BUILDING ENDOVASCULAR SYNERGIES

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In-stent Restenosis: the Achille's Heel of SFA Stenting

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Balloon Angioplasty versus Implantation of Nitinol Stents in the Superficial Femoral Artery

Martin Schillinger, M.D., Schila Sabeti, M.D., Christian Loewe, M.D., Petra Dick, M.D., Jasmin Amighi, M.D., Wolfgang Mlekusch, M.D., Oliver Schlager, M.D., Manfred Cejna, M.D., Johannes Lammer, M.D., and Erich Minar, M.D.

CONCLUSIONS

In the intermediate term, treatment of superficial-femoral-artery disease by primary implantation of a self-expanding nitinol stent yielded results that were superior to those with the currently recommended approach of balloon angioplasty with optional secondary stenting.

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Vascular Medicine

Sustained Benefit at 2 Years of Primary Femoropopliteal Stenting Compared With Balloon Angioplasty With Optional Stenting

Martin Schillinger, MD; Schila Sabeti, MD; Petra Dick, MD; Jasmin Amighi, MD; Wolfgang Mlekusch, MD; Oliver Schlager, MD; Christian Loewe, MD; Manfred Cejna, MD; Johannes Lammer, MD; Erich Minar, MD

Conclusions—At 2 years, primary stenting with self-expanding nitinol stents for the treatment of superficial femoral artery obstructions yields a sustained morphological benefit and a trend toward clinical benefit compared with balloon angioplasty with optional stenting. (*Circulation*. 2007;115:2745-2749.)

« Unresolved problems of SFA stenting »

- In-stent restenosis
- Stent fractures

Schillinger, *EuroPCR*, 2008

Vienna, Resilent, Fast *et al*...

	FAST	Vienna Study	Resilient
Mean lesion length	45.2mm	101mm	61.8mm
ISR rate @ 12mo	**32%**	**36%**	**20%**
Fracture rate	12%	2%	2.9%

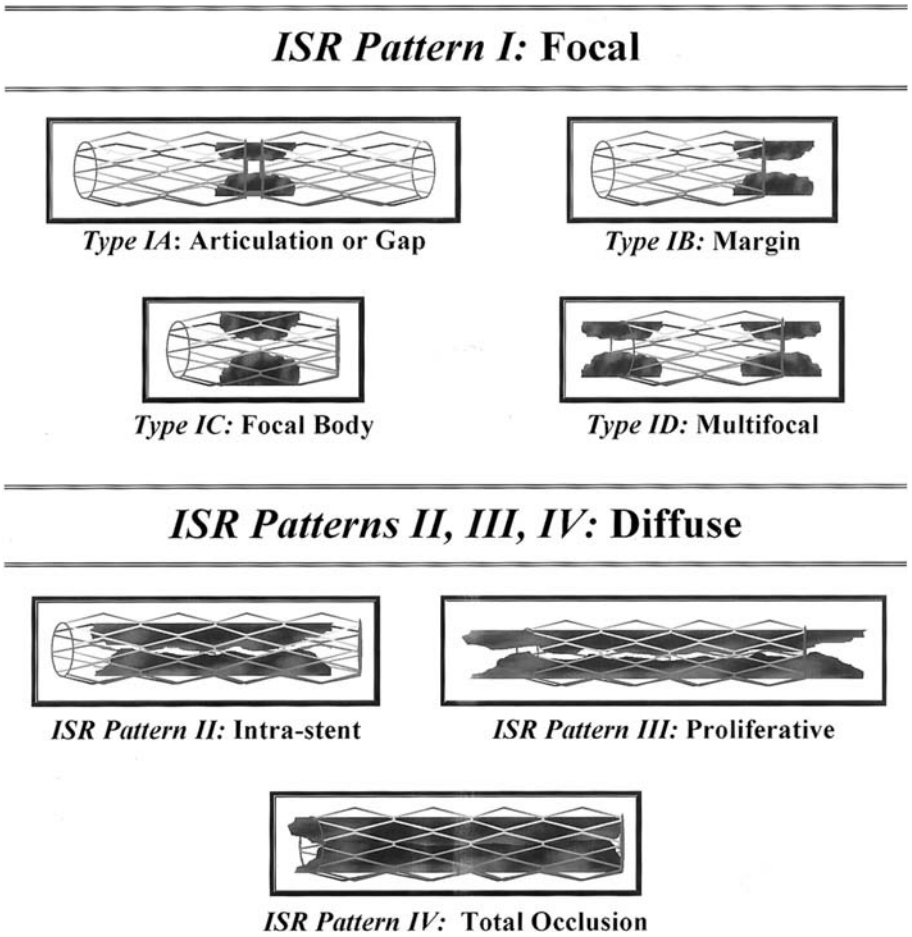
Definitions

ISR can be defined clinically or angiographically.

- **Clinically**, it is defined as the presentation of recurrent ischaemia
- **Angiographically**, ISR is the presence of >50% diameter stenosis in the stented segment.

Teirstein PS, *N Engl J Med*, 1997

Angiographic classification



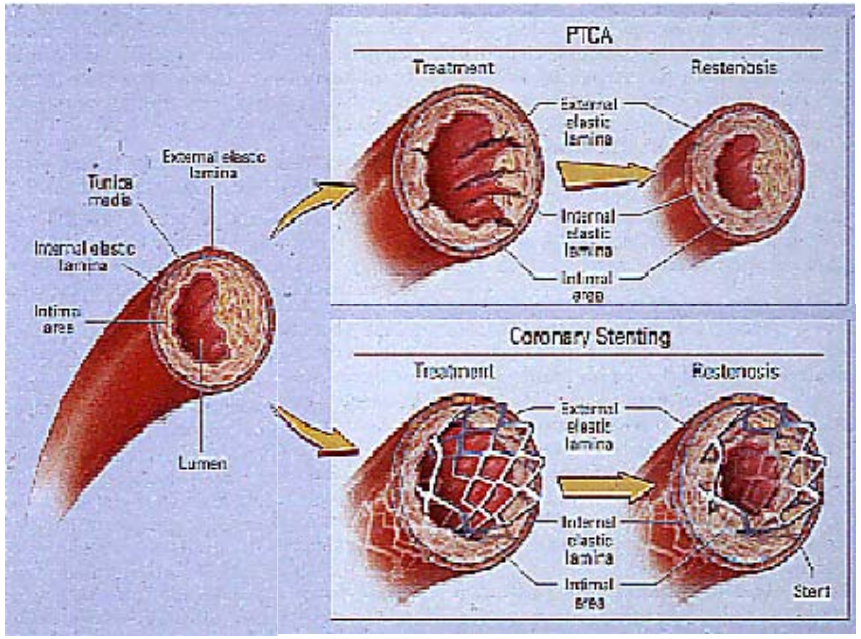
Mehran R, Circulation, 1999

In-stent restenosis *versus* remodeling

~~Elastic recoil~~

Intimal hyperplasia

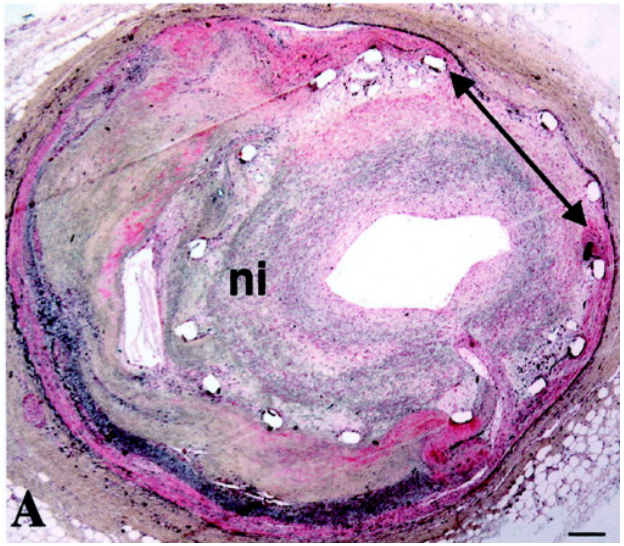
~~Constrictive remodeling~~

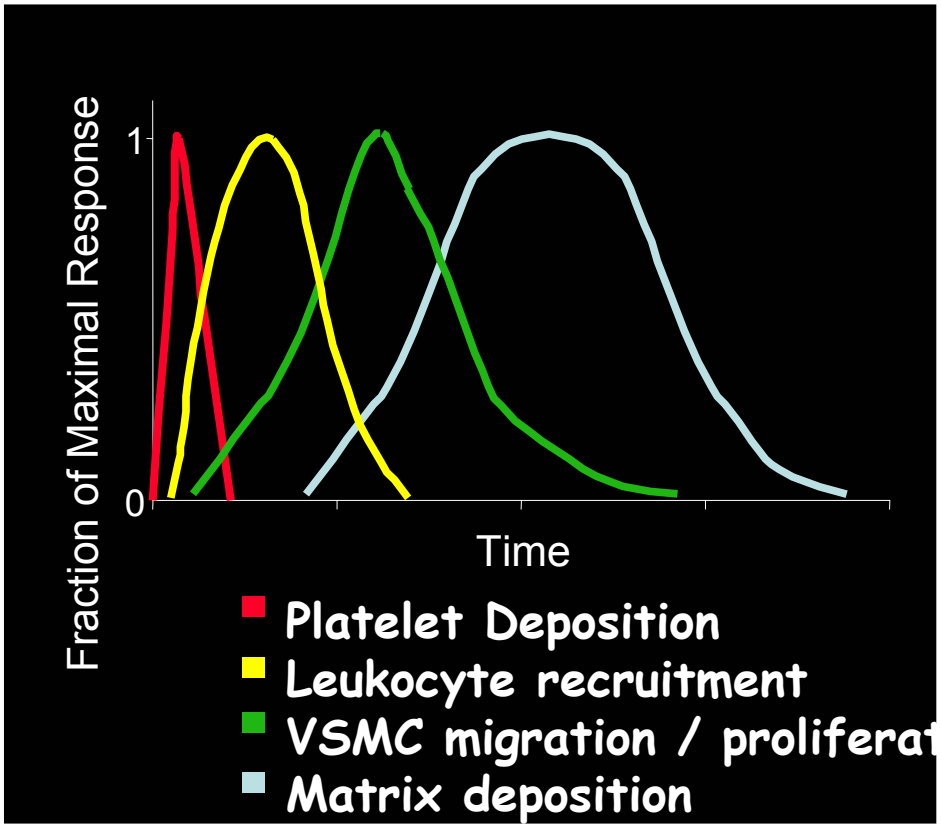


Bittl, *N Engl J Med*, 1996

Intimal hyperplasia

Inflammation / SMCs / ECM





Hoffmann. *Circulation*, 1996

ISR in cardiac arteries ≠ ISR in peripheral arteries

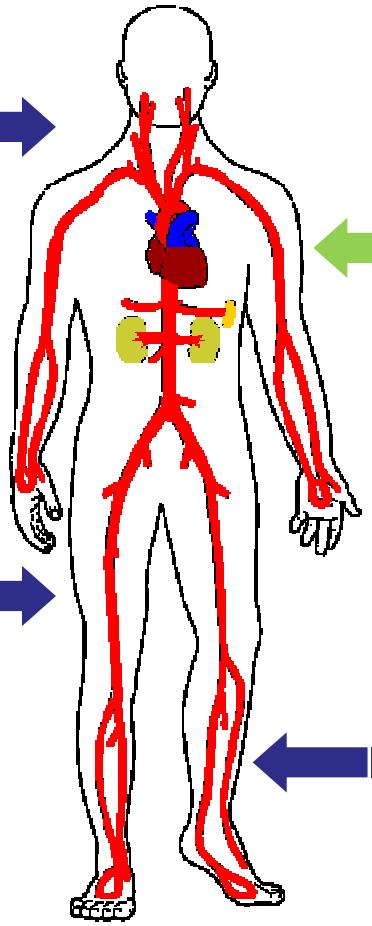
DIFFERENCES AND COMMONS IN PATHOLOGY AND REACTION ON STENTS BETWEEN CARDIAC AND PERIPHERAL ARTERIES

Frank D KOLODGIE, Gaku NAKAZAWA, Giuseppe SANGIORGI,
Elena R. LADICH, Allen P BURKE, Renu VIRMANI

Crucial point to understand and to prevent ISR in peripheral arteries

Various ISR rates @ 1-year according locations

Carotid arteries
<10%



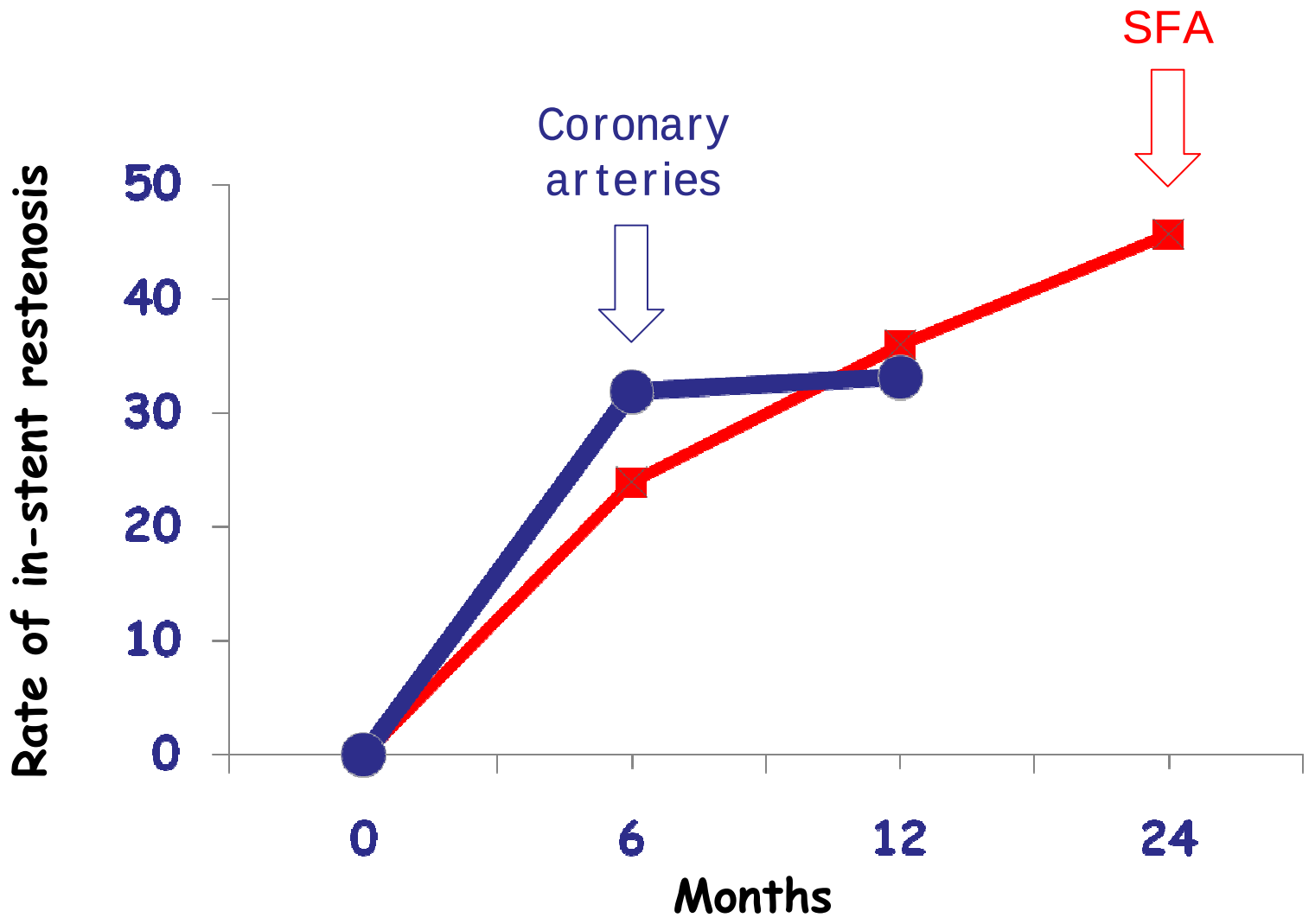
Coronaries arteries
20-30%

SFA 30-40%

Below the knee arteries
30-50%

Virmani, ESVB, 2007

Time courses of ISR



Kastrati A, Circulation, 1993; Schillinger, Circulation, 2007

DES in cardiac and peripheral arteries

Coronary arteries: 0% @ 9 mo

Ravel, ESC, Stockholm, 2001

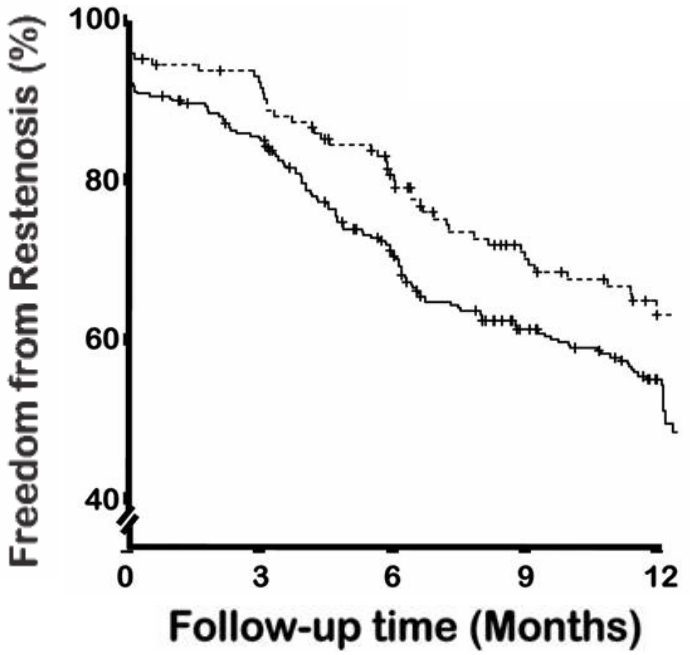
SFA:	**20% @ 18 mo**	Duda, J Endovasc Ther, 2005
Vertebral:	**62.5% @ 6 mo**	Lugmayr, Rofo, 2004
Renal:	**18.7% @ 6 mo,**	Rabbia, CIRSE conference, 2006
BLK arteries:	**37% @ 12 mo**	Siablis, J Endovasc Ther, 2005

Which specific factors could influence in-stent restenosis of SFA

- Cardio-vascular risk factors
- Endogenous factors
- Exogenous factors

Effect of smoking on ISR

Cumulative freedom from restenosis after endovascular treatment of femoropopliteal artery



smokers and heavy smokers
versus
nonsmokers and light smokers

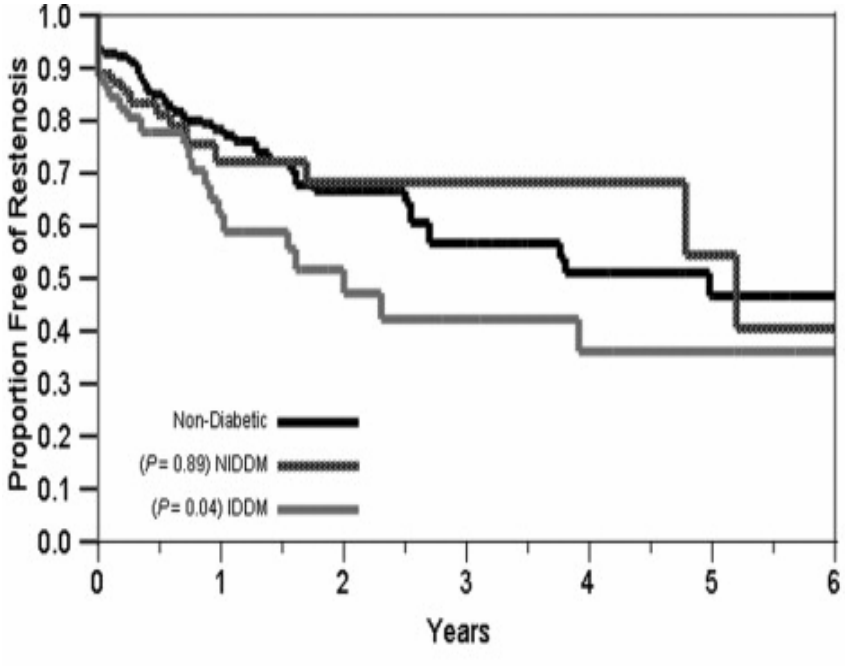
P= .0093

Does smoking prevent from ISR ?

Schillinger, *Radiology*, 2004

Impact of diabetes mellitus on restenosis

- Nondiabetic patients
- Noninsulin-dependent diabetic
- Insulin-dependent diabetic



Insulin-dependent diabetes confers an increase of the rate of restenosis

Bakken, *J Vasc Surg*, 2007

Endogenous factors

- Genomic
- Blood flow
- Plaque

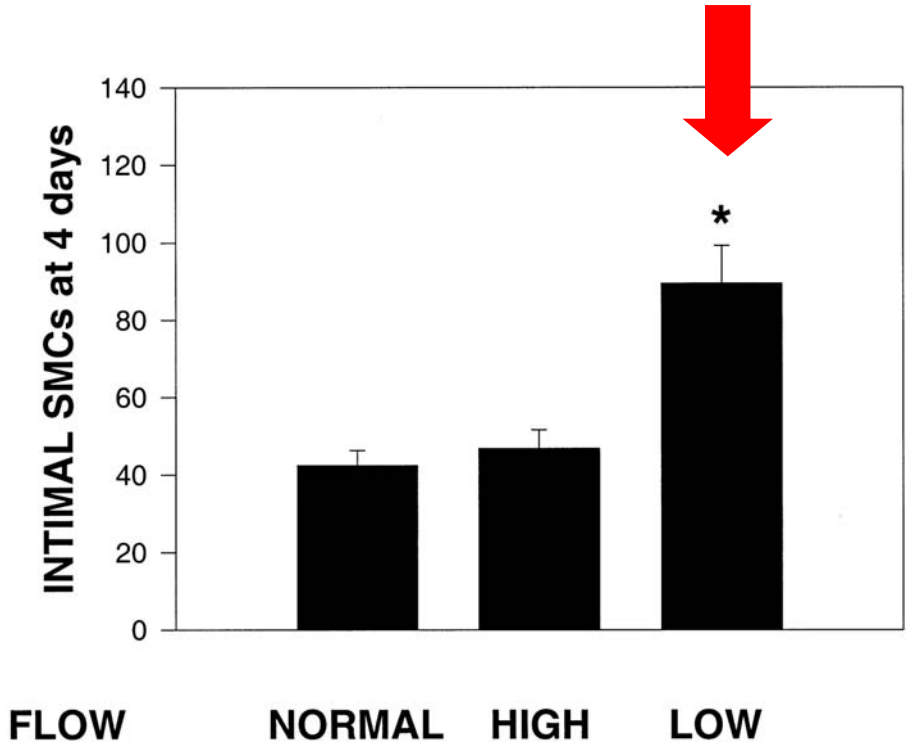
Genomic

Some people develops more ISR than others
Phenotype / Gene and protein expression

Nelson, *J Vasc Surg*, 2007

The blood flow influences restenosis

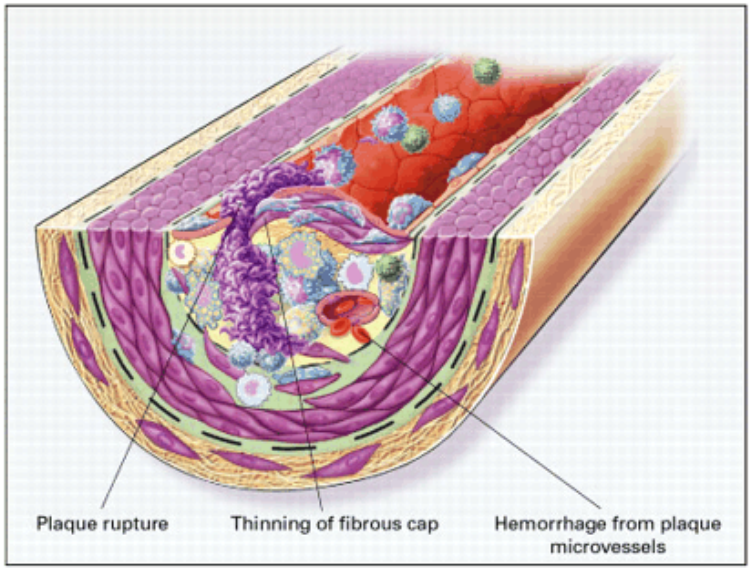
Intimal hyperplasia in vessels with low blood flow was significantly more



Ward, Arterioscler Thromb Vasc Biol, 2001

Atheromatous plaque

- SMC, calcifications, lipids, inflammatory cells, ECM



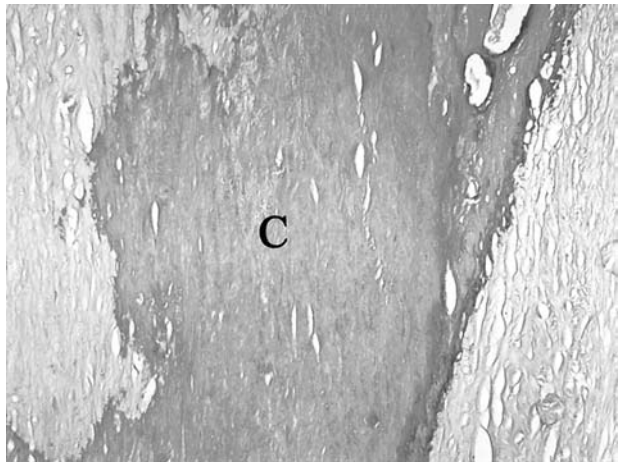
- Type of plaque differs according location

Ross R, *N Engl J Med*, 1999

Calcifications morphology in atheroma

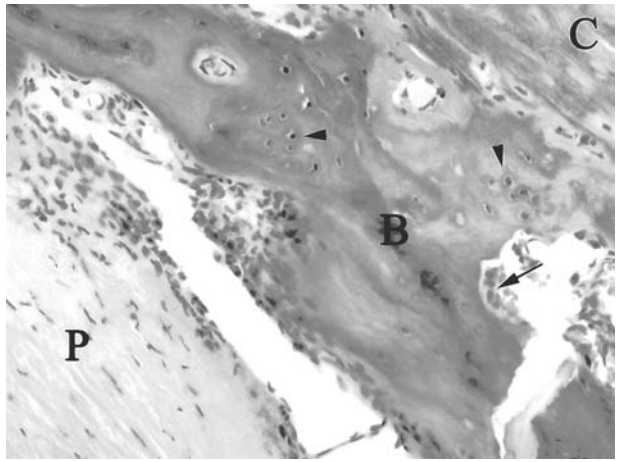
- Small and large calcifications

  Sheetlike calcifications



- Bone formation

  Bone formation and large sheets of calcification are associated with non ulcerated, stables plaques

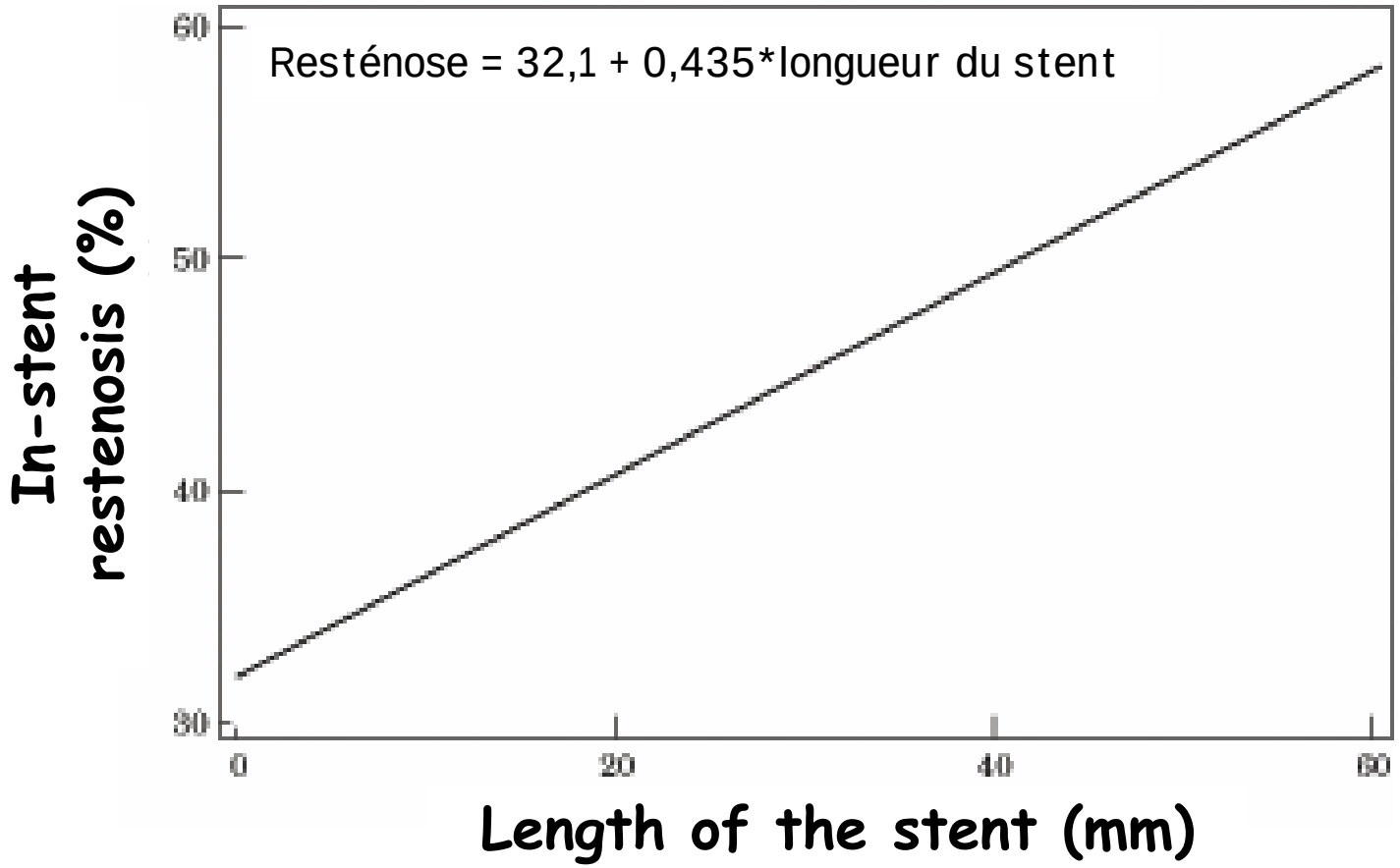


Hunt, Stroke, 2002

The type of plaque influences ISR ?

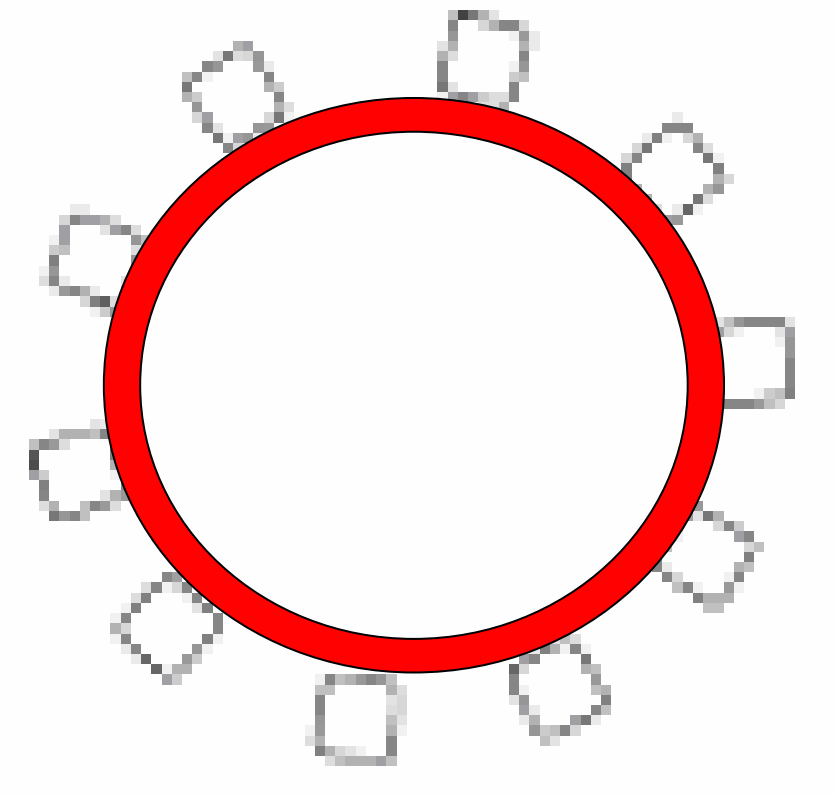
Gouëffic, Fondation de l'avenir, 2007

ISR and length of the lesion

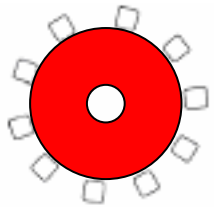


Foley, Eur Heart J, 2001

ISR and vessel area



10-11mm² : 4%



3-4mm²: 30%

De Feyter, Circulation, 1999

Exogenous factors:

Stent

« A stent is not just a stent »

To treat SFA disease we should make sure of:

Flexibility
Profile
Trackability

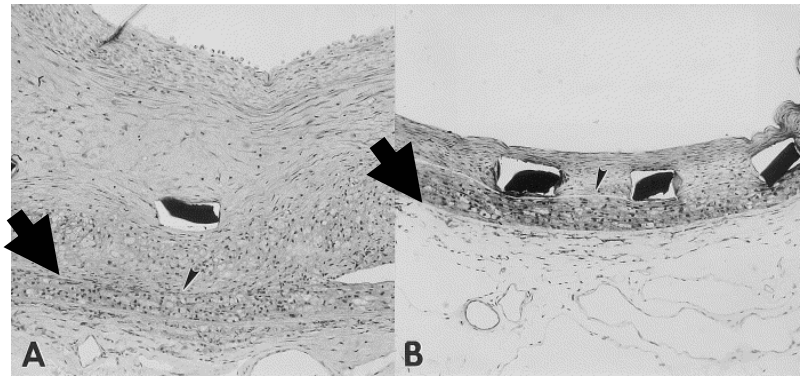
Radial strength
Schaffolding

Biocompatibility
Good fatigue properties
Corrosion resistance

Impact of stent asymmetry on ISR

Stent asymmetry could be caused by tortuosity and calcification

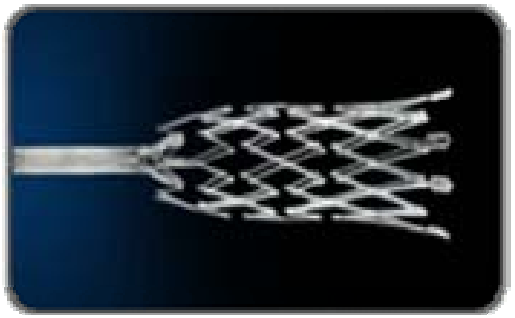
Stent asymmetry increases ISR



Stent designs could reduce asymmetric stent expansion and ISR

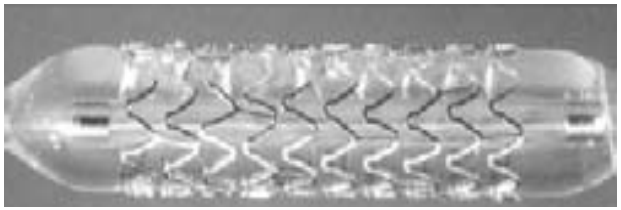
Schulz, Heart, 2000

Self expanding *versus* balloon expanded stents



Nitinol

Schillinger, N Engl J Med, 2007

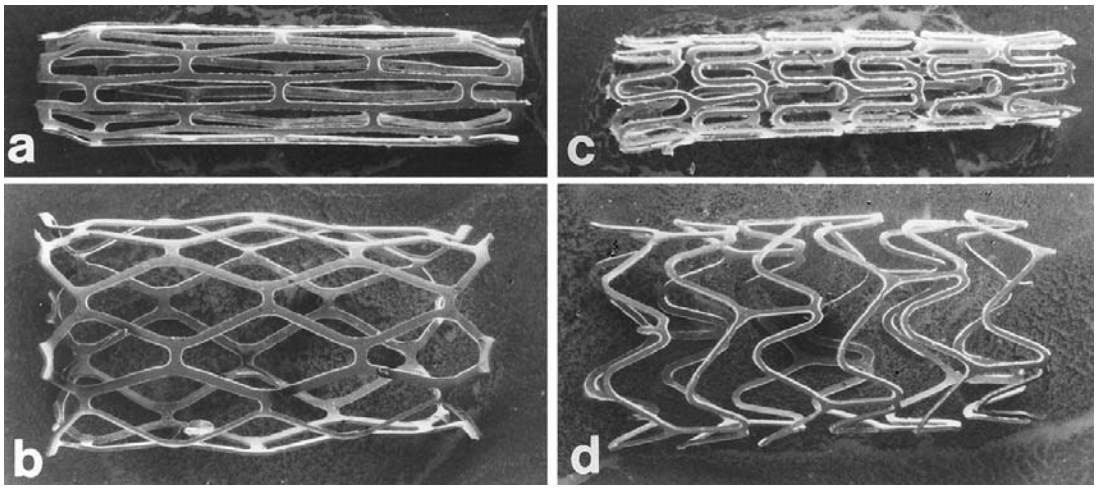


316L

Becquemin, J Vasc Surg, 2003

Cell design

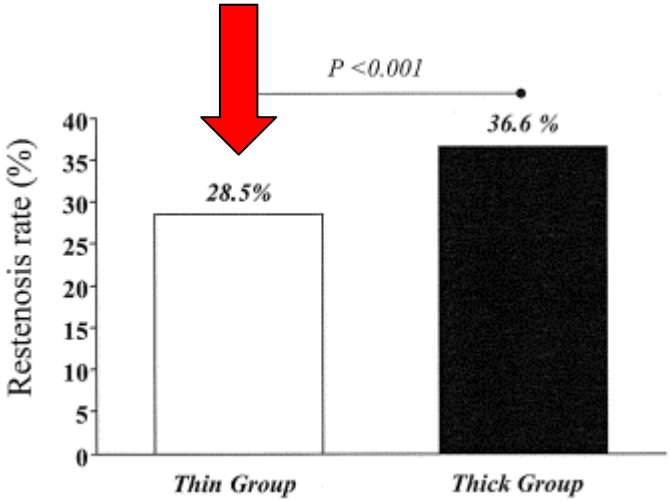
Close cells **Open cells**



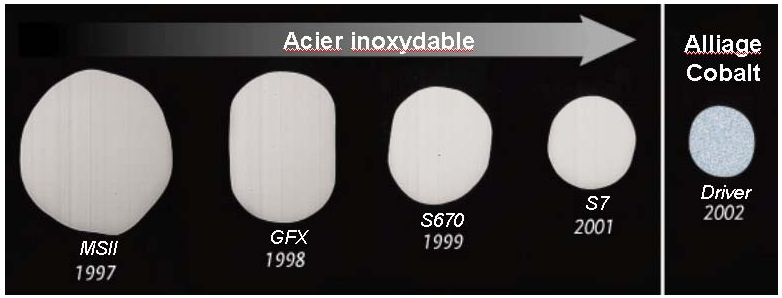
- Flexibility - Stent asymmetry
- Corrosion and fatigue

Gurbel, J Invasive Cardiol, 2002

ISR and strut thickness



Strut thickness is an independent predictor of ISR



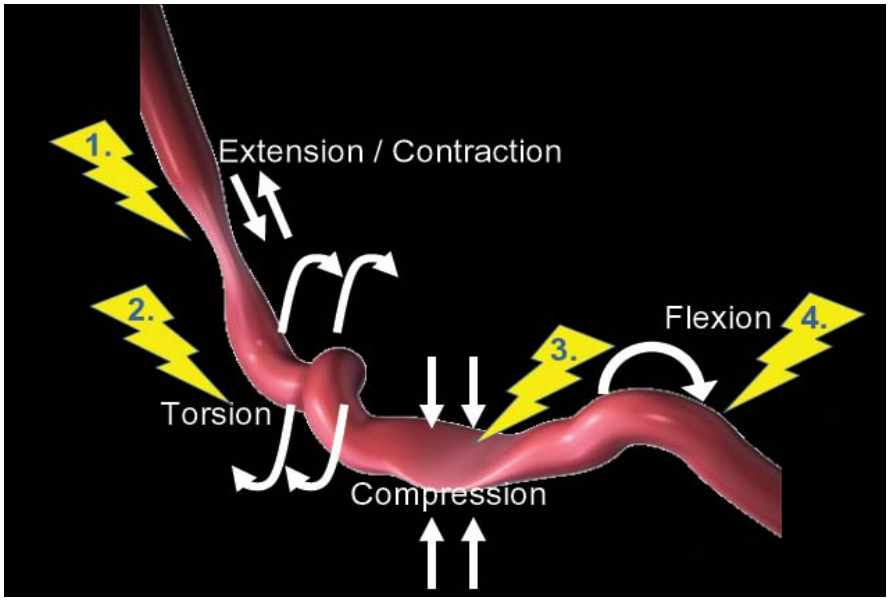
With thin struts:

-increase of fatigue
-decrease of radial strength

Briguori, J Am Coll Cardiol, 2002

ISR and stent fractures

Mechanical characteristics of the SFA



ISR and fracture

	FAST	Vienna Study	Resilient
Mean lesion length	45.2mm	101mm	61.8mm
ISR rate @ 12mo	**32%**	**36%**	**20%**
Fracture rate	12%	2%	2.9%

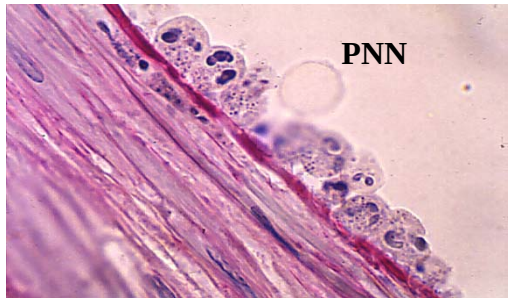
Lower fracture rate does not seem to be associated to a decrease of ISR

Take-home message

- ISR is the main problem of SFA stenting
- Intimal hyperplasia is ISR
- SFA ≠ cardiac arteries
- Specific treatment and devices to treat SFA

Intimal hyperplasia and inflammation

Day 1



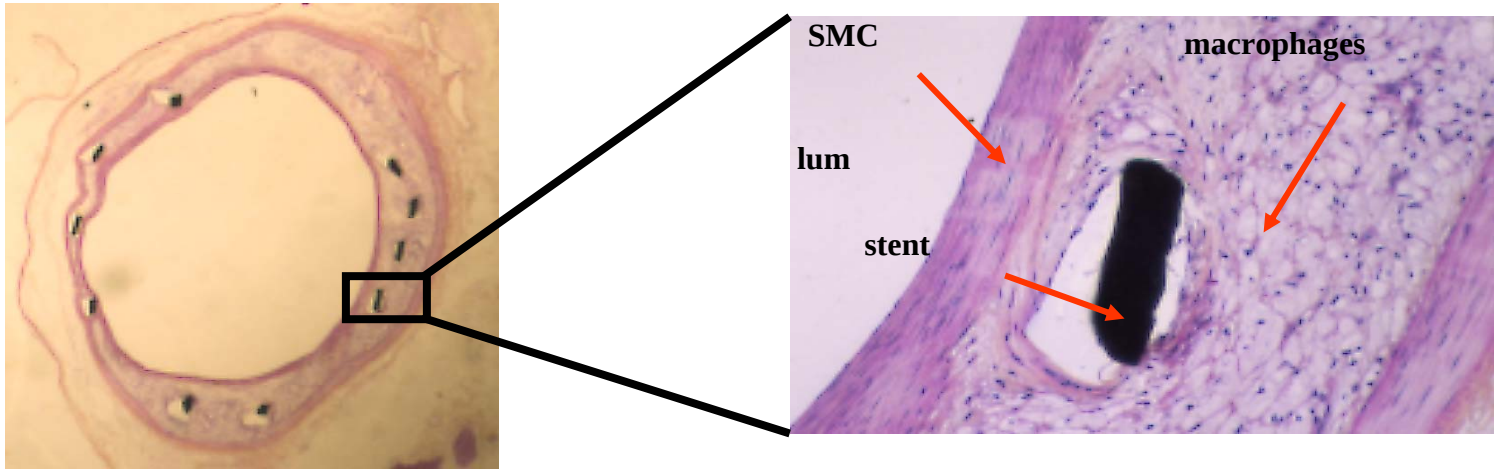
Inflation

Rupture of the fibrous plaque

Struts

Stent >>> ballon

Day 28



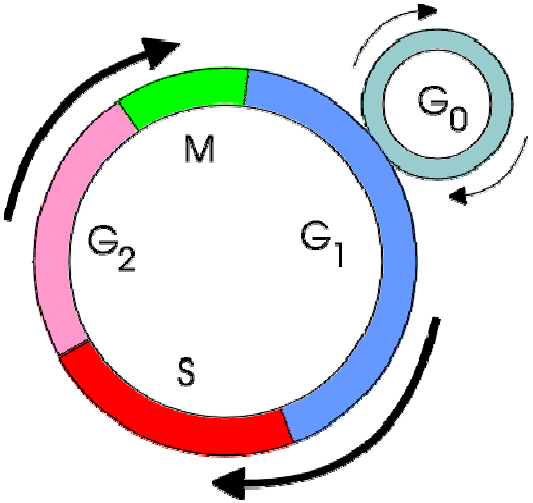
Feldman, Circulation, 2000

Migration and proliferation of smooth muscle cells

Proliferation

48h – media

96h - intima

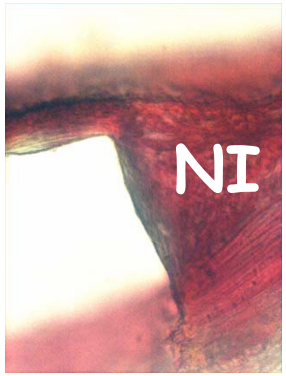


Migration

Phenotype

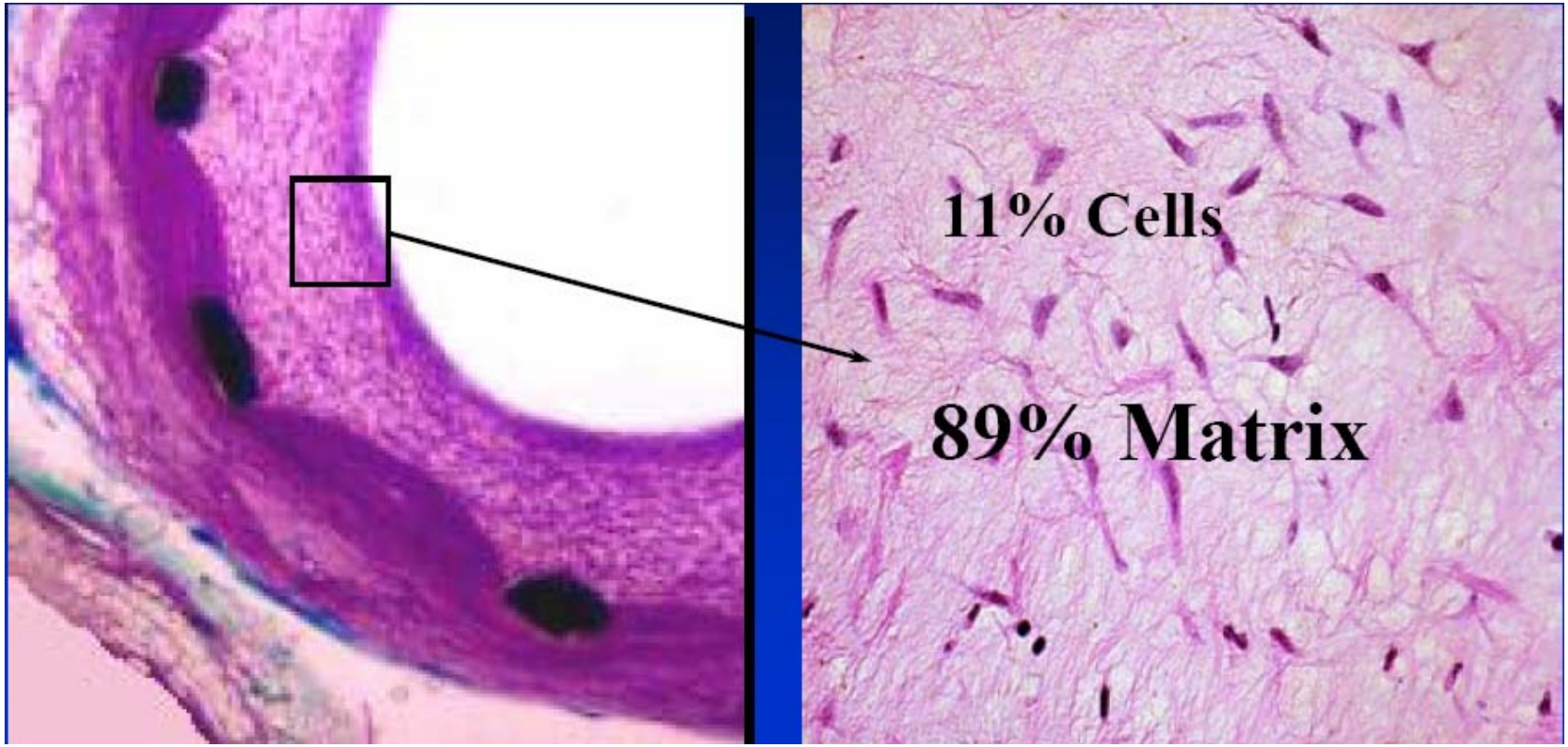
Cell contact

Extra cellular matrix



Clowes, Lab Invest, 1983

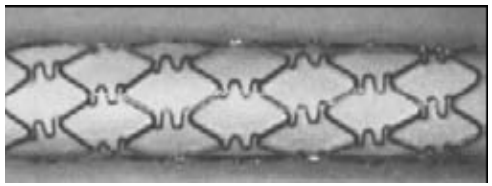
Extra Cellular Matrix



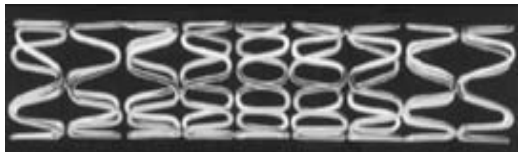
Goueffic, *Atherosclerosis*, 2007

Geometrical stent design

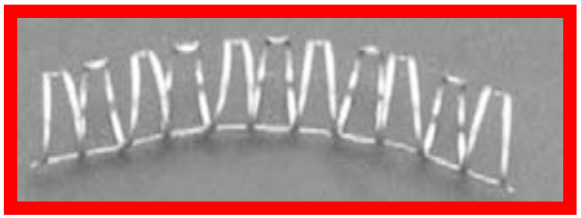
Tube



Modular



Coil



TAUX ELEVE DE RESTENOSE

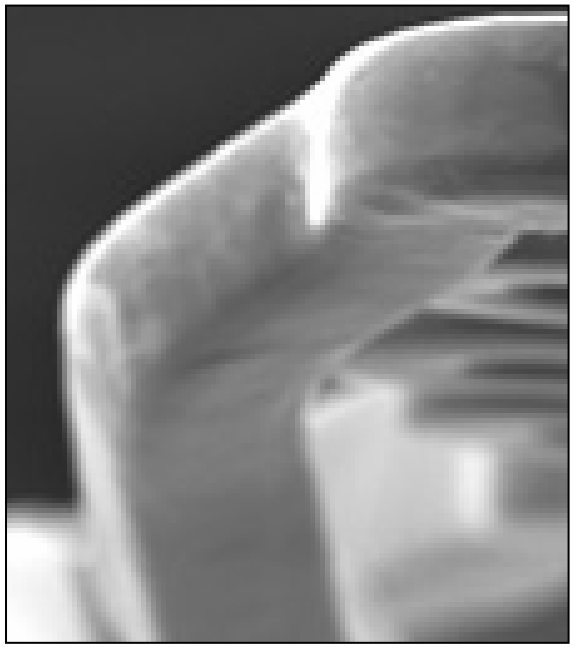
Très flexible

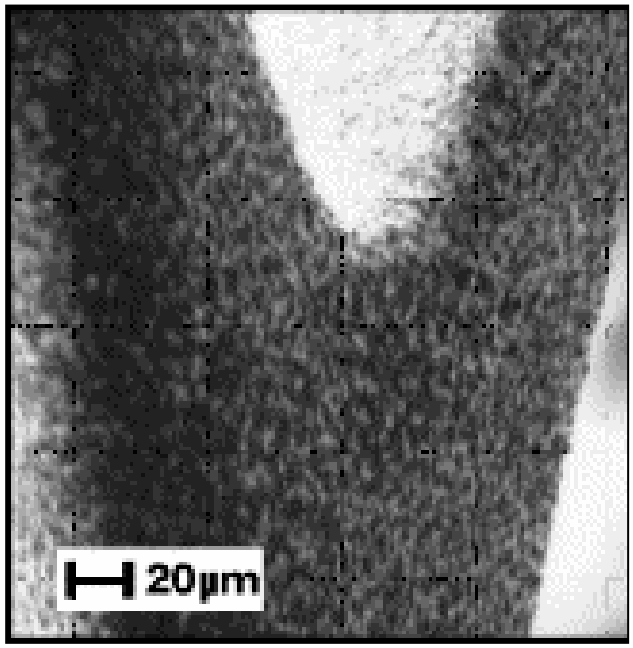
Force radiale faible

Prolapsus du tissu

Lansky, circulation, 2000

Etat de surface lisse ou rugueux





Hyperplasie intimale
Thrombose
Fracture

Sgura, Herz, 2002