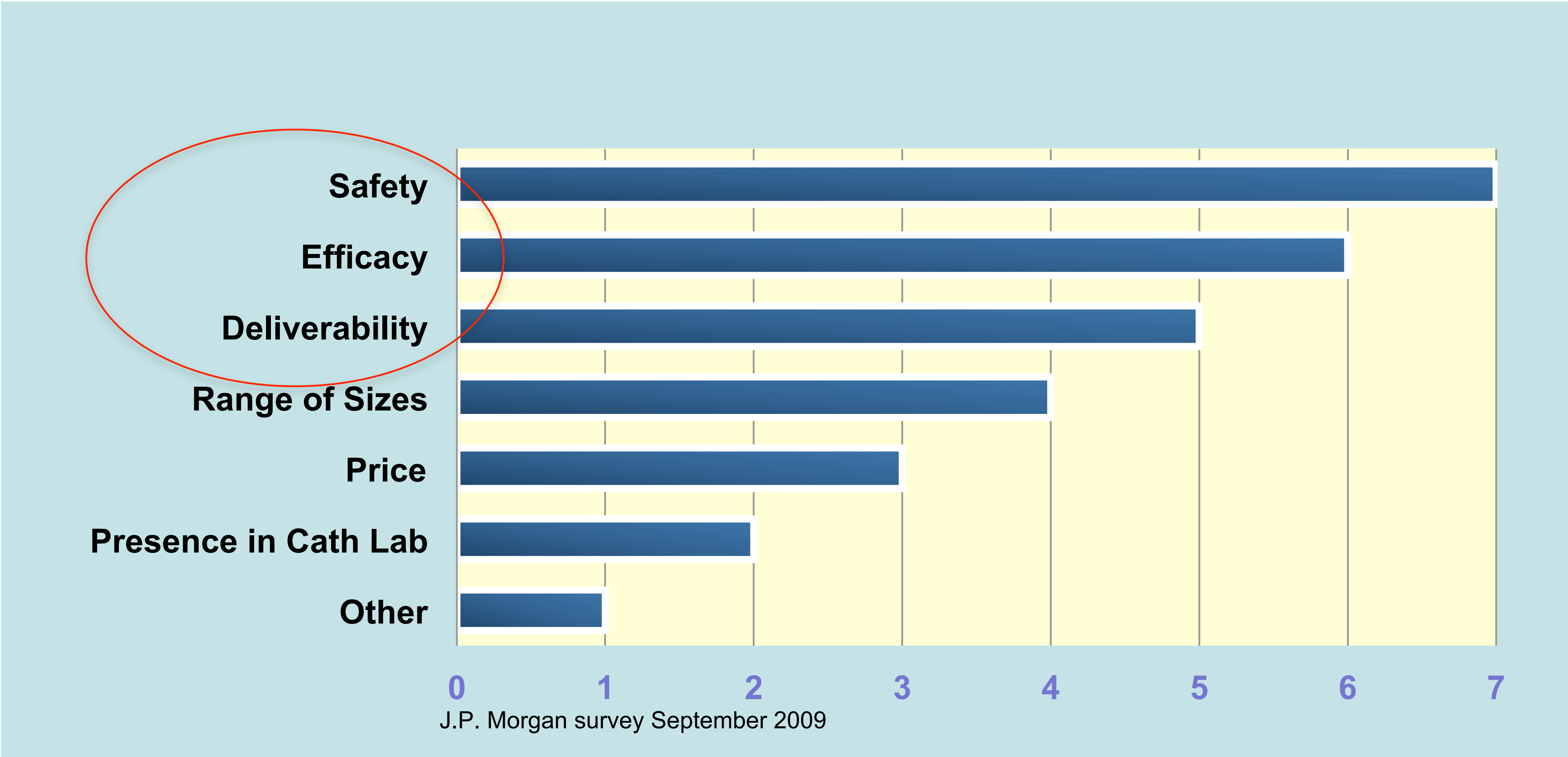
- **Lesion characteristics**
  - Sub-total occlusion (no cross risk) → Lowest profile
  - Location of the stenosis → Hybrid stent design
  - Calcification within the lesion → Balloon design
  - Vessel tortuosity (not getting to the lesion) → Superior trackability

Stent Design

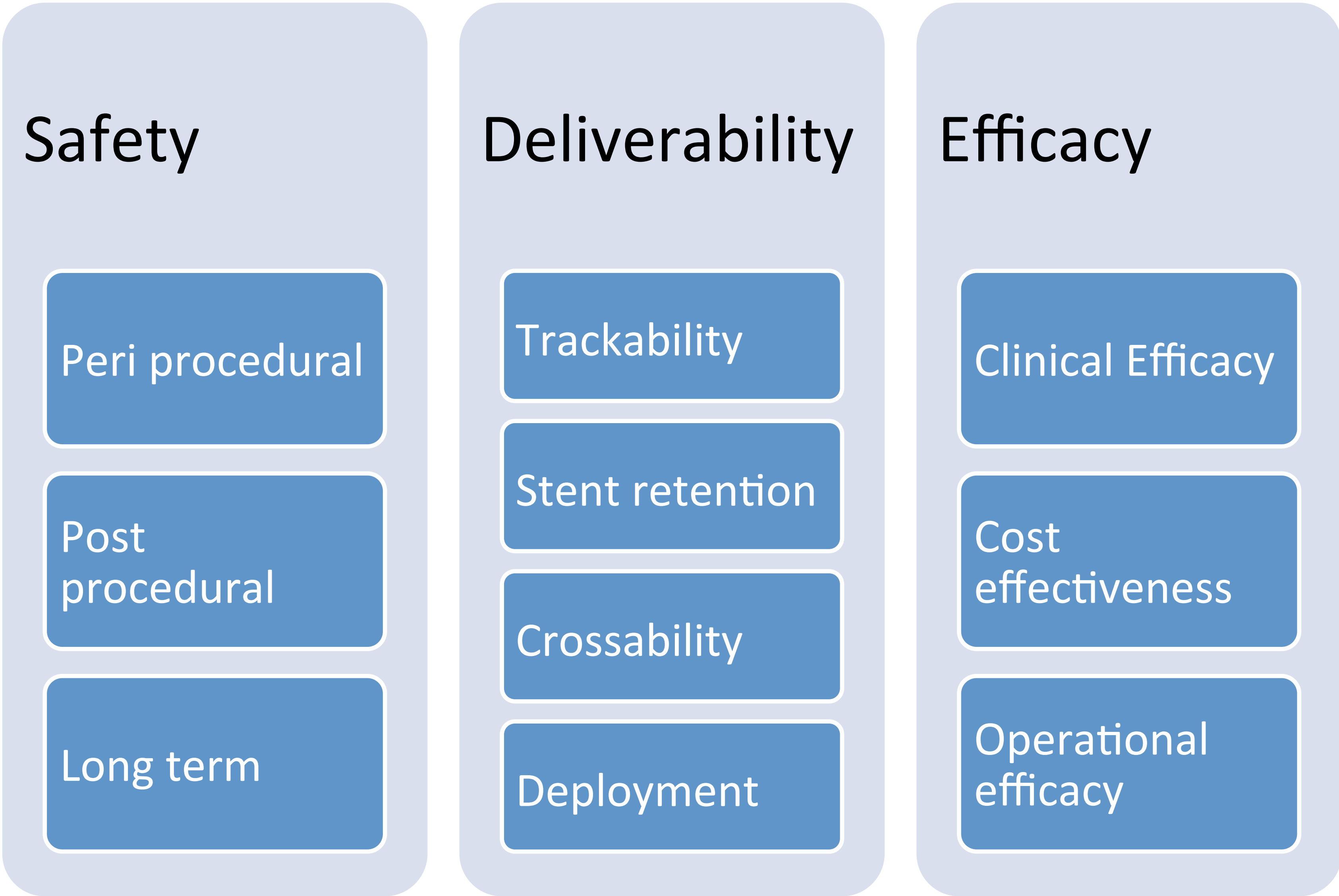


Ultra Thin Stent Struts
.0031″ (81μm)

Factors Driving Stent Selection



Stenting


Safety
Peri procedural
Post procedural
Long term
Deliverability
Trackability
Stent retention
Crossability
Deployment
Efficacy
Clinical Efficacy
Cost effectiveness
Operational efficacy

Role for Bare Metal Stents

Patients who can not take Plavix reliably

- Non-compliance due to Plavix cost and/or reliable use?
- Upcoming surgery?
- Plavix resistance/intolerance non-compliance

AMI patients

- Unknown patient history to determine Plavix compliance capabilities?

Large Vessels

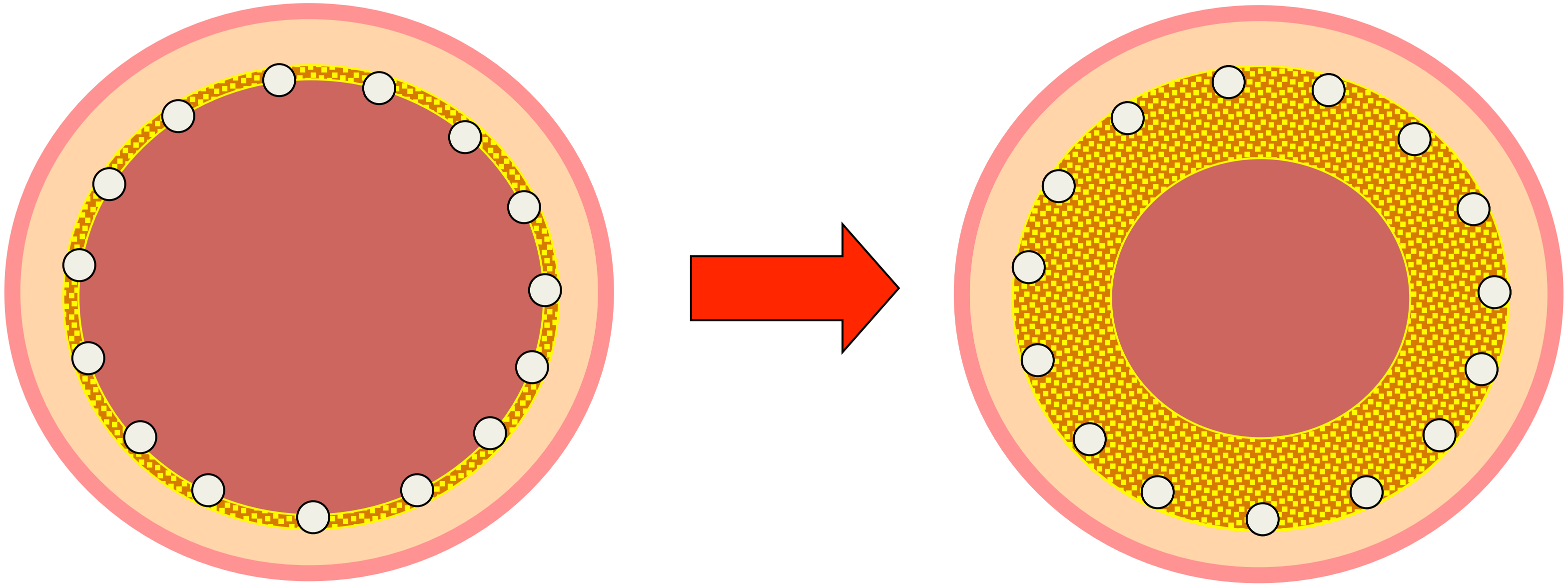
Thrombosis risk outweighs restenosis risk?
Patients who can not take Plavix reliably?

Risk and impact of restenosis. . .

. . . versus Thrombosis and hemorrhage

In-Stent Restenosis

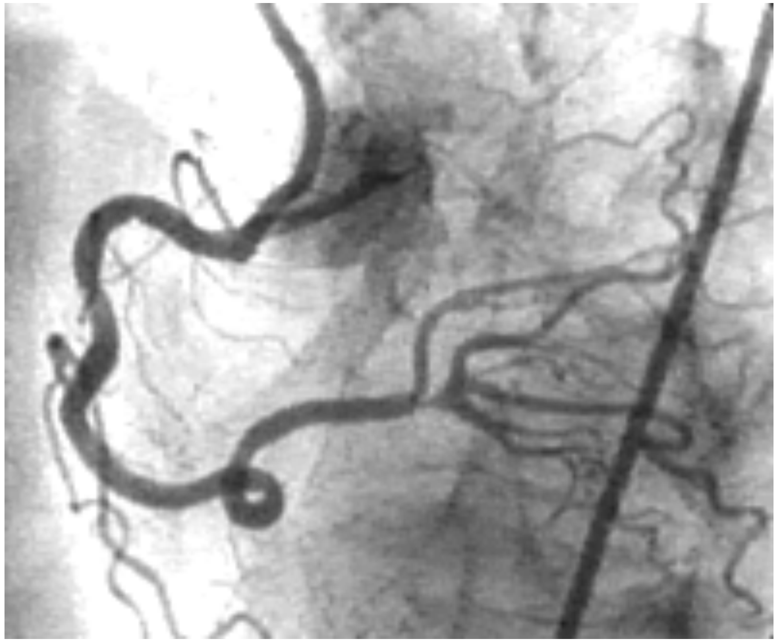
- Stents provide a scaffold against negative remodeling of the vessel, but induce a greater amount of neointimal hyperplasia
- In-stent restenosis is caused almost entirely by tissue in-growth



Stent Characteristics

- **Deliverability**
  - Trackability
  - Flexibility
  - Pushability
  - Crossability

  Poor performing stents will not be able to navigate tortuous vessels and cross challenging lesions



- **Good clinical outcomes**
  - Efficacy (restenosis)
  - Safety (MACE, ST)

Myriad of parameters influencing deliverability and clinical outcomes

- Stent strut
- Stent crowns and connectors
- Stent patterns, closed and open cells
- Metal-to-artery ratio
- Unsupported surface area
- Vessel scaffolding
- Recoil
- Radial strength
- Foreshortening
- Flexibility and conformability
- Radiopacity
- Self-expandable vs. Balloon-expandable
- Balloon outside the stent / Overhang
- Stent jail
- Apposition

Foreshortening

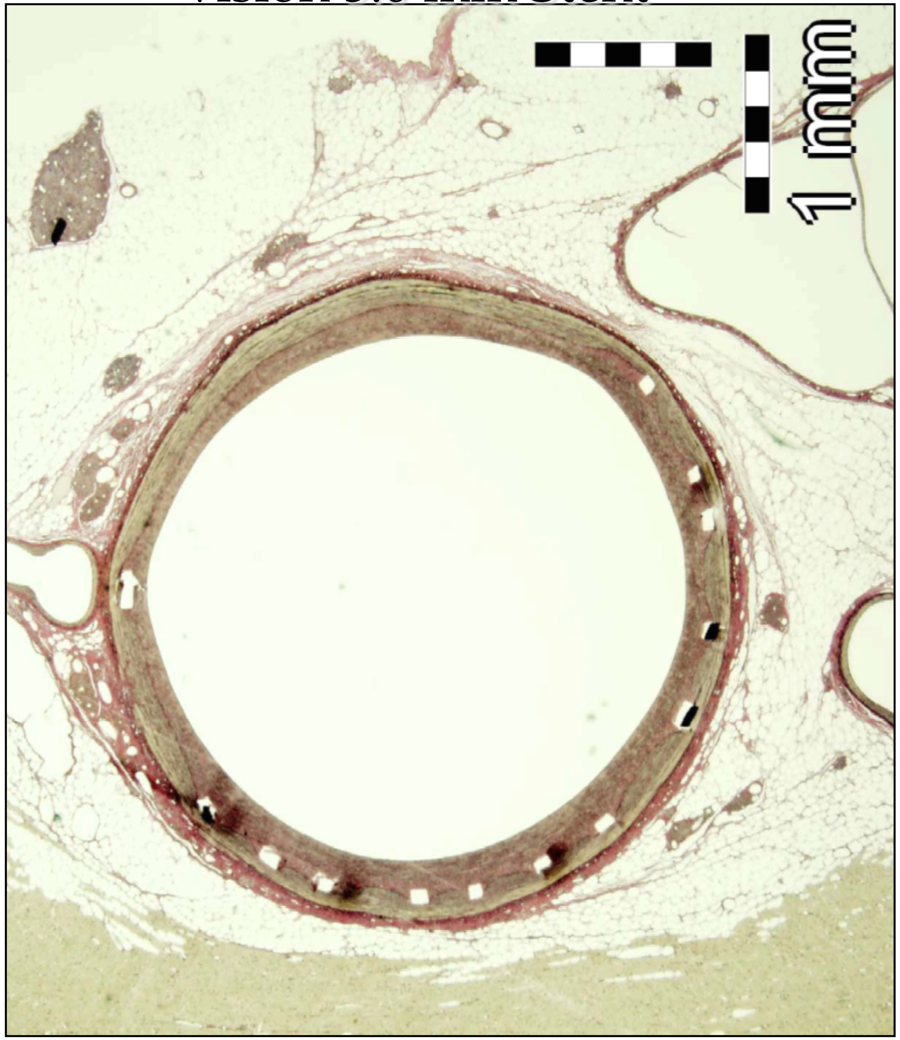
Stent Design Is a Balancing Act of Trade-offs impacting Deliverability and Clinical Outcomes

Scaffolding
Radial Strength
Recoil
Radiopacity
Expansion range

Flexibility
Conformability
Metal in vessel
Profiles

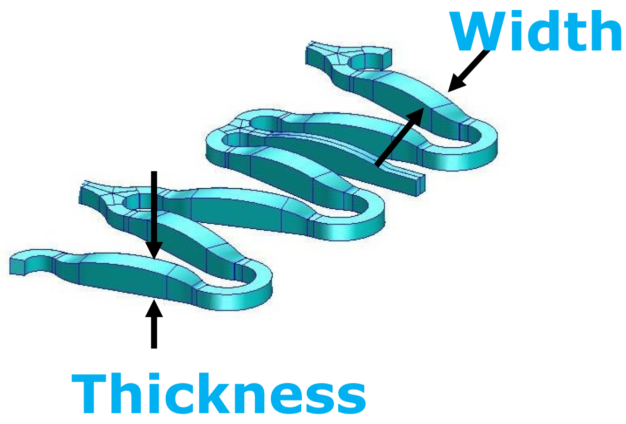
Histopathology (Porcine Model) 90 Days Vision

Vision 3.0 mm Stent



Stent Struts

Definition of STENT STRUT: the strands of metal that make up the underlying stent structure.

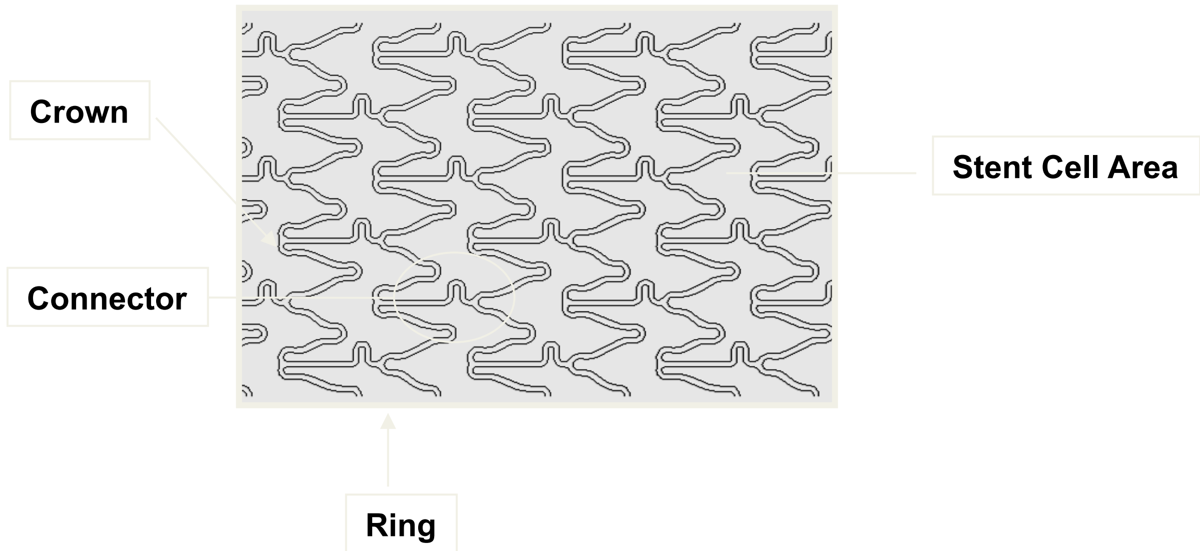


- Strut thickness
- Strut width
- **Clinical Implications**
  - Thin struts are associated with reduced restenosis
  - Thinner struts can have more recoil

Stent Crowns and Connectors

- **Stent crowns/crest**: the stent struts are formed into curved, repeating patterns creating **rings** around the circumference of the stent – each pattern repeat is called a crown or a **crest**

- **Connectors:** strut segments that connect the crowns to one another to form the **stent cell**

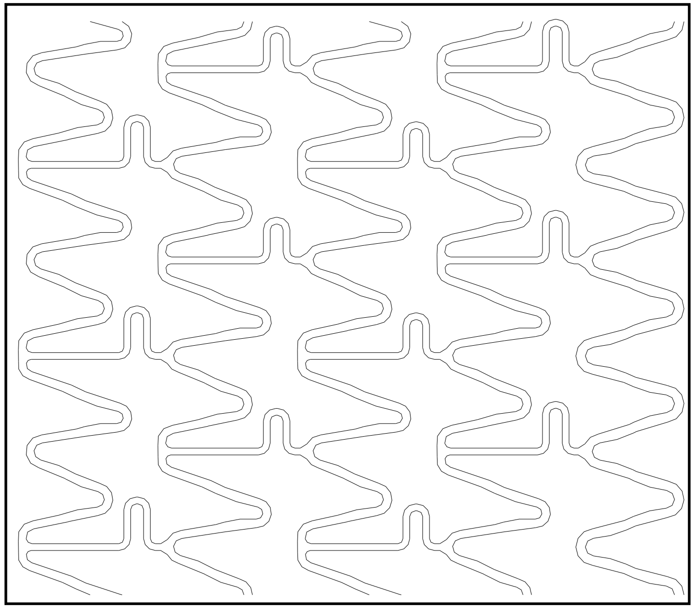


Number of Connectors per Ring

More connectors

Less flexible

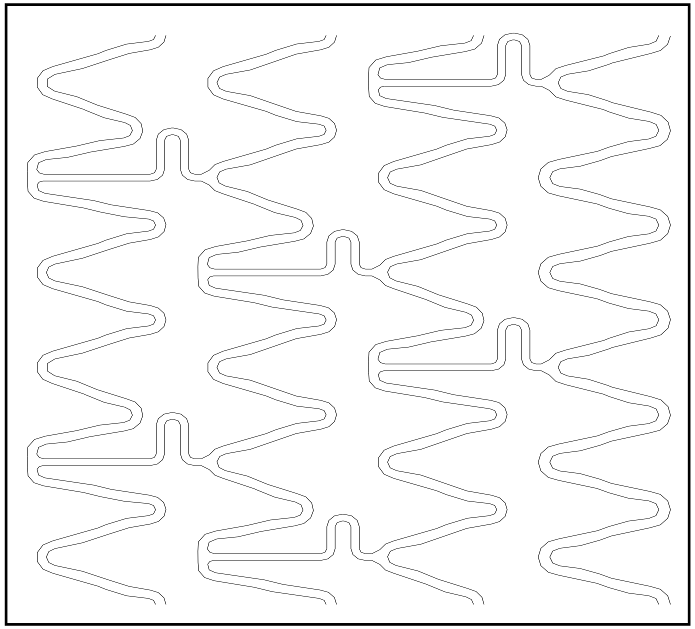
More scaffolding



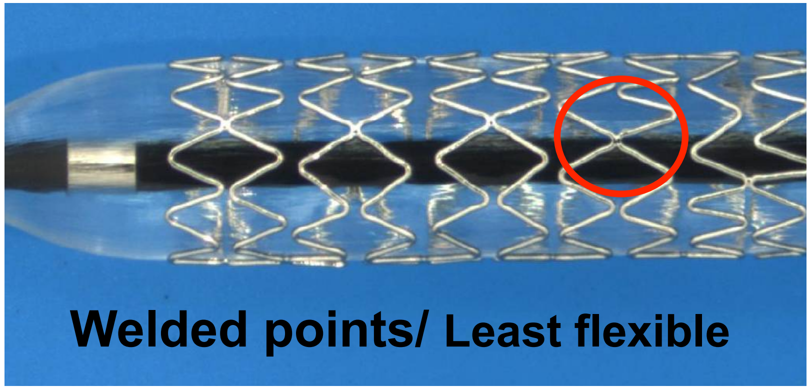
Less connectors

More flexible

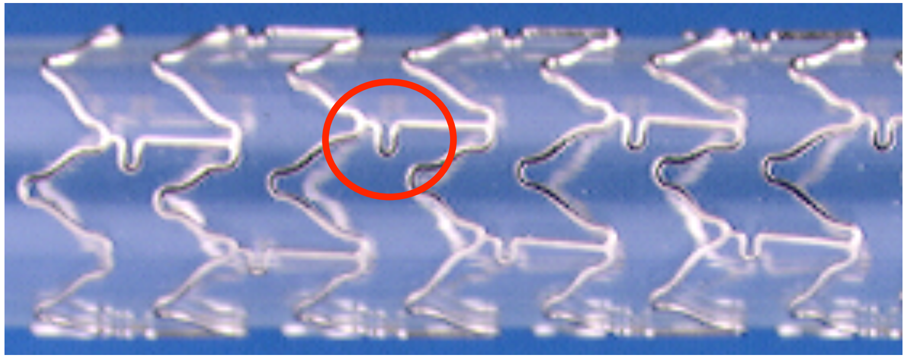
Less scaffolding

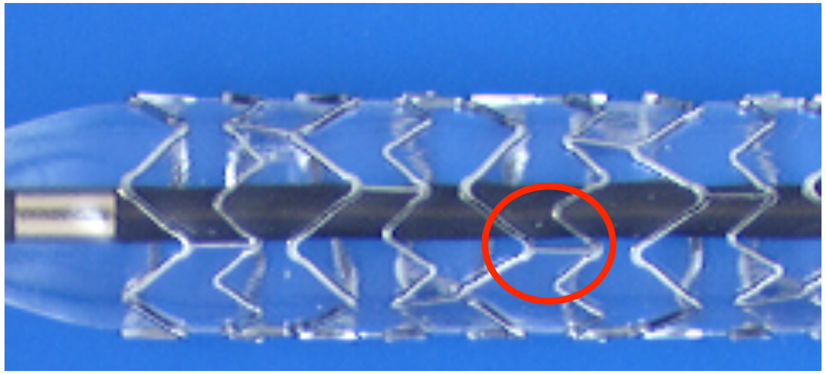


Connector Design

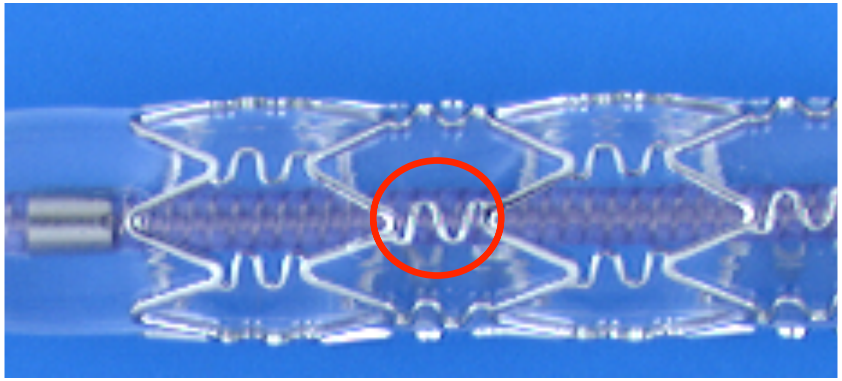


Welded points/ Least flexible



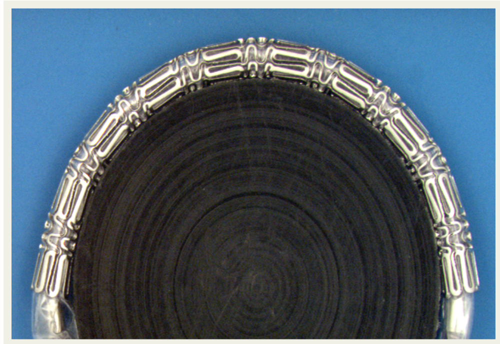


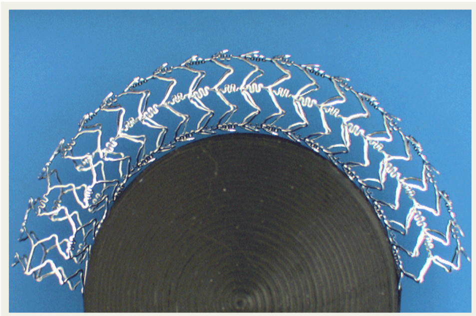
Straight link/ Less flexible

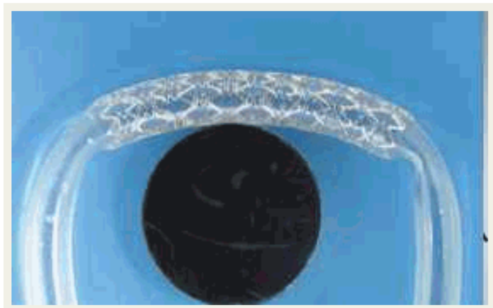


Curved link/ More flexible

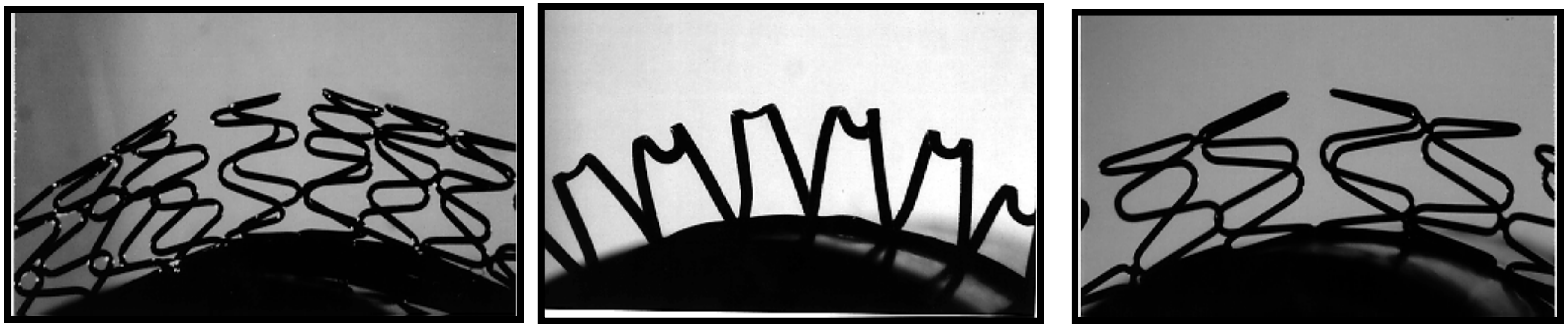
Flexibility and Conformability







Scaffolding



Terminology: Metal-to-Artery Ratio

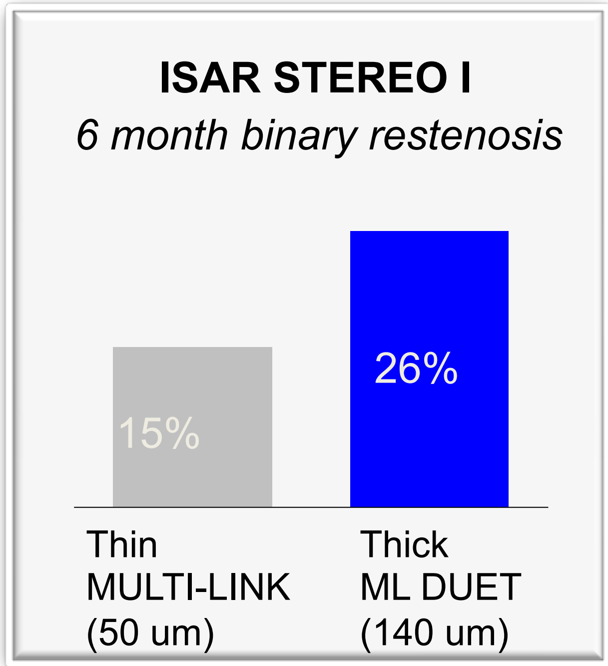
Definition of METAL-TO-ARTERY RATIO: Ratio of metal surface area of the stent to the surface area of the artery that the stent is covering

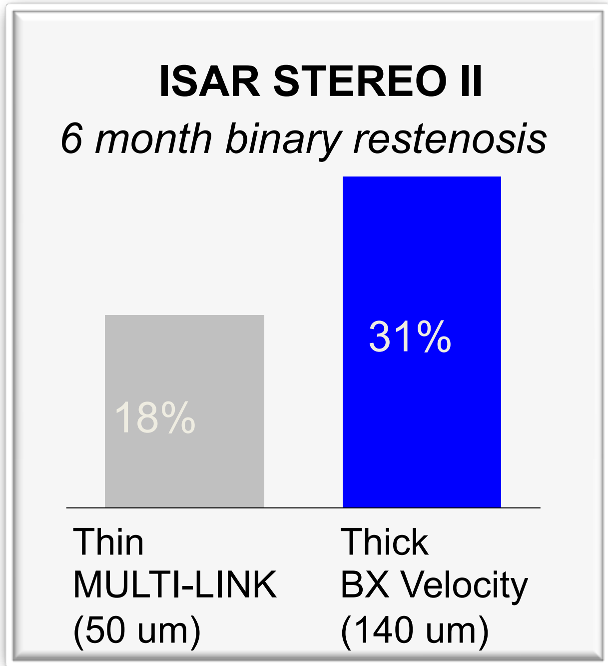
Clinical Implications

- Excessive metal may result in greater thrombogenicity and neointima hyperplasia
- Loss of flexibility
- Reduced side branch access

Thin Strut Advantage: Less Injury and Long-Term Restenosis

Reduce deep wall trauma





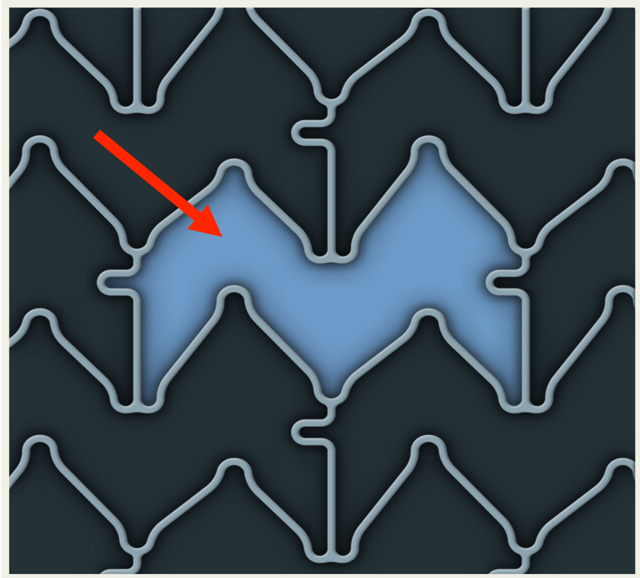
Struts thickness have a significant impact on long-term restenosis after stent implantation.[1,2]

1. Kastrati, et al. Intracoronary stenting and angiographic results strut thickness effect on restenosis outcome (ISAR-STEREO) trial. Circulation 2001; 103:2816-2821.
2. Pache, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. JACC 2003; 41:1283-8.

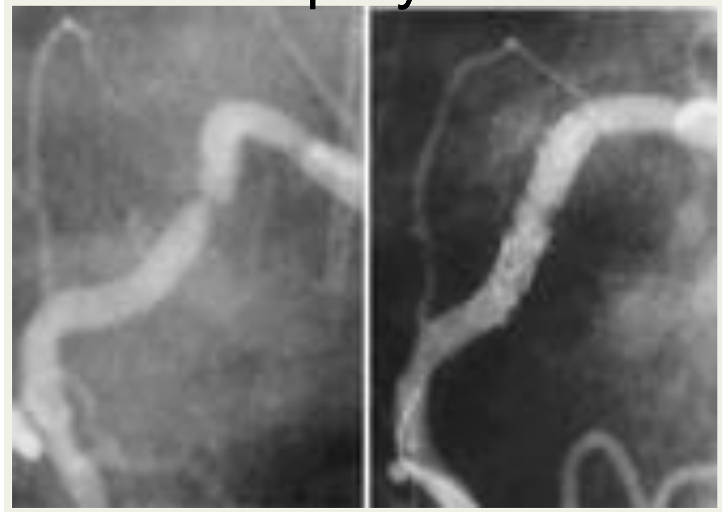
Unsupported Surface Area

Area of the vessel wall which lies

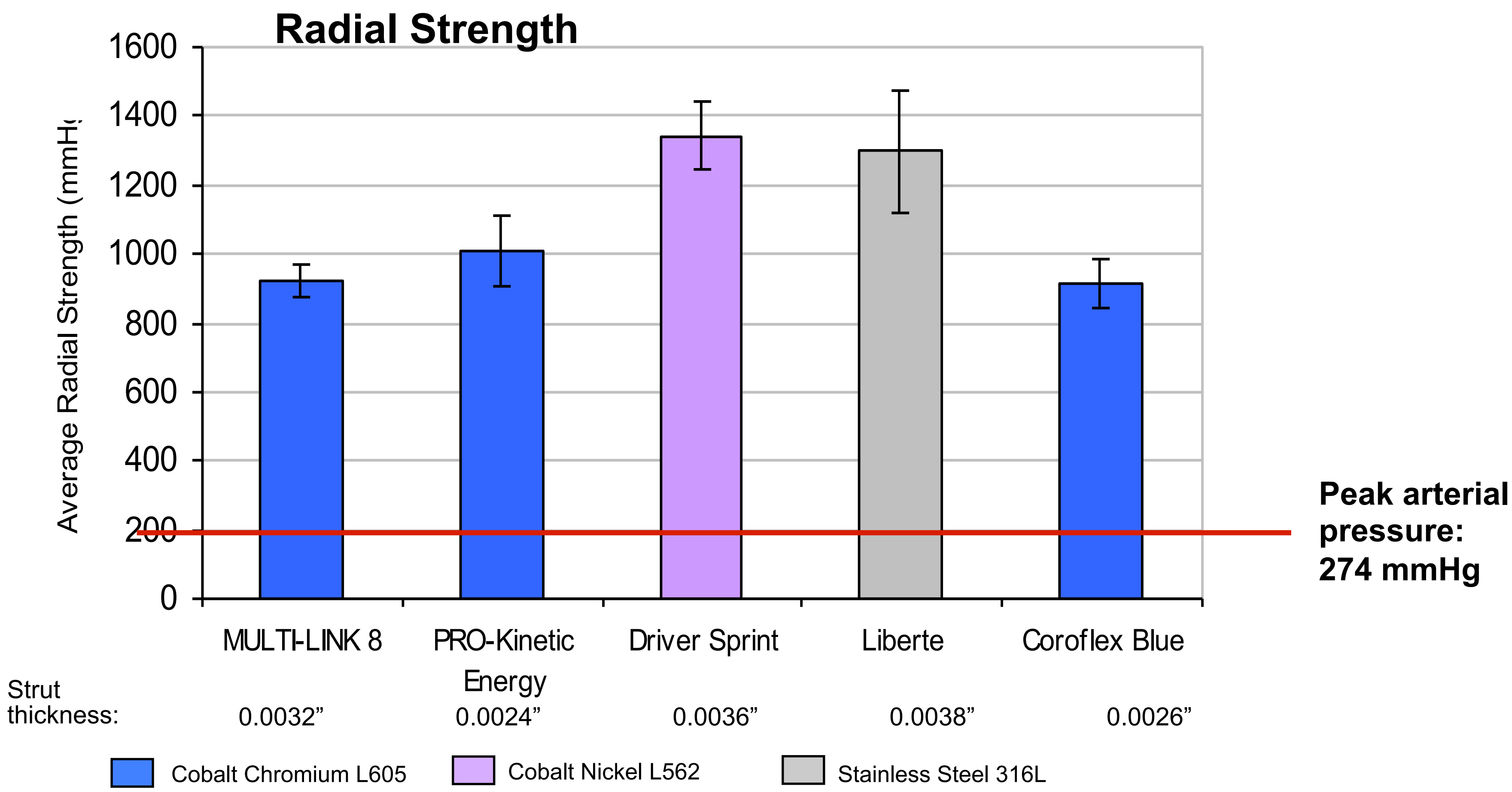
between the stent struts



Tissue prolapse
after stent deployment



Currently Marketed Stents Have Sufficient Radial Strength to Withstand Arterial Pressure



Agrawal et al, Biomaterials: Vol. 13, #3, 1992. .

Considerations for Pre-dilatation
Lesion Considerations

- Lesion Characteristics
  - Eccentric
  - Calcified/Resistant
  - Chronic Total Occlusion
- Lesion Length
  - Complete coverage
  - Vessel injury beyond stent edges
- Vessel Diameter
  - Dissection risk with small or tapered vessels

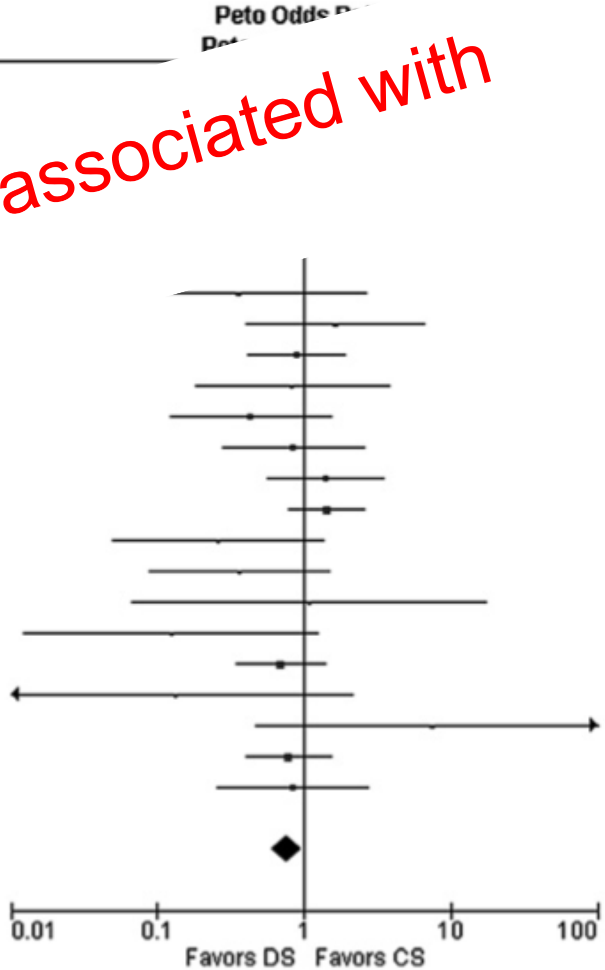
Finet G, et al. Heart (2003) 89:84-90.

Results from DS Meta-Analysis

Study or Subgroup	Direct stenting Events	Direct stenting Total	Conventional stenting Events	Conventional stenting Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Airoldi et al.	3	140	3	131	2.0%	0.93 [0.19, 4.70]
BET	3	173	10	165	4.3%	0.31 [0.10, 0.9
Brueck et al.	9	171	9	164	5.9%	0.96
CK TEST	4	59	9	44	3.9	
CONVERTIBLE	2	101	5	10		
Cuisset et al.	3	25	7			
Danzi et al.	0	61				
DECIDE	1					
DIRAMI						
DIRECT						1.88]
						.82 [0.18, 3.76]
					.4%	0.43 [0.12, 1.52]
				124	4.3%	0.84 [0.28, 2.57]
			8	200	6.2%	1.39 [0.55, 3.49]
			19	454	15.1%	1.44 [0.79, 2.60]
	1	37	5	40	1.9%	0.26 [0.05, 1.36]
	2	102	6	104	2.7%	0.36 [0.09, 1.48]
ure trial	1	39	1	42	0.7%	1.08 [0.07, 17.57]
Ozedmir et al.	0	25	3	25	1.0%	0.12 [0.01, 1.25]
PREDICT	14	198	20	201	10.7%	0.69 [0.34, 1.40]
Sabatier et al.	0	65	2	65	0.7%	0.13 [0.01, 2.15]
SWIBAP	2	197	0	199	0.7%	7.50 [0.47, 120.38]
TRENDS	16	379	21	395	12.1%	0.79 [0.41, 1.52]
VELVET	5	200	6	201	3.7%	0.83 [0.25, 2.76]
Total (95% CI)		**3412**		**3391**	**100.0%**	**0.76 [0.60, 0.96]**
Total events	135		173			

Heterogeneity: $Chi^2 = 25.02$, $df = 22$ ($P = 0.30$); $I^2 = 12\%$
Test for overall effect: $Z = 2.35$ ($P = 0.02$)

"23% reduction in the odds of MI associated with Direct Stenting"



Piscione et al. Heart 2010:96:588-594

Rationale for direct-stenting

Comparison of Direct Stenting With Conventional Stent Implantation in AMI (HORIZONS-AMI) : At 1-year follow-up, direct compared to conventional stenting was associated with a significantly lower rate of all-cause death (58% reduction) and stroke, with non-significant differences in TLR, MI, Stent Thrombosis and major bleeding.

	Direct (n=698)	Conventional (n=1830)	*P-value*
All-cause death	**1.6 %**	3.8 %	p=0.01
Cardiac death	**1.2 %**	2.7 %	p=0.02
Stroke	**0.3 %**	1.1 %	p=0.049

Möckel et al. ***Am J Cardiol 2011****:108:1697-1703*

Potential Clinical Benefits of Direct Stenting

- **Post procedural**
  - Greater rates of TIMI grade 3 flow ($p<0.0001$)
  - Less distal embolization (final slow reflow $p=0.04$)
  - Improved ST segment resolution (Relative at 60 mins $p=0.01$)
- **1-Year Follow-Up**
  - Reduced All-Cause Death ($p=0.01$)
  - Lower stroke ($p=0.049$)

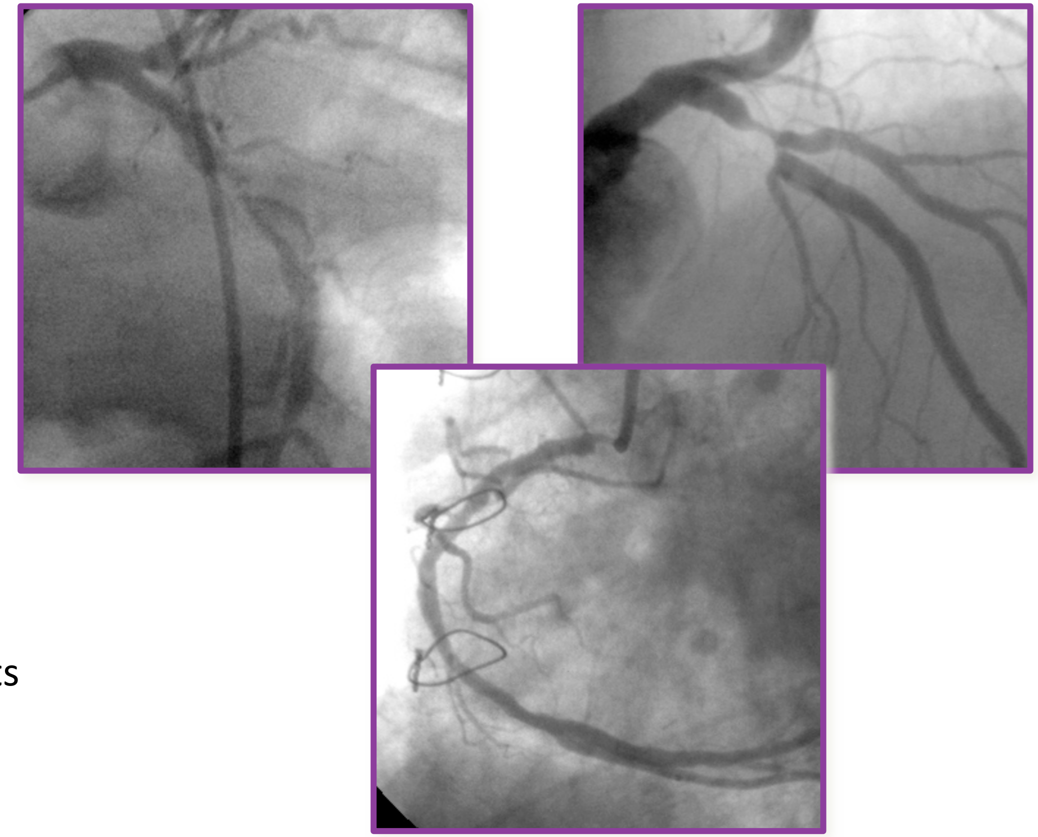
Möckel et al. Am J Cardiol 2011; 108:1697-1703)

Additional Benefits of Direct Stenting

- **Shorter fluoroscopy time**
- **Less use of contrast**
- **Less material usage**
- **Lower procedure time**

When Considering Post-dilatation Clinically:

- Vessel expansion
- Resistant lesions
  - Calcific
  - Fibrotic
- Complex Lesions
  - Bifurcation
  - Ostial Lesions
  - Long Lesions
  - Small Vessels
  - In-Stent Restenosis
  - Multiple overlapping stents

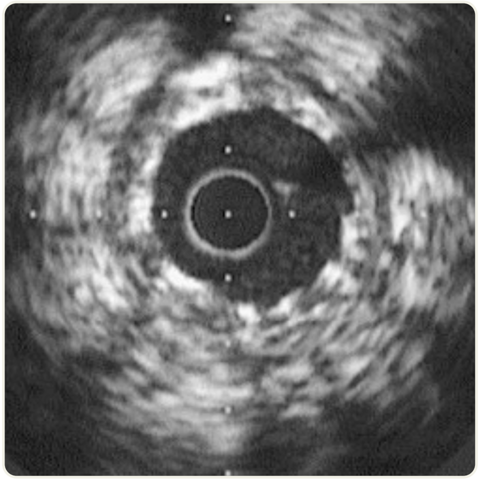


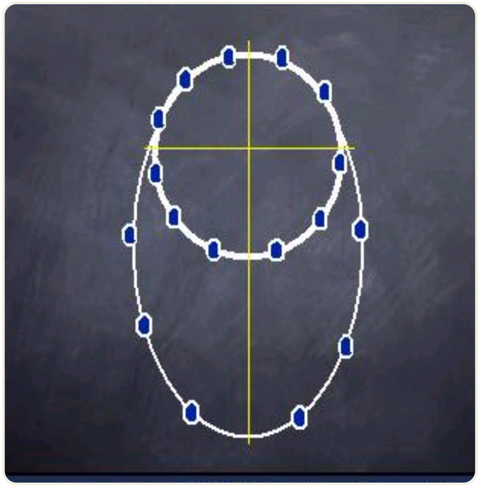
Romagnoli, Enrico et al.,
"Drug Eluting Stenting The Case for Post Dilatation," JACC, 2008.

Post-dilatation: Potential Advantages / Disadvantages

- Potential Advantages
  - More complete stent apposition
  - Restenosis reduction
  - Avoidance of thrombosis
  - Decreased rate of TVR
    (target vessel revascularization)
  - Uniform drug delivery

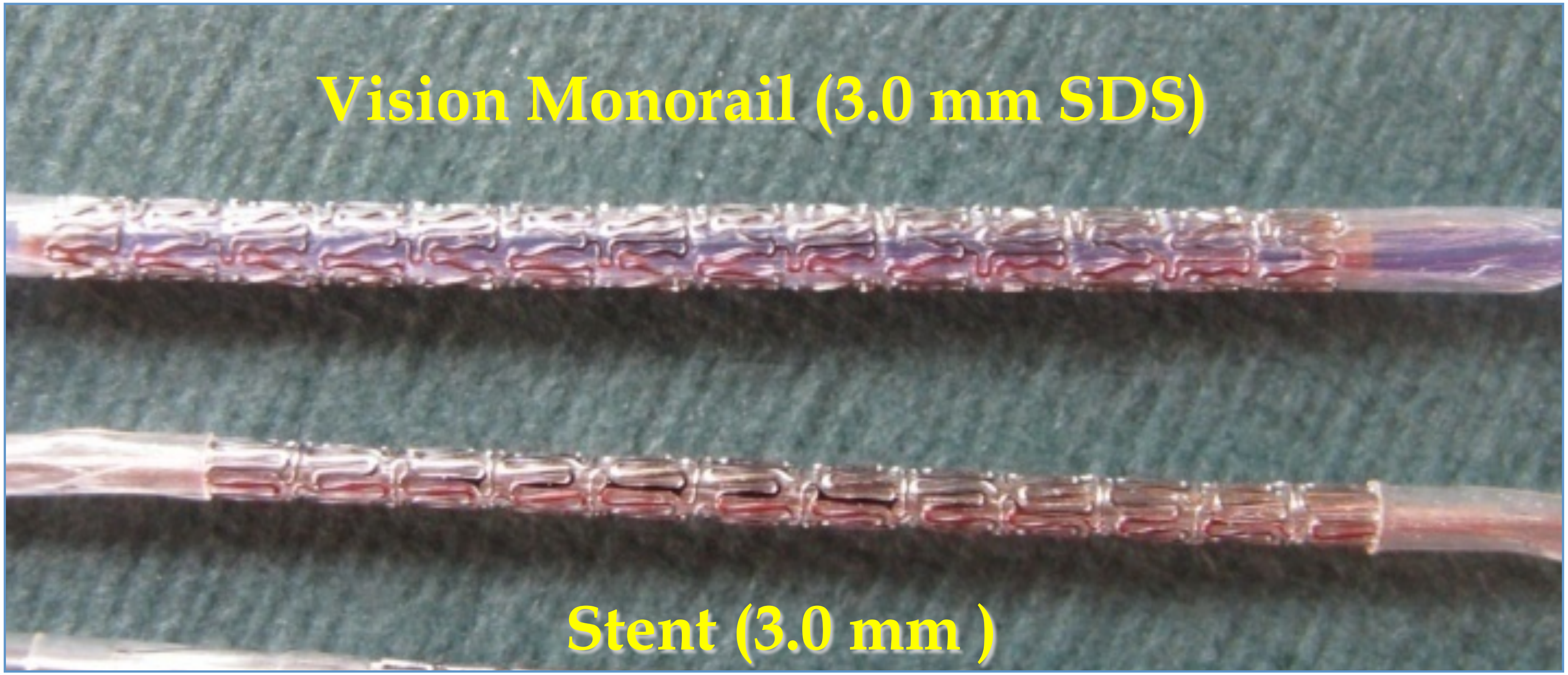
- Potential Disadvantages
  - Additional vessel injury





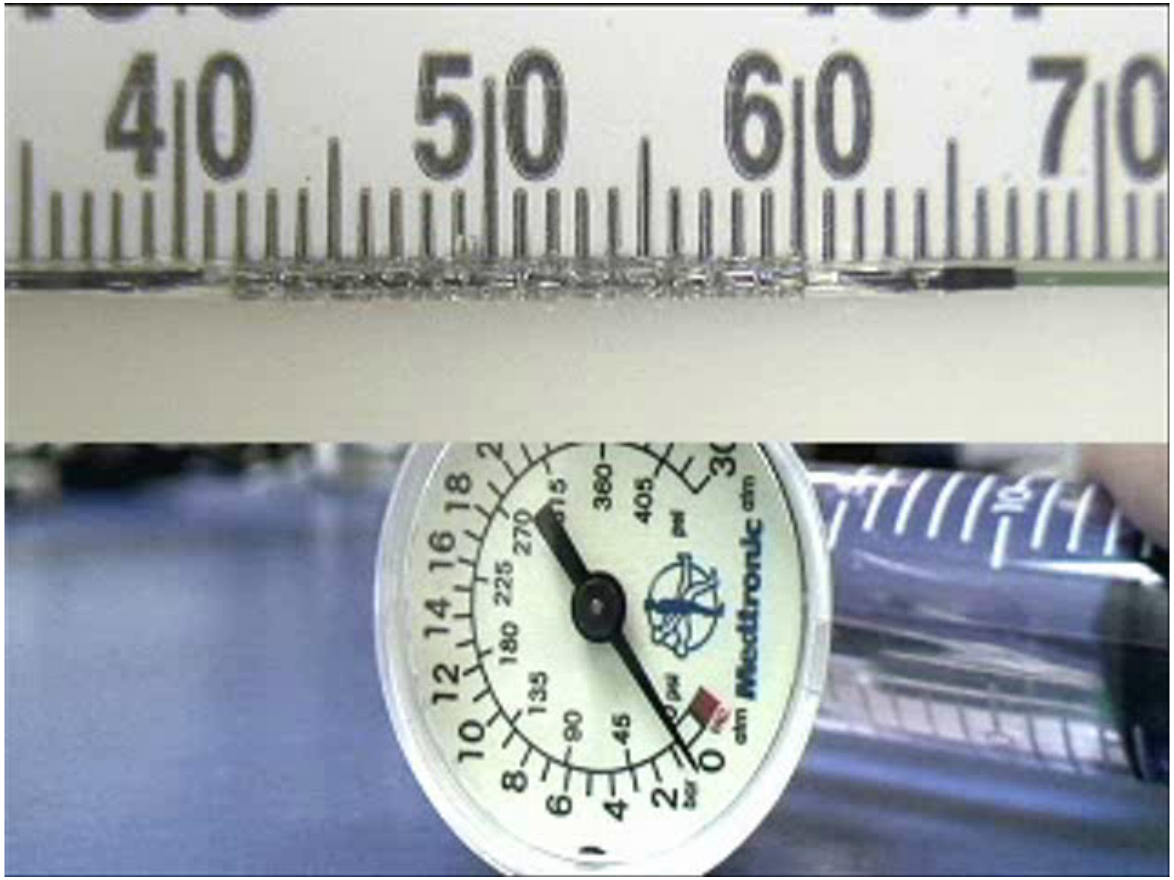
Henry K. et al., "The Perfect Fit: Getting the Most out of Your Coronary Stent," Cath Lab Digest, 2005.

Comparative Profiles

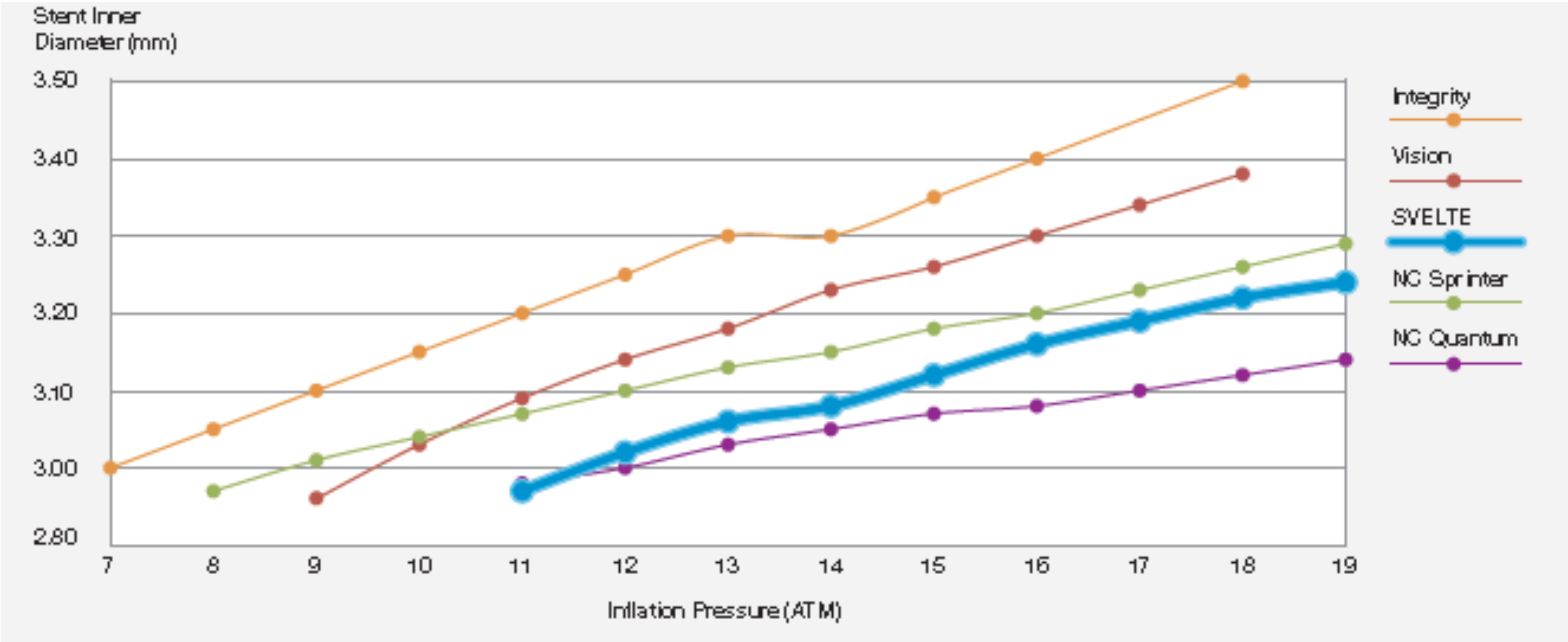


Balloon Inflation Control

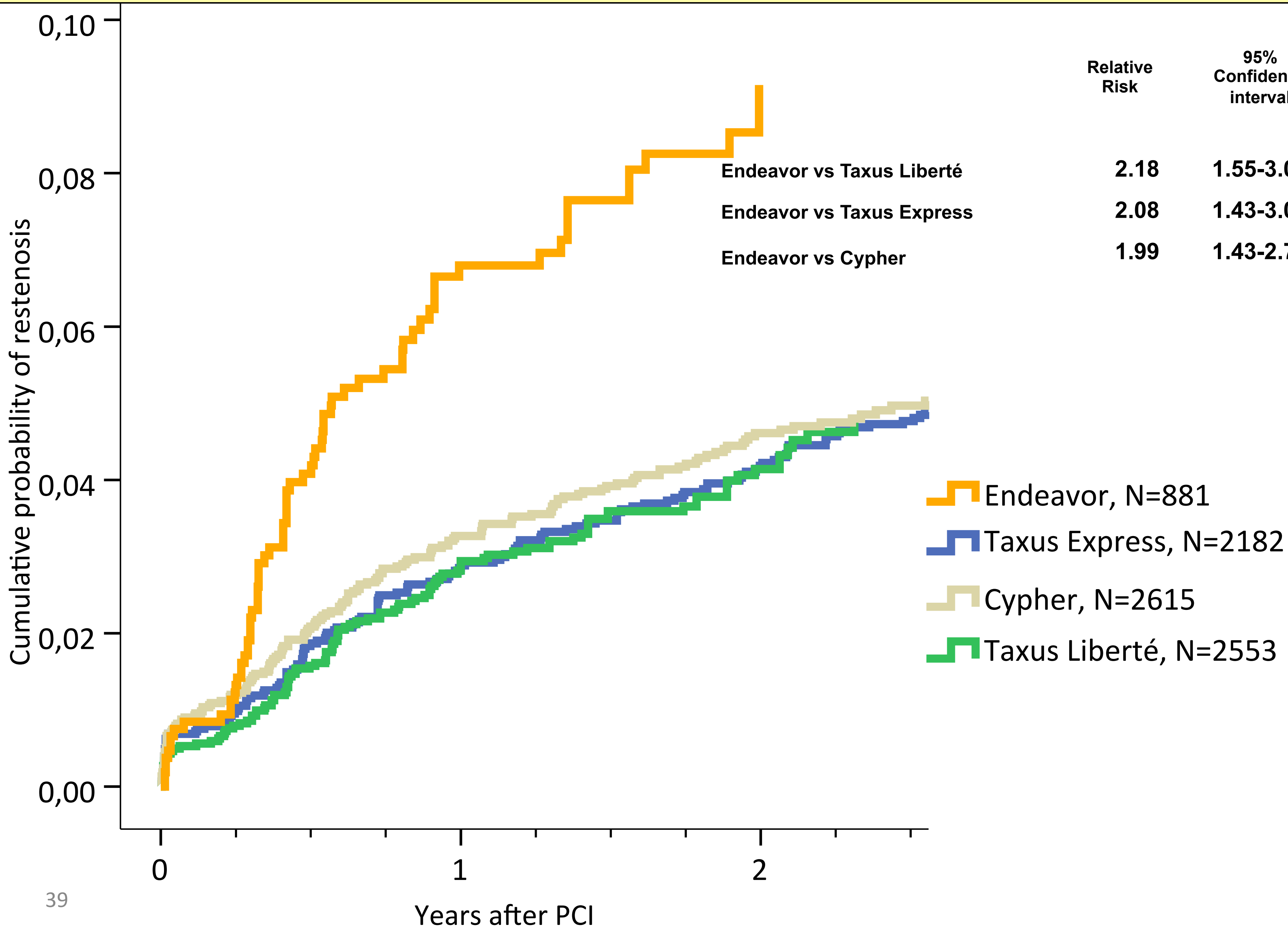
Typical Nylon Balloon



Compliance Comparison



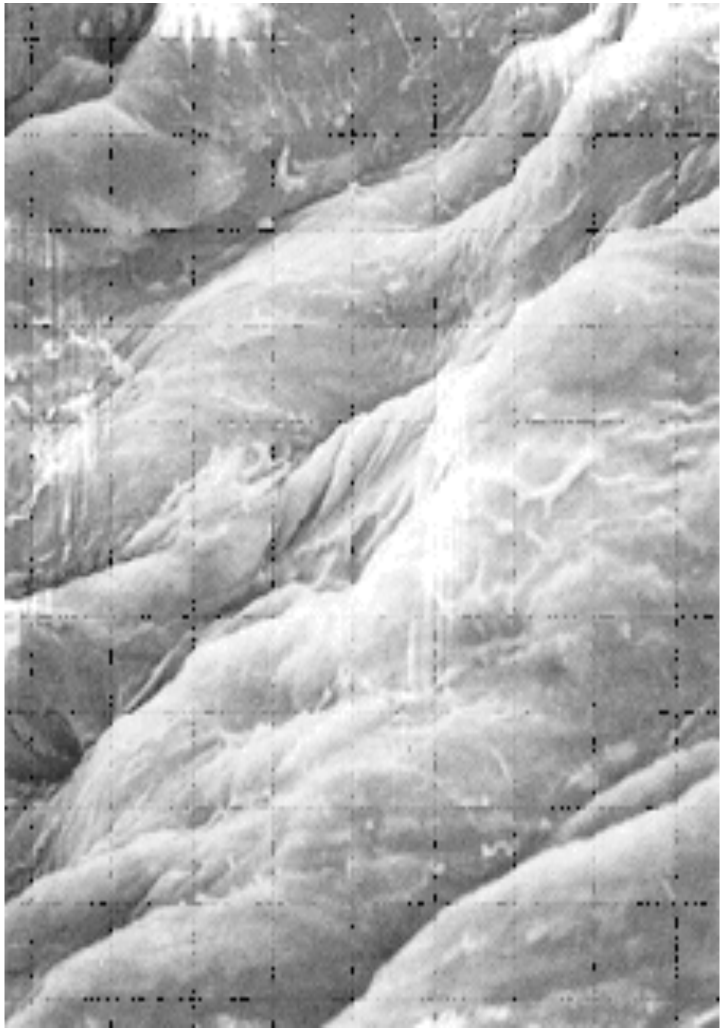
Diabetes, Adjusted



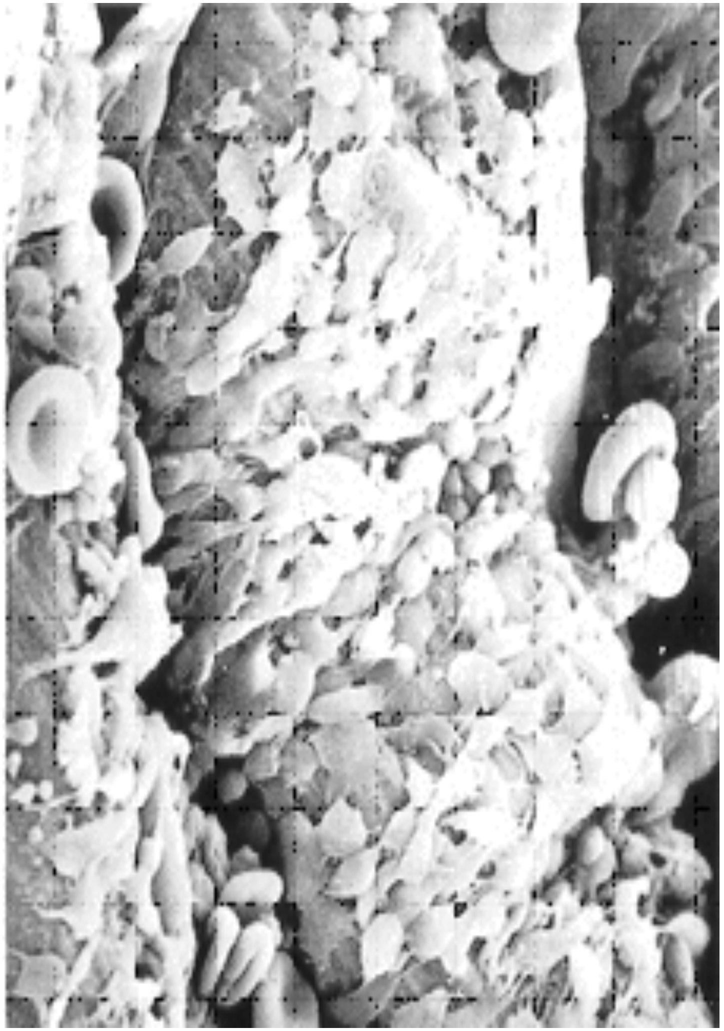
	Relative Risk	95% Confidence interval
Endeavor vs Taxus Liberté	2.18	1.55-3.07
Endeavor vs Taxus Express	2.08	1.43-3.00
Endeavor vs Cypher	1.99	1.43-2.77


Tout va bien
tout va bien,
tout va bien,
tout va bien
...

Endothelial Layer



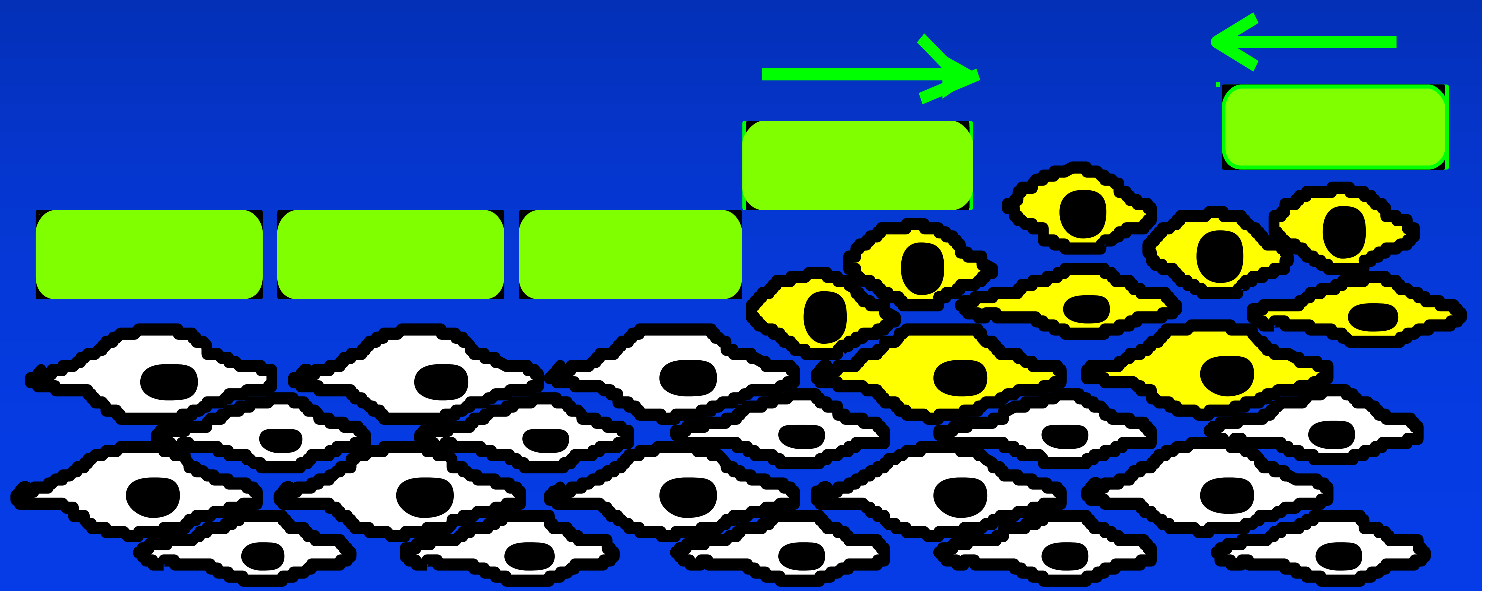
Normal

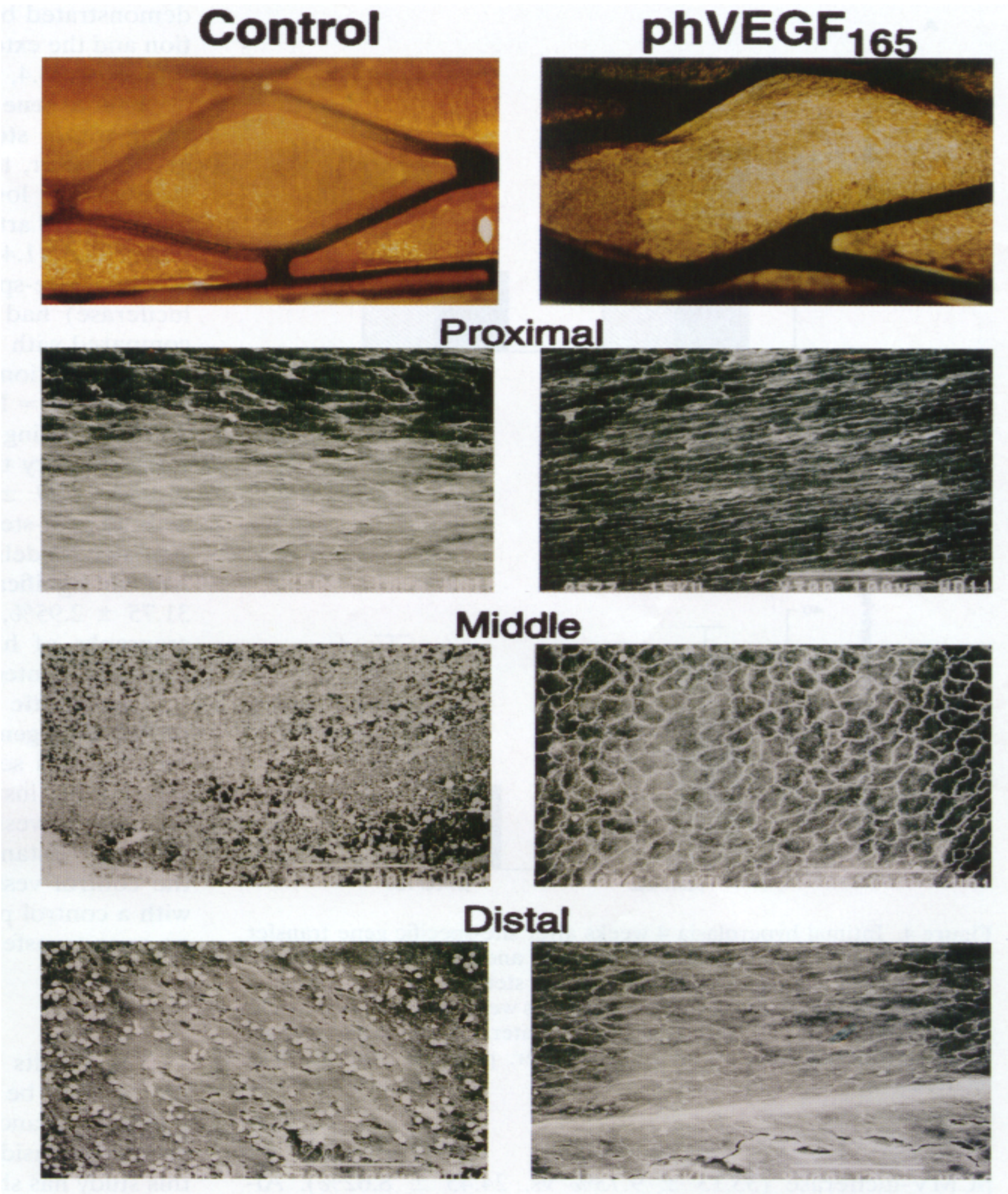


Ischemic

VEGF

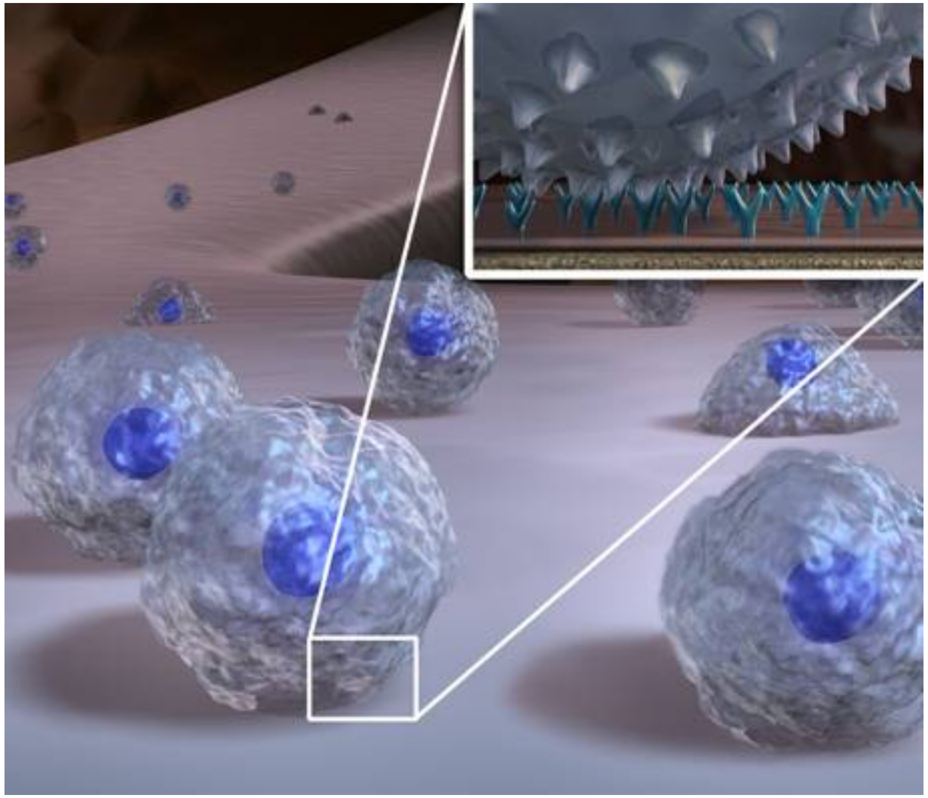
Direct application of VEGF to the intimal surface of balloon-injured artery accelerates re-endothelialization and reduces neointimal thickening.

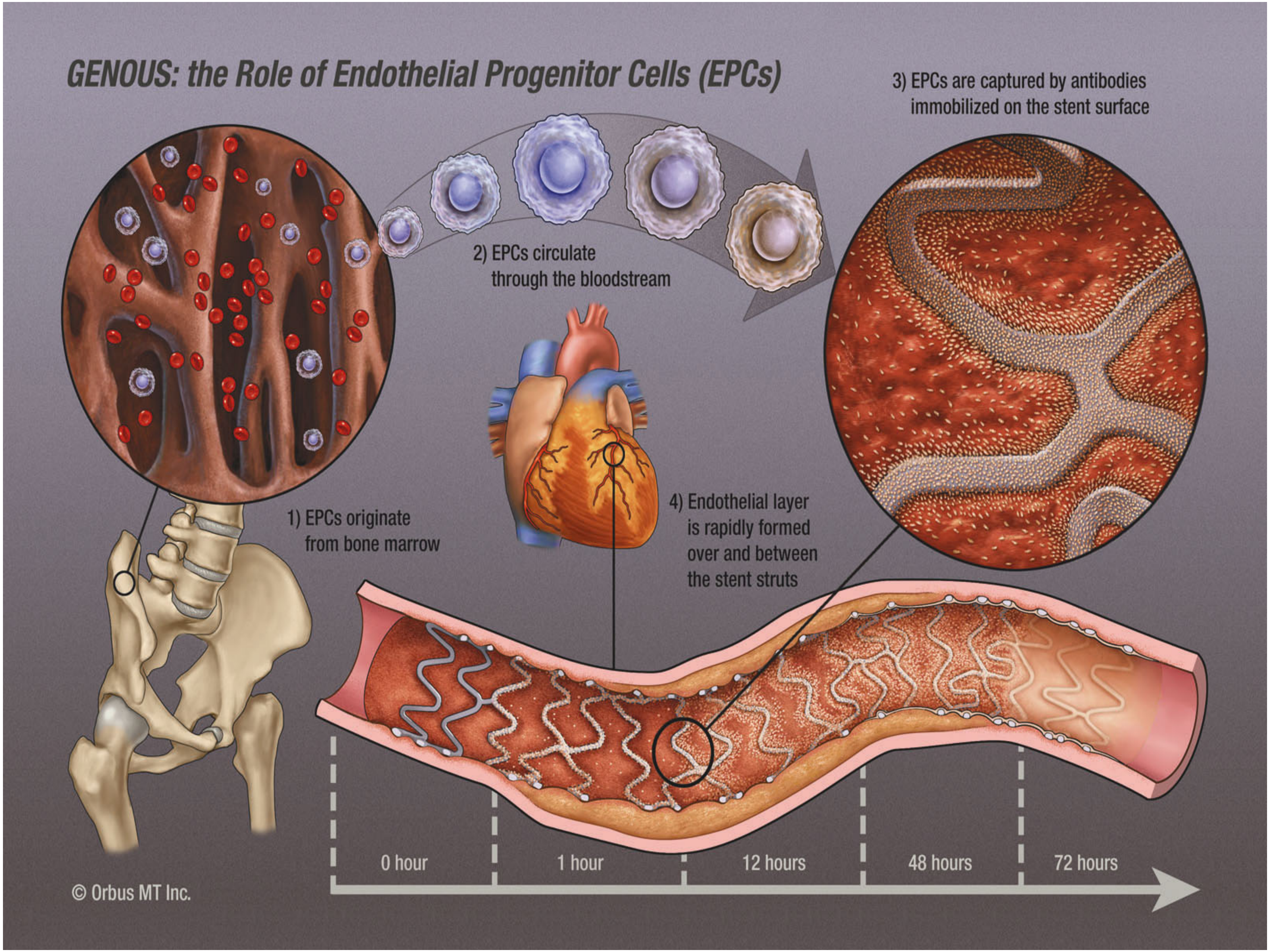




Van Belle
JACC
1997;
29:1371-9

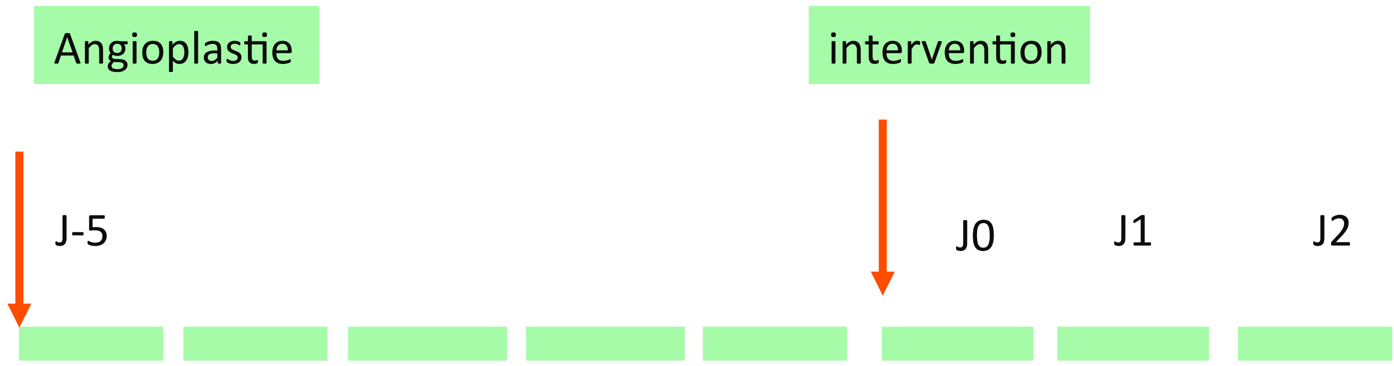
Antibodies specific to EPCs are immobilized on the stent surface and capture circulating EPCs.





GENOUS: the Role of Endothelial Progenitor Cells (EPCs)
1) EPCs originate from bone marrow
2) EPCs circulate through the bloodstream
3) EPCs are captured by antibodies immobilized on the stent surface
4) Endothelial layer is rapidly formed over and between the stent struts
0 hour
1 hour
12 hours
48 hours
72 hours
© Orbus MT Inc.

En Pratique:



Aspirine	2mg/kg	0/+	0/+	0/+		0/+	0/+	Reprise si arrêt
Plavix	10 mg/kg	0	0	0	0	0		Reprise

Coronary stenting and surgery, a complex situation to manage. Usefulness of endothelial progenitor cells capture.

Philippe Longere, MD, François Vochelet, MD,
Alain Tavildari, MD, Marie Rose Clergeau, MD,
Bertrand Olive, MD, Jean Marc Pigassou, MD,
Luc Maillard, MD, PhD
Clinique Axium, Aix en Provence, France

Method :

In real life conditions, 11 patients, 7 male, 4 female, 77.4+/-7.37 year old, presented an acute coronary syndrom with severe coronary artery lesions and an urgent surgical indication underwent PTCA with exclusive one or more Genous stent (Orbus Medical).

Single unique bolus of 10 mg/kg of clopidogrel associated to 2 mg/kg of aspirin was given at least 6 hours prior PTCA.

Surgery was planed to be performed at day 5 following half pool platelet renewal. Inform consent was obtained for all patients.

Results :

1.72+/-0.78 stent was implanted for a total lenght of 28+/-12 mm and a mean diameter of 3.0+/-0.5 mm.

All target selected lesions included left main (n=1), LAD (n=9), CX (n=3), RCA (n=6) were treated with angiographic success.

Mean ventricular ejection fraction was 55.0+/-0.5.

Surgery was performed in average at day 5 under aspirin alone (2 mg/kg) with success of the planed surgical act (colectomy, prostatectomy, cholesterolemy, mammectomy, gastrectomy, peripheral arteriel graft) with no complication.

Results (2) :

Intra veinous nitrate was used for patients presenting incomplete revascularisation and distal lesions.

Only one patient needed a blood transfusion.

At one month no event was observed
(death, myocardial infarction, repeat PTCA, cerebral event, stent thrombosis).

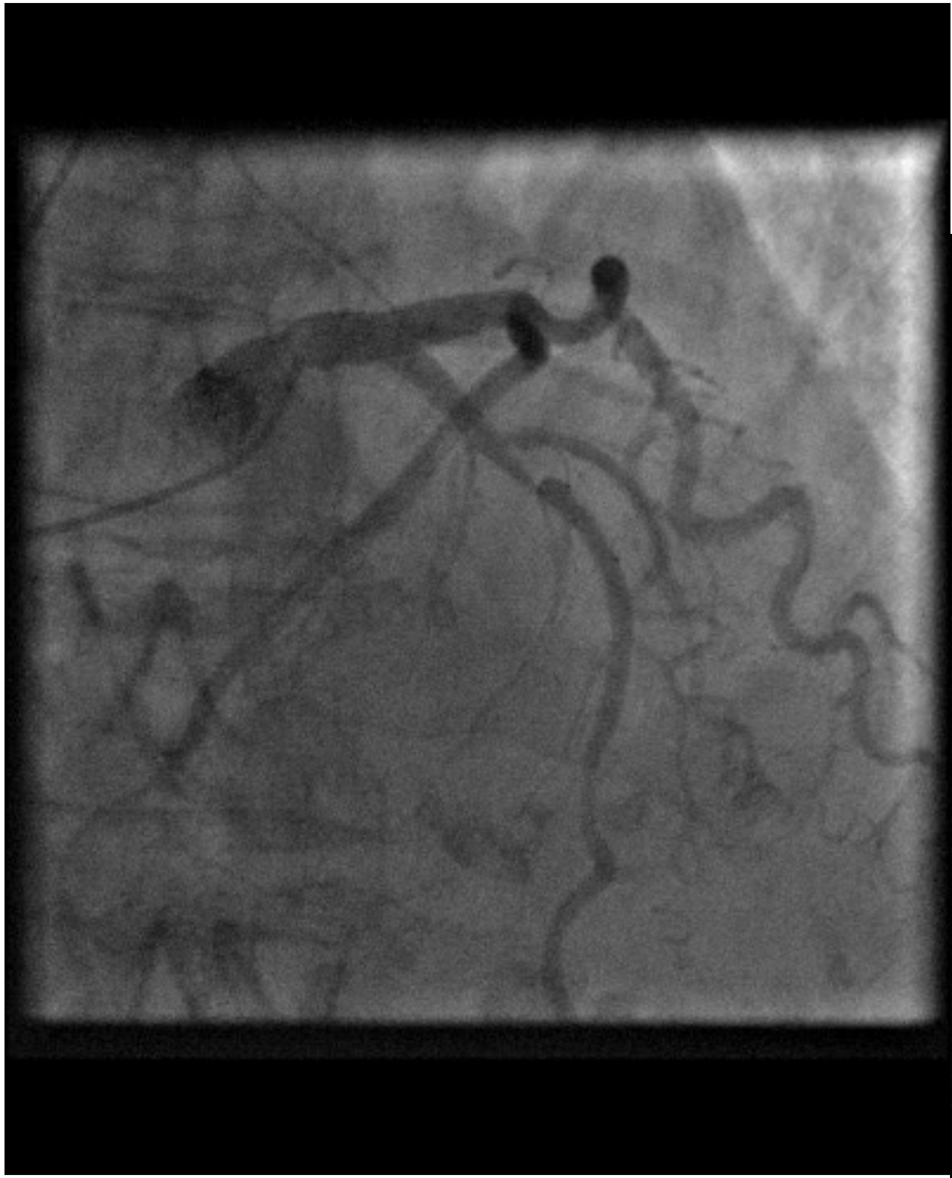
Conclusion :

Single bolus of clopidogrel for high risk evolutive coronary artery lesions treated with Genous stent allow a surgical act at day 5 under aspirin alone in good condition with no complication in this short serie.

Those preliminary data can serve as an impetus for multi-center studies.

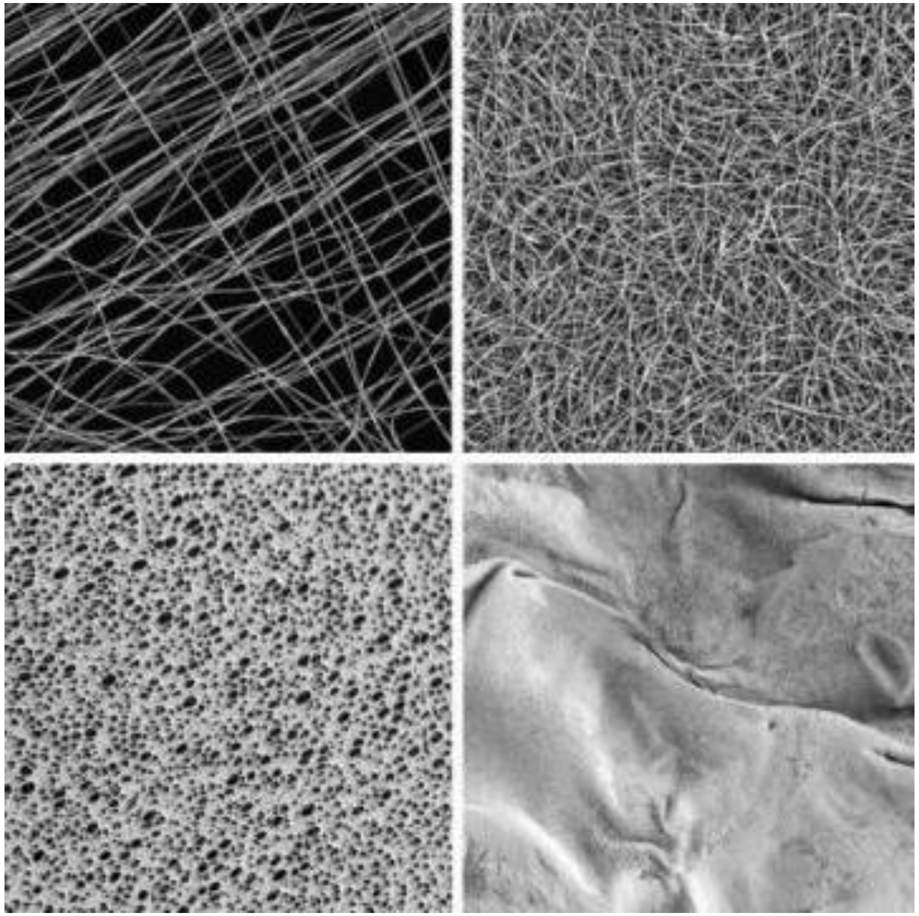
Mme P….. 82 ans, autonome
ATCD : ATCD ATC IVA moyenne BMS un an auparavant
sur lésion bitronculaire (CD 50%) , FEVG 45%
FRCV : Age, HTA
Présentation : OAP avec SCA (Lésion sous endocardique antérieure et élévation troponine) à J2 PTH sous aspirine

Coronarographie : Radiale G




Que faites vous?

Polyzene®-F represents a quantum leap in synthesized inorganic polymers.



A NanoThin surface treatment of Polyzene®-F increases the biocompatibility of the stent and does not trigger the coagulation cascade, which in turn leads to thrombosis reduction.

The Catania Stent (CeloNova BioSciences, Newnan, GA), a cobalt chromium stent with a modified, open-cell design, is surface-modified by the NanoThin Polyzene®-F polymer.

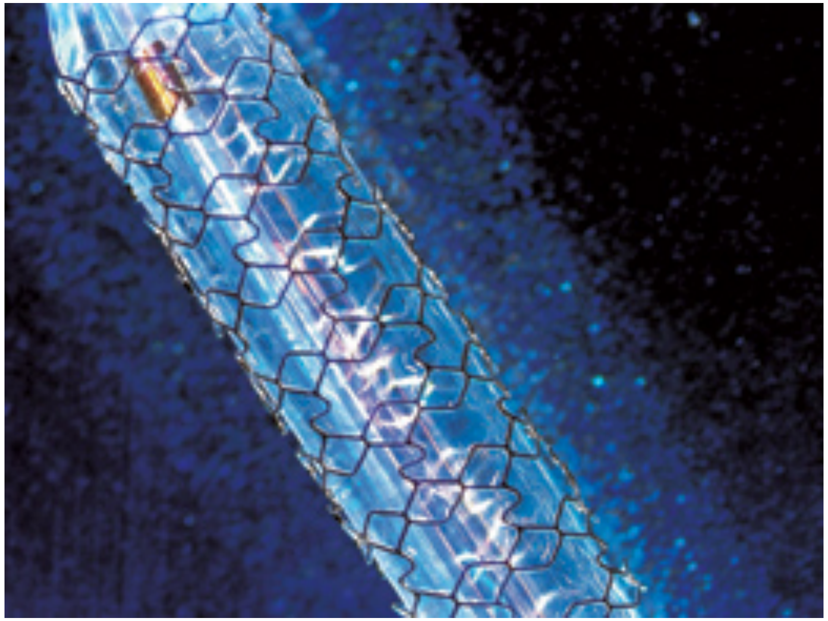
Preclinical studies demonstrate that Polyzene-F has very positive effects.

Polyzene-F has very low surface thrombogenicity.

This polymer has anti-inflammatory and bacterial resistance qualities, as well as a pro-healing effect.

The final result is a very low rate of stent thrombosis.

This stent also has a high rate of endothelialization compared to bare-metal and drug-eluting stents



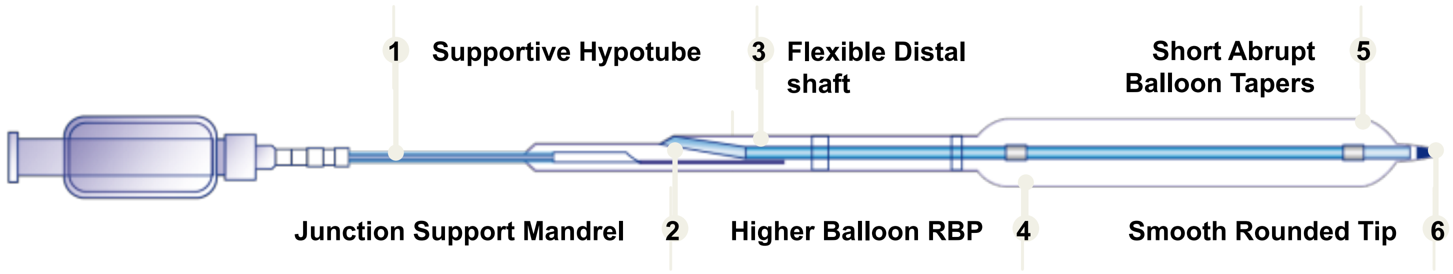
What is an Ideal Stent?

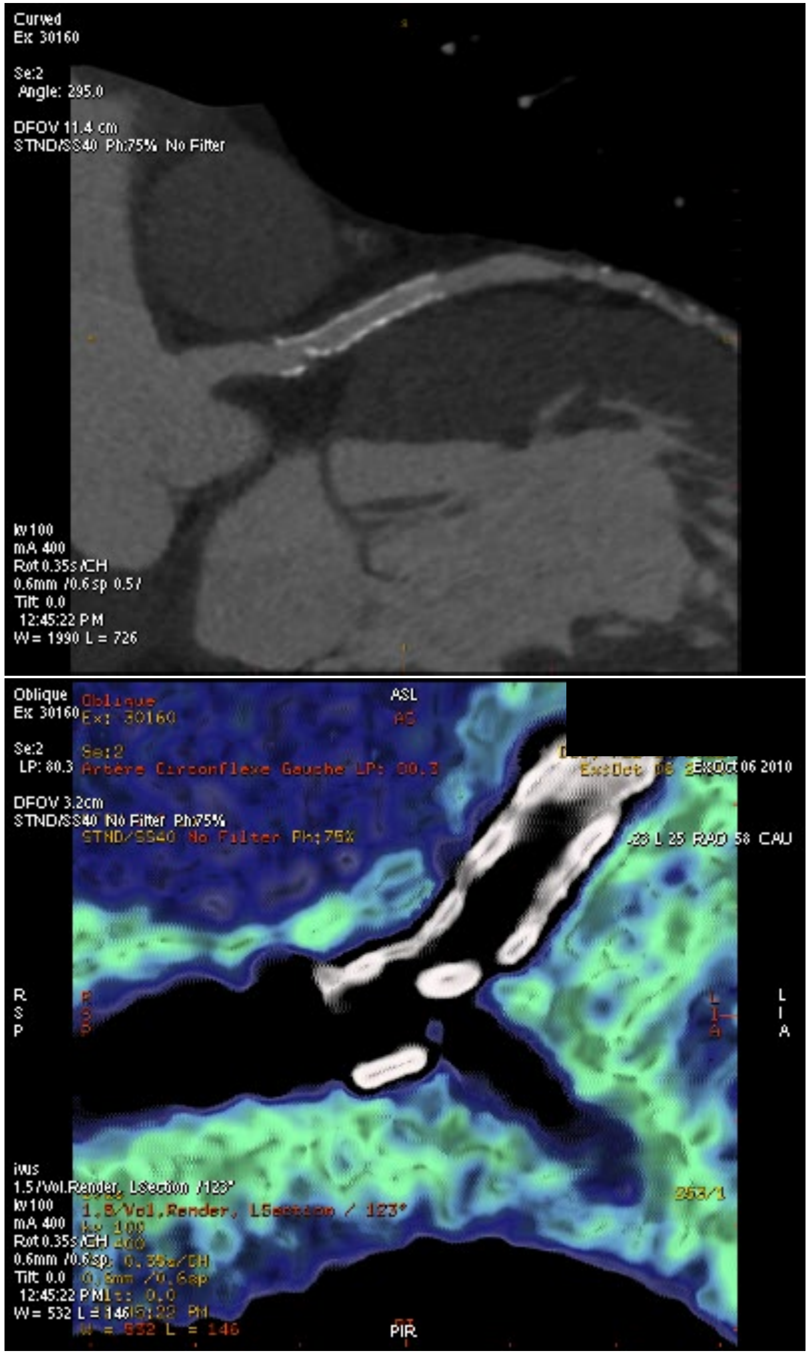
Ideal Stent

- Flexibility & conformability
- Good scaffolding
- High radial strength with minimal recoil
- Good visibility
- Minimal foreshortening
- Low restenosis rate and good safety
- Low cost

Ideal Stent

- Side-branch accessibility
- Appropriate metal-to-artery ratio
- Biocompatibility
- Optimal stent delivery system
- Variety of sizes and lengths

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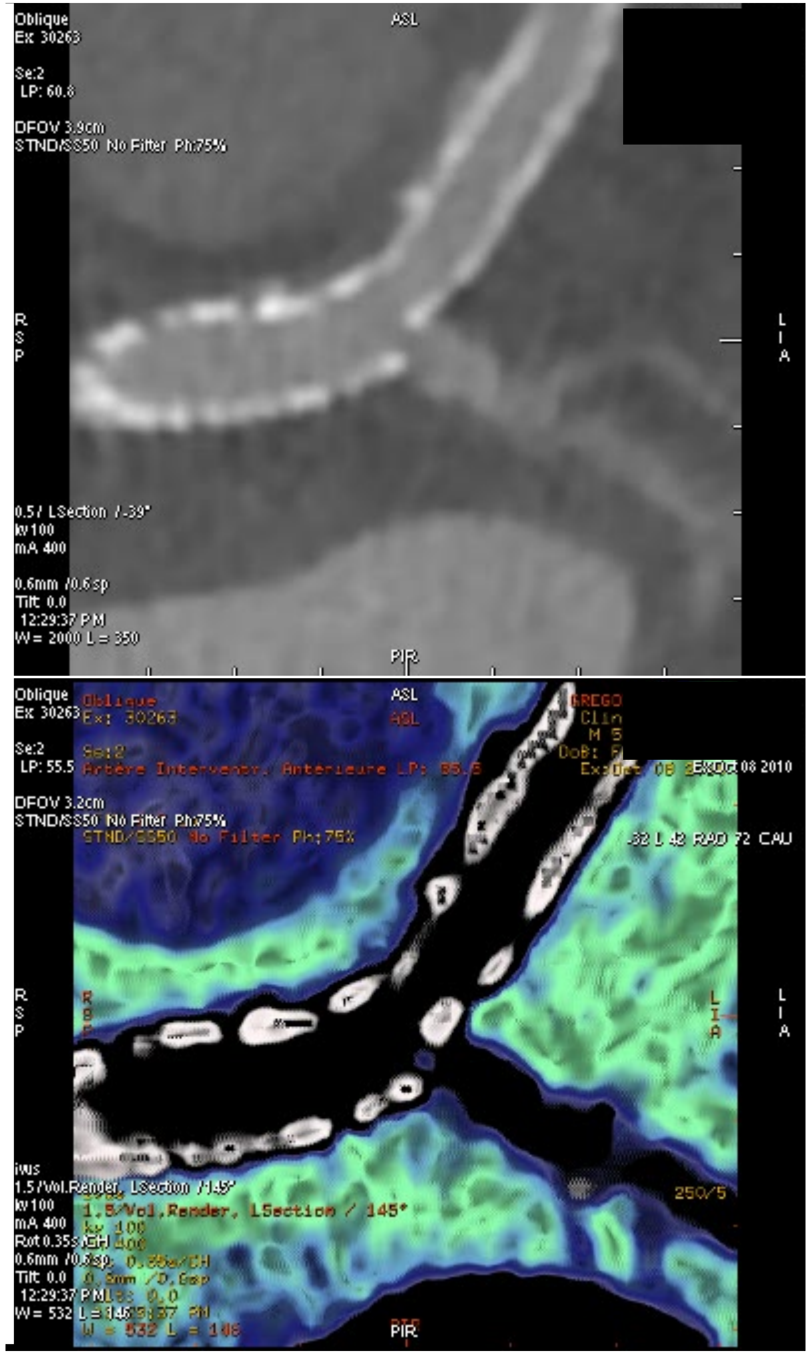
STND/SS40 Ph:75% No Filter
Oblique
Artère Circonflexe Gauche
DFOV 3.2cm
STND/SS40 No Filter Ph:75%
ASL
PIR

SMS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Se:2
LP: 60.8
DFOV 3.9cm
STND/SS50 No Filter Ph:75%
ASL
PIR
Artère Interventr. Antérieure
DFOV 3.2cm
STND/SS50 No Filter Ph:75%

Kiss

Summary

- Stents enable treatment of many lesion types
- Stent design influences deliverability and clinical outcomes
- Not all BMS are the same; not all DES are the same