Safety and Efficacy of the S.M.A.R.T Control Stent for Iliao-femoral Occlusive Disease in Contemporary Clinical Practice

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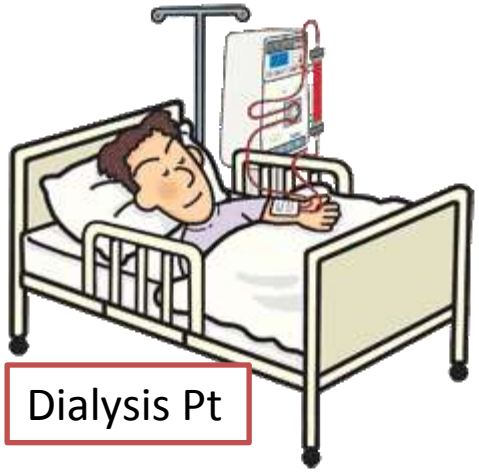
Current pattern of clinical consequences in Japan

-Why is prevalence of PAD patients with **AI** lesions now increasing??-

DM Pt

PAD Pt

AI lesion

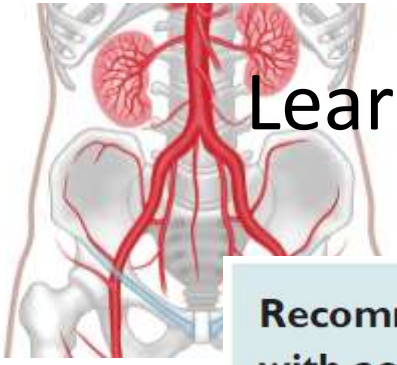


Dialysis Pt

Diabetes mellitus (DM) and **renal Insufficiency (RI)** are the predominant risk factors on the likelihood of developing PAD.

This situation is not only a clinical but also an economic challenge which contributes to an **increasing prevalence of vascular disease** in every country.

Aortoiliac (AI) arterial lesions are found **in one third** of patients with symptomatic peripheral artery disease (PAD).



Learn From ESC 2011 guideline -Aorto-Iliac lesions-

Recommendations for revascularization in patients with aortoiliac lesions

Recommendations	Class[a]	Level[b]
When revascularization is indicated, an endovascular-first strategy is recommended in all aortoiliac TASC A–C lesions.	I	C
A primary endovascular approach may be considered in aortoiliac TASC D lesions in patients with severe comorbidities, if done by an experienced team.	IIb	C
Primary stent implantation rather than provisional stenting may be considered for aortoiliac lesions.	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
TASC = TransAtlantic Inter-Society Consensus.

General agreement of endovascular reconstruction for severe aortoiliac occlusive disease -From TASC II guideline-

- The technical and initial clinical success of endovascular reconstruction of iliac stenoses exceeds **90%** in all reports in the literature.

(**100%** for focal iliac lesions, whereas **80 to 85%** long segment iliac occlusions)

⇒ Recent device developments geared towards treatment of total occlusions.

- Factors negatively affecting the patency of such interventions include
  - ✓ **Quality of run off vessels**
  - ✓ **Severity of ischemia**
  - ✓ **Length of diseased segments**
  - ✓ **Female gender** decrease patency of external iliac artery stents

These fait accompli mentioned in TASC II documents was built based on traditional research published around 2000-2005. It doesn't reflect recent clinical practice.

TASC II

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

Contemporary Outcomes After Endovascular Treatment for Aorto-Iliac Artery Disease

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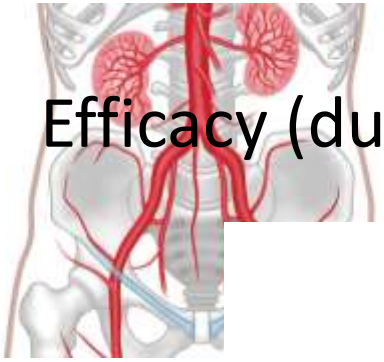
Background: The patency and complications in aorto-iliac (AI) stenting remain poorly understood. The aim of this paper was to investigate the safety and efficacy after AI stenting.

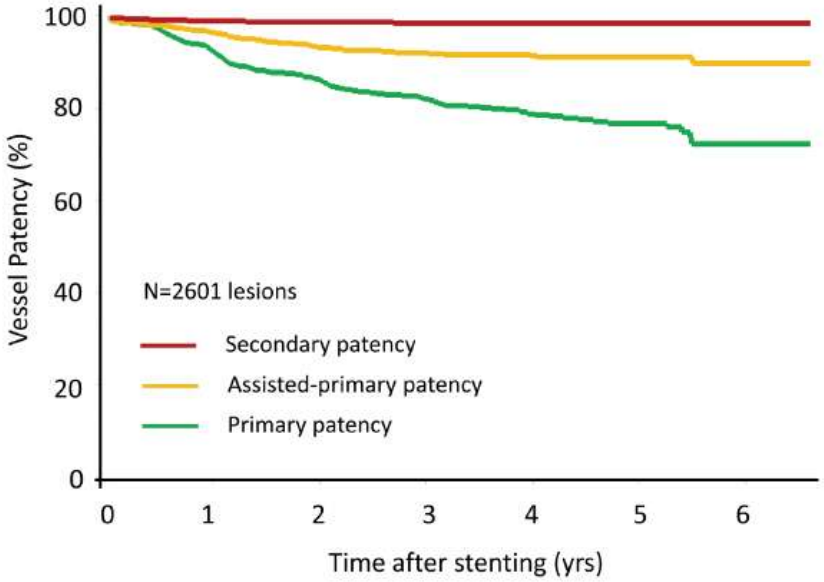
Methods and Results: This study was performed as a large-scale multicenter, retrospective registry. A total of 2,147 consecutive patients with AI disease were enrolled. The safety endpoints were procedure success, complications and 30-day mortality. The efficacy endpoints were primary, assisted primary and secondary patency, overall survival, freedom from major adverse cardiovascular events (MACE; all-cause death, myocardial infarction and stroke), and major adverse cardiovascular and limb events (MACLE; any repeat revascularization for limb and leg amputation in addition to MACE). Procedure success, complication rate and 30-day mortality were 97.6%, 6.4% and 0.7%. Primary patency was 92.5%, 82.6% and 77.5% at 1, 3 and 5 years, assisted primary patency was 97.0%, 92.7% and 91.9% at 1, 3 and 5 years and secondary patency was 99.0%, 98.7% and 98.5% at 1, 3 and 5 years. The overall survival rate was 95.0%, 87.6%, and 79.3% at 1, 3 and 5 years. The cause of death was cardiovascular in 44.1%. Freedom from MACE (MACLE) was 93.3% (89.9%), 84.4% (76.7%), and 74.9% (66.8%) at 1, 3 and 5 years. Female gender, diabetes, renal failure, absence of aspirin, reference vessel diameter <8.0 mm and outflow lesion were found to be independent predictors of primary patency.

Conclusions: The safety and efficacy after AI stenting are feasible compared to surgical reconstruction.

Key Words: Aorto-iliac disease; Endovascular therapy; Patency; Stents



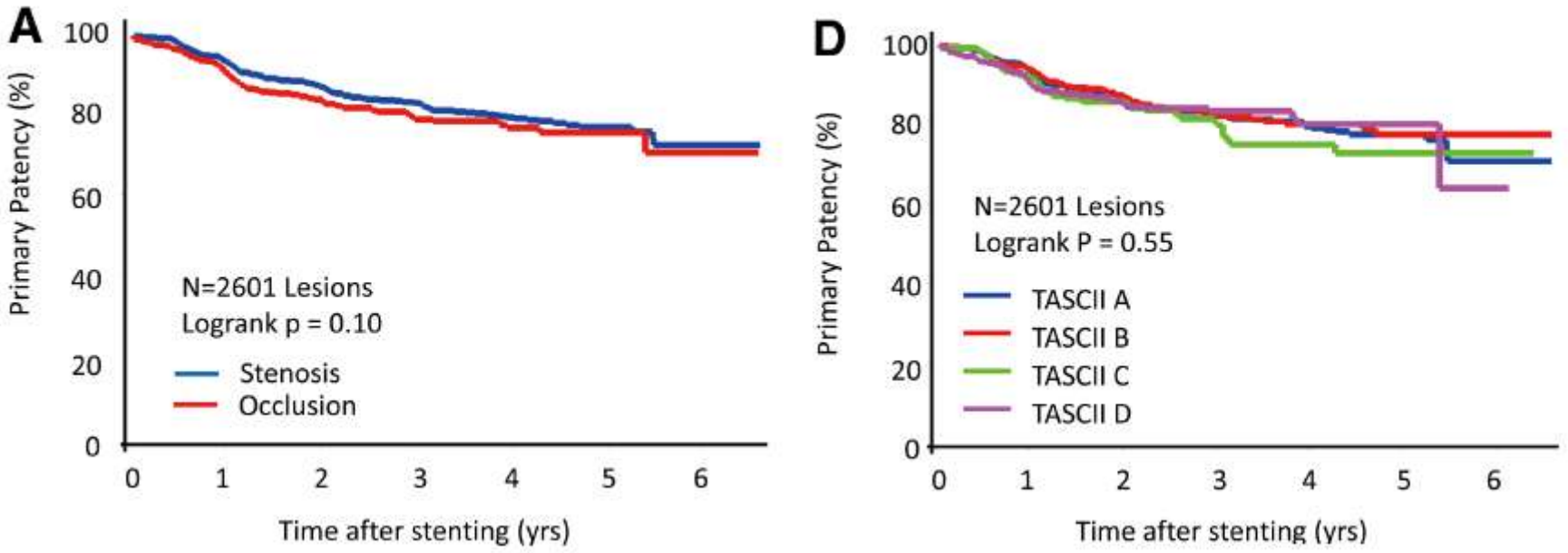
Efficacy (durability) of EVT with stenting for AIOD



		0	1	2	3	4	5	6
Primary Patency	No. at risk	2601	1963	1340	784	373	128	26
	%	100	92.5	86.3	82.6	79.3	77.5	73.1
Assisted-primary patency	No. at risk	2601	2054	1434	852	422	150	31
	%	100	97.0	94.0	92.7	91.9	91.9	90.6
Secondary Patency	No. at risk	2601	2095	1498	897	450	160	34
	%	100	99.0	98.9	98.7	98.5	98.5	98.5

The overall primary patencies were 92.5%, 82.6% and **77.5**% at 1, 3 and 5 years, assisted-primary patencies were 97.0%, 92.7% and **91.9%** at 1, 3 and 5 years and the secondary patencies were 99.0%, 98.7% and **98.5%** at 1, 3 and 5 years

Efficacy (durability) of EVT with stenting for AIOD



Left (A): primary patency between stenosis and occlusion (77.8% vs. 76.5% at 5-year, Logrank p=0.10),
Right (D): primary patency among TASCII category (TASCII A, B, C, D; 77.8%, 78.0%, 73.3%, 80.5% at 5-year, Logrank p=0.55)

There are no direct comparisons of long-term outcomes among stents

Table 2. Lesion Characteristics

Use of stent	
Self-expandable stent	2,282 (70.3)
Luminexx	452
SMART	1,683
Self X	67
Wall RP	80
Balloon-expandable stent	963 (29.3)
Palmaz	348
Express LD	615

A half of lesions were treated with S.M.A.R.T stent in REAL-AI registry.

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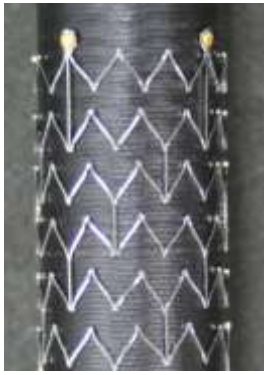
S.M.A.R.T.

VS.

Luminexx

Selfex



Zilver

Wall

Express LD

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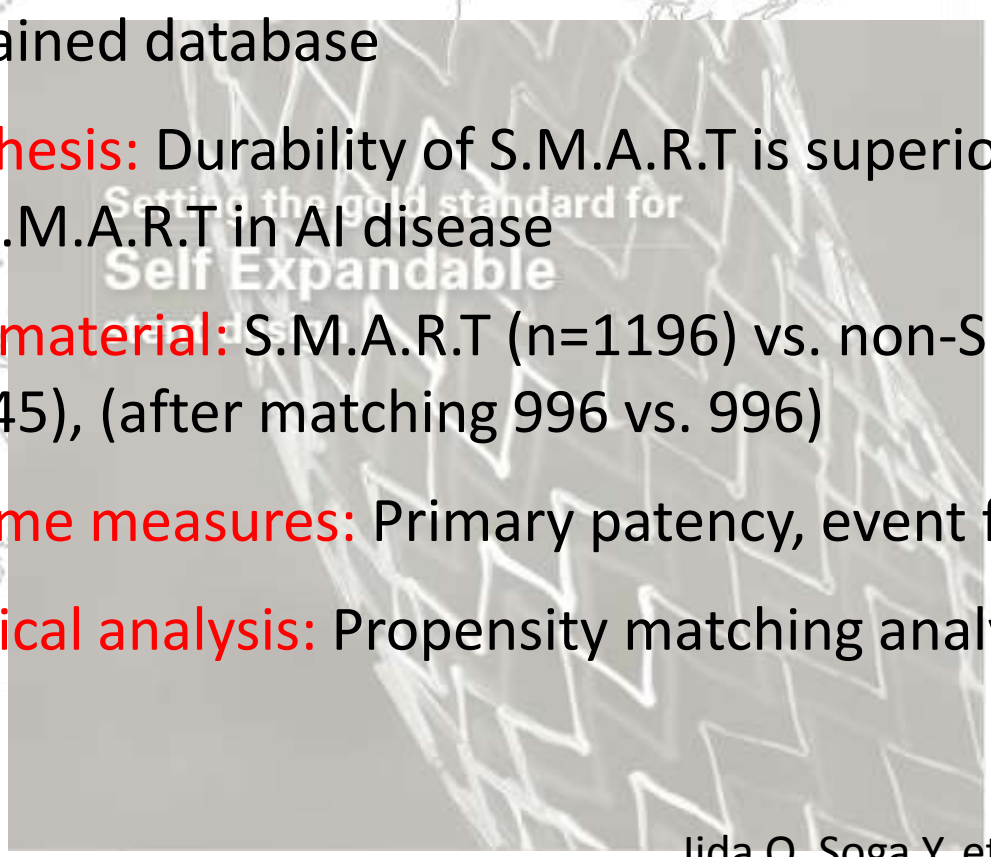
- **Study design:** Retrospective analysis for prospectively maintained database
- Hypothesis: Durability of S.M.A.R.T is superior to that of non- S.M.A.R.T in AI disease
- Study material: S.M.A.R.T (n=1196) vs. non-S.M.A.R.T (n=1345), (after matching 996 vs. 996)
- Outcome measures: Primary patency, event free survival
- Statistical analysis: Propensity matching analysis



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	Before propensity score matching			After propensity score matching		
Variables	S.M.A.R.T stent group	Non-S.M.A.R.T stent group	P value	S.M.A.R.T stent group	Non-S.M.A.R.T stent group	P value
Patients characteristics						
Diabetes mellitus (DM)	47% (576)	49% (652)	0.87	49% (485)	46% (462)	0.32
Renal insufficiency (Cre>1.5mh/dL)	26% (308)	27% (365)	0.42	20% (203)	18% (183)	0.26
History of heart failure	11% (132)	13% (178)	0.10	12% (115)	11% (110)	0.77
Lower limb characteristics						
Critical limb ischemia/Claudicatior	22% (260)/ 78% (936)	14% (186)/ 86% (1159)	**<0.0001**	18% (182)	16% (155)	0.22
ABI before procedure	0.59±0.25	0.64±0.24	**<0.0001**	0.62±0.23	0.62±0.23	0.60
Lesion Characteristics						
TASC A and B/C and D	71% (853)/ 29% (343)	76% (1017)/ 24% (328)	**0.01**	74% (739)	72% (716)	0.27
Lesion length (mm)	58±40	46±38	**<0.0001**	52±35	51±39	0.30
Vessel diameter (mm)	8.0±1.4	8.2±2.8	**0.01**	8.1±1.3	8.0±1.4	0.83
Lesion calcification	49% (587)	54% (722)	**<0.0001**	51% (506)	51% (508)	0.92
Outflow lesions	42% (497)	34% (457)	**<0.0001**	38% (380)	37% (364)	0.49

Limb and Lesions background in S.M.A.R.T stent group is statistically worse than those in non-S.M.A.R.T stent group.

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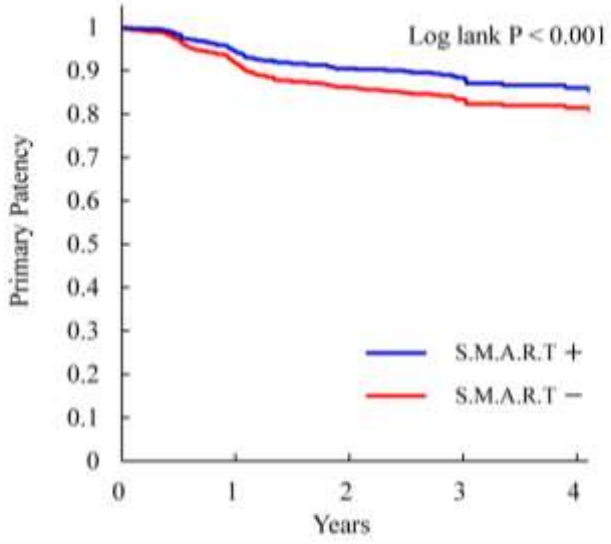
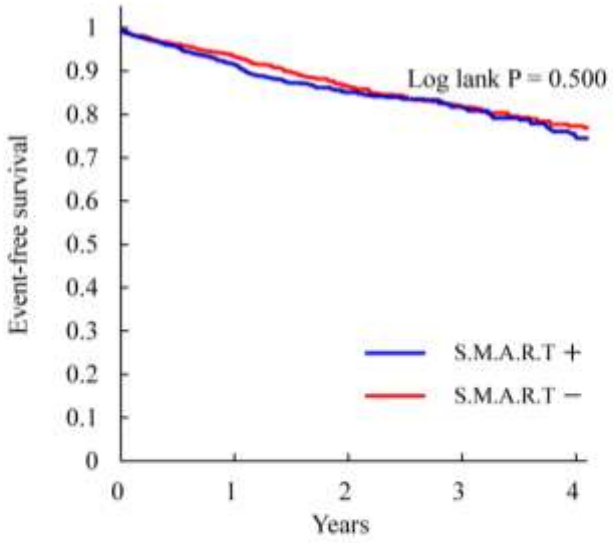
Primary patency and event-free survival



years		0	1	2	3	4
at risk	−	996	767	564	347	167
	−	996	754	494	271	130
%	−	100	94.4	90.5	88.4	86.0
	−	100	92.5	86.5	81.0	76.4
SE	−	0	0.008	0.011	0.013	0.016
	−	0	0.009	0.012	0.015	0.019

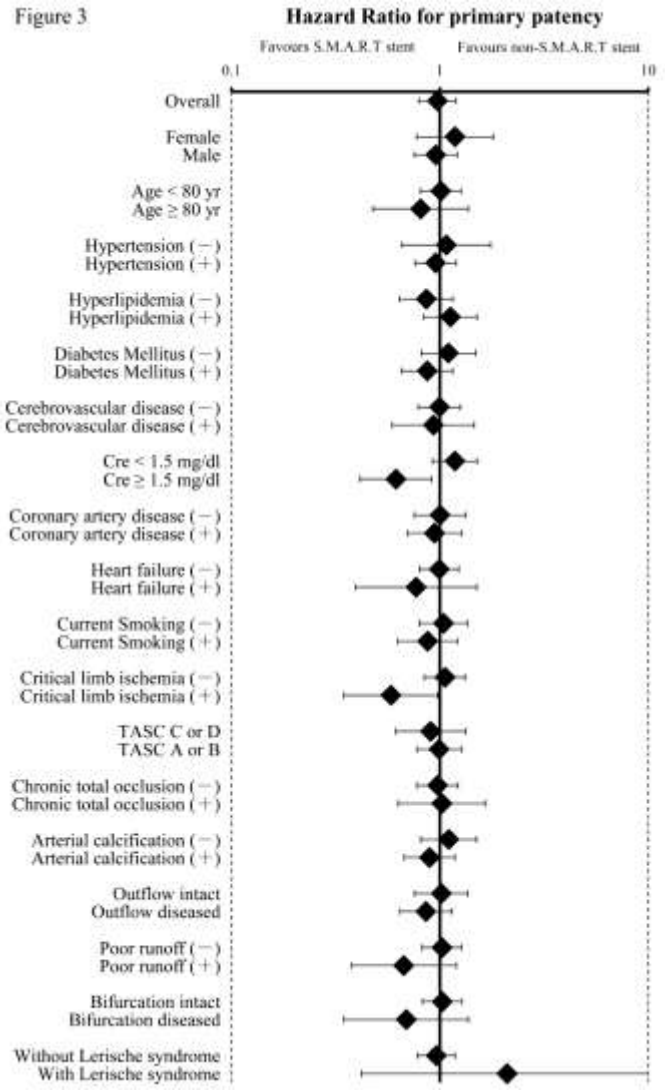
After matching



years		0	1	2	3	4
at risk	−	996	778	520	282	139
	−	996	801	597	383	197
%	−	100	91.5	85.1	81.7	75.0
	−	100	93.3	86.4	81.7	77.3
SE	−	0	0.009	0.012	0.015	0.021
	−	0	0.008	0.012	0.014	0.017

After matching

Safety and Efficacy of the S.M.A.R.T Control Stent for Aorto-Iliac Occlusive Disease in Contemporary Clinical Practice



- Use of the S.M.A.R.T. stent was associated with greater primary patency in patients with **renal insufficiency (Cr>1.5)** and **critical limb ischemia**.
- However, in **CLI patients**, the use of S.M.A.R.T stent was not significantly associated with primary patency after adjustment for TASC classification and the presence of outflow lesions; the adjusted HR was **0.605 [0.358, 1.025] (p = 0.062)**.
- On the other hand, in patients with **elevated creatinine levels (>= 1.5 mg/dl),** the use of SMART stent was still significantly associated with the outcome after the same adjustment; the adjusted HR was **0.575 [0.386, 0.857] (p = 0.007).**

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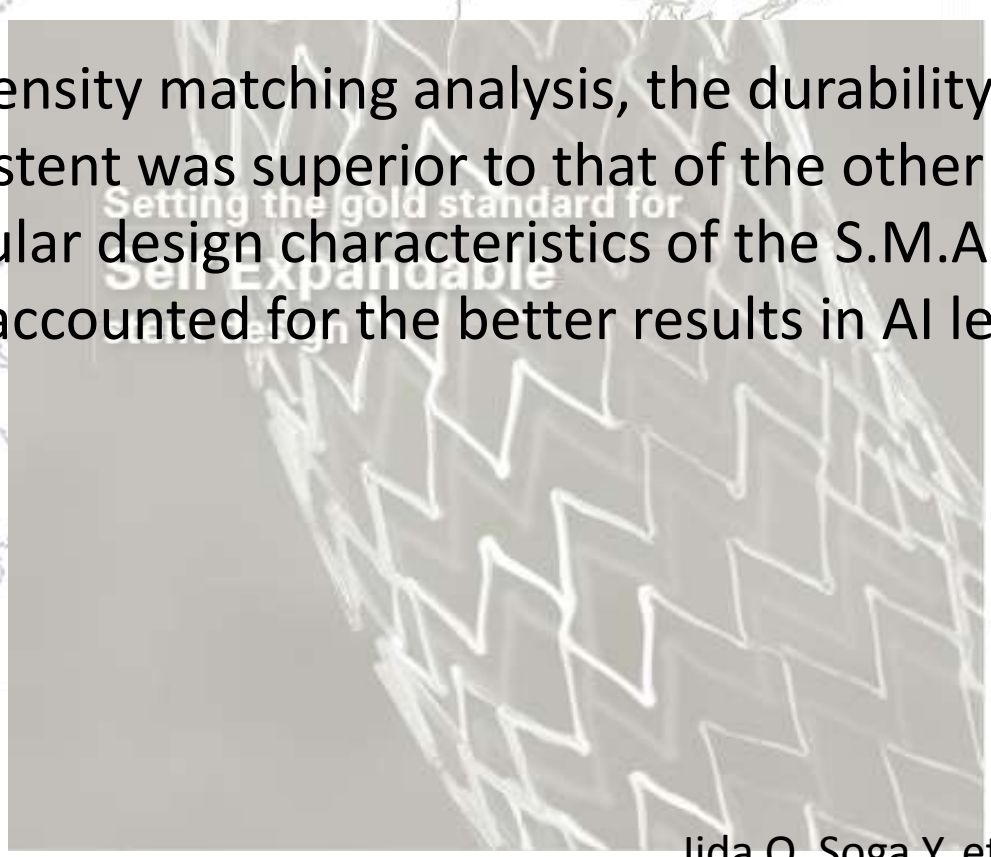
Safety and Efficacy of the S.M.A.R.T Control Stent for Aorto-Iliac Occlusive Disease in Contemporary Clinical Practice

After propensity matching analysis, the durability of S.M.A.R.T. stent was superior to that of the other stents. The particular design characteristics of the S.M.A.R.T. stent may have accounted for the better results in AI lesions.



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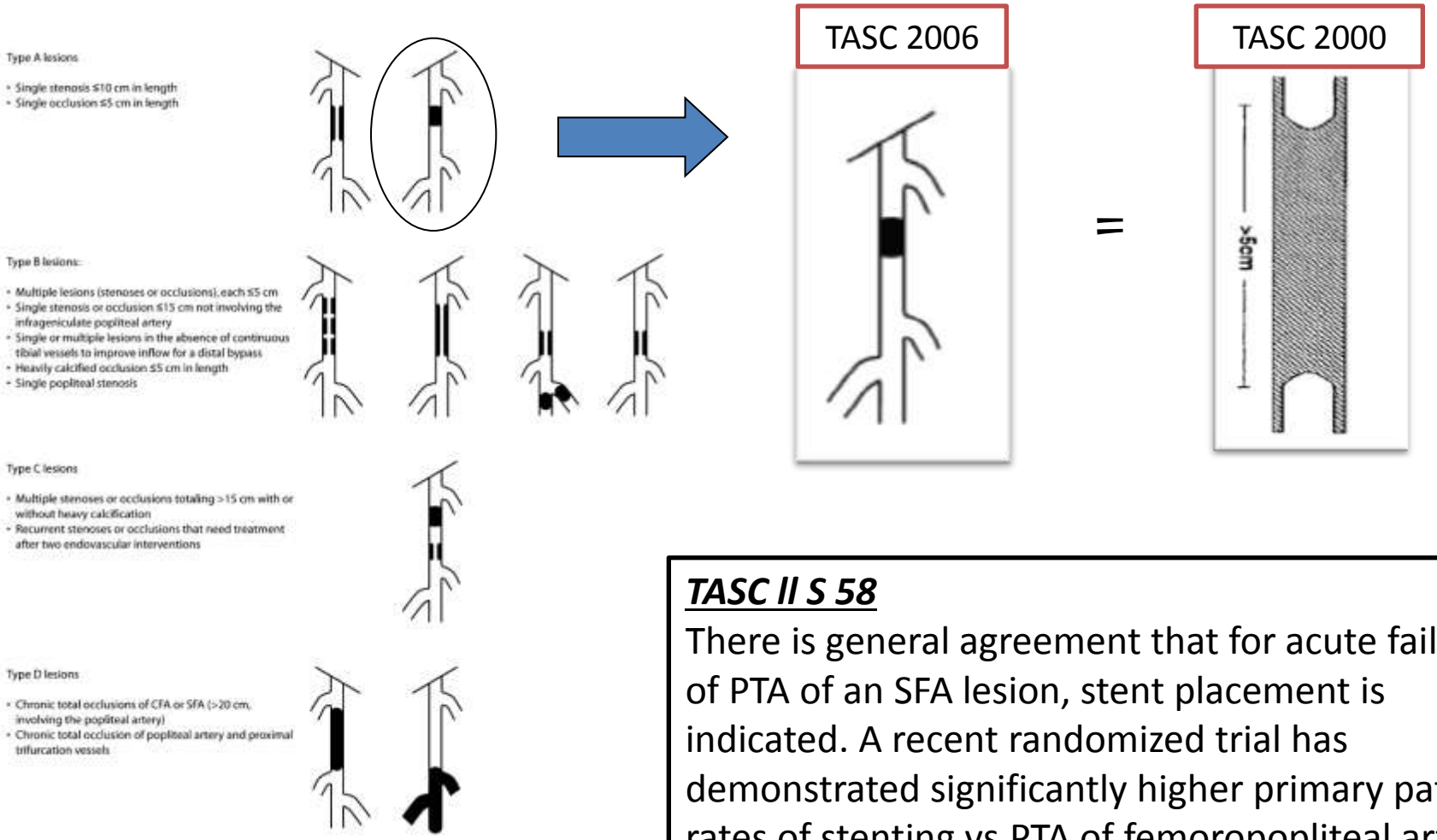
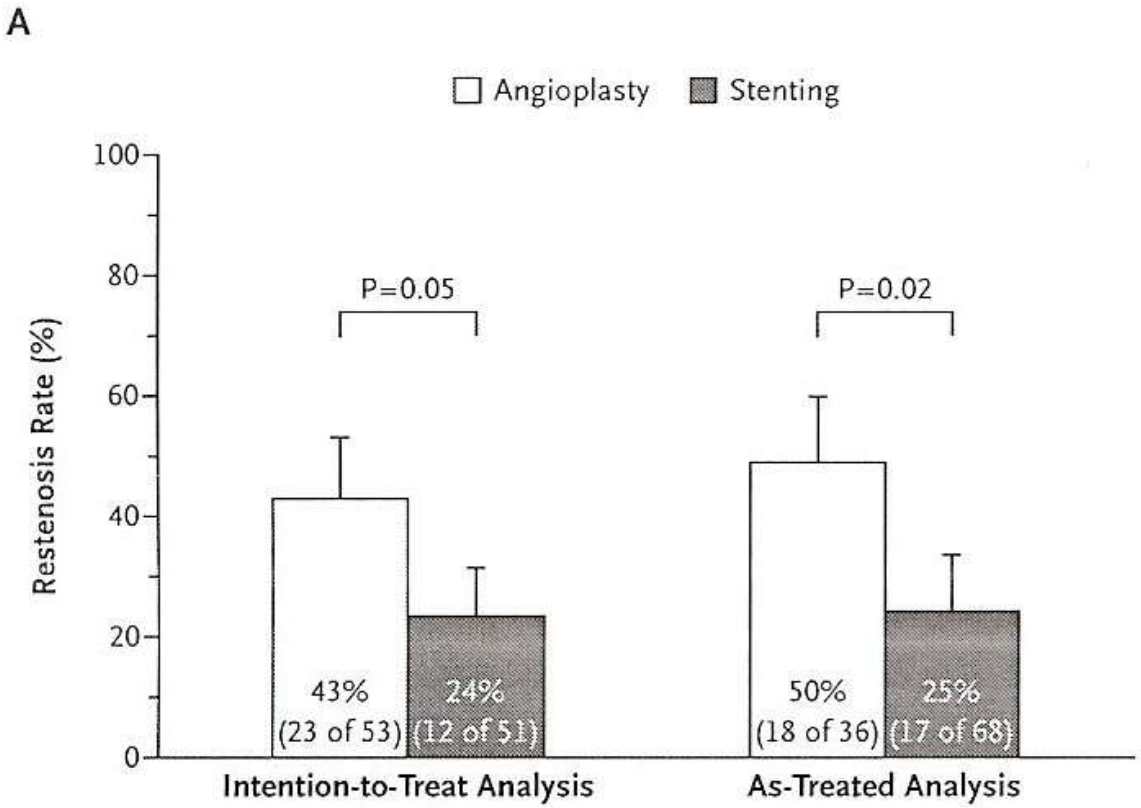
TASC II classification of Femoro-Popliteal lesions (TASC 2006 documents)



TASC II S 58

There is general agreement that for acute failure of PTA of an SFA lesion, stent placement is indicated. A recent randomized trial has demonstrated significantly higher primary patency rates of stenting vs.PTA of femoropopliteal artery lesions TASC A and B at 1-year follow up.

ABSOLUTE trial (Absolute/Dynalink stent, Abott)



Absolute stent (Abott)

Scillinger M et al. N Engl J Med 2006; 354:1879-88

RESILIENT 1-and 2-Year Clinical Outcome

Life stent, BARD

Stent Fracture rate
12 month 3.1%
18 month 3.8%

Laird JR et al. Circ Cardiovasc Interv. 2010;3:267-76.

Learn From ESC 2011 guideline

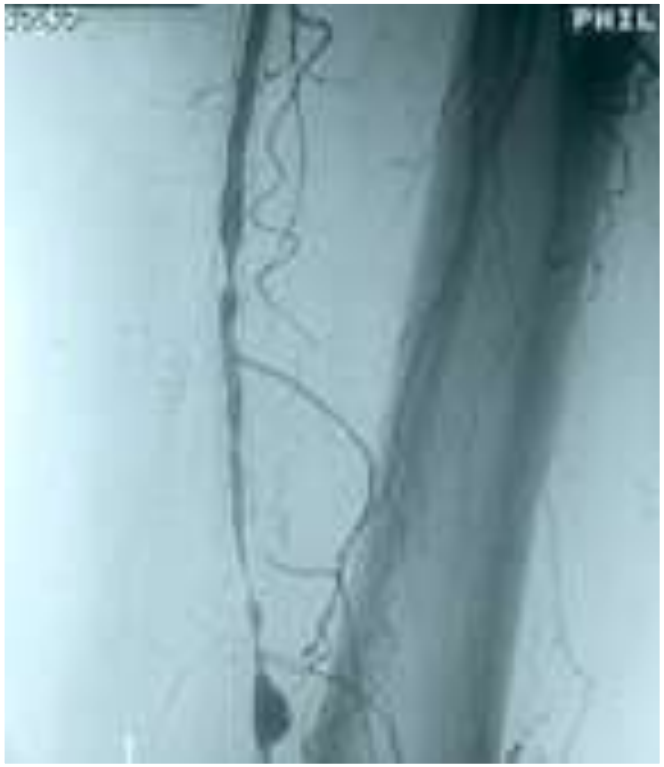
Recommendations for revascularization in patients with femoropopliteal lesions

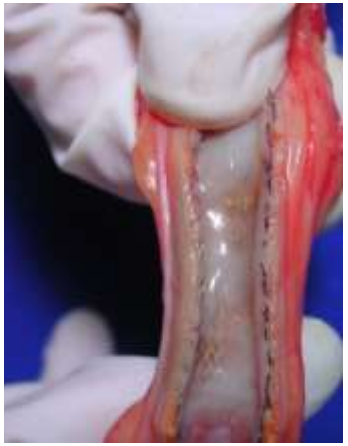
Recommendations	Class[a]	Level[b]	Ref[c]
When revascularization is indicated, an endovascular-first strategy is recommended in all femoropopliteal TASC A–C lesions.	I	C	-
Primary stent implantation should be considered in femoropopliteal TASC B lesions.	IIa	A	285, 286, 291
A primary endovascular approach may also be considered in TASC D lesions in patients with severe comorbidities and the availability of an experienced interventionist.	IIb	C	-

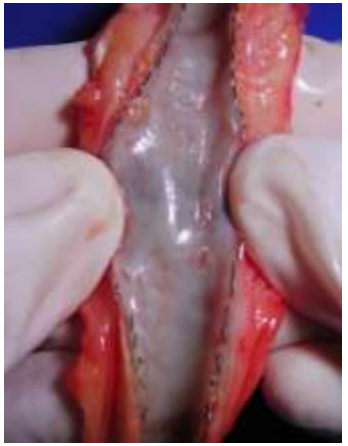
- TASC II A-C lesions
  ⇒ **Endovascular-first** strategy
  *Primary stent **should** be considered in TASC **B**
- TASC II D
  ⇒ **Primary endovascular approach may** be considered in
  1) Pts with severe comorbidities
  2) availabilities of experienced interventionist

Eur Heart J. 2011;32:2851-906

Clinical Issues after SFA Revascularization

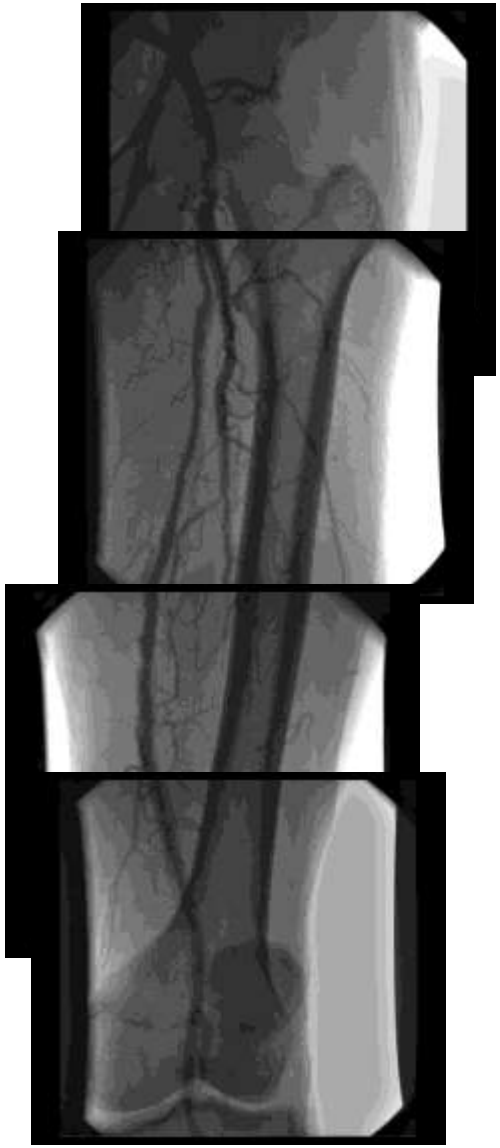


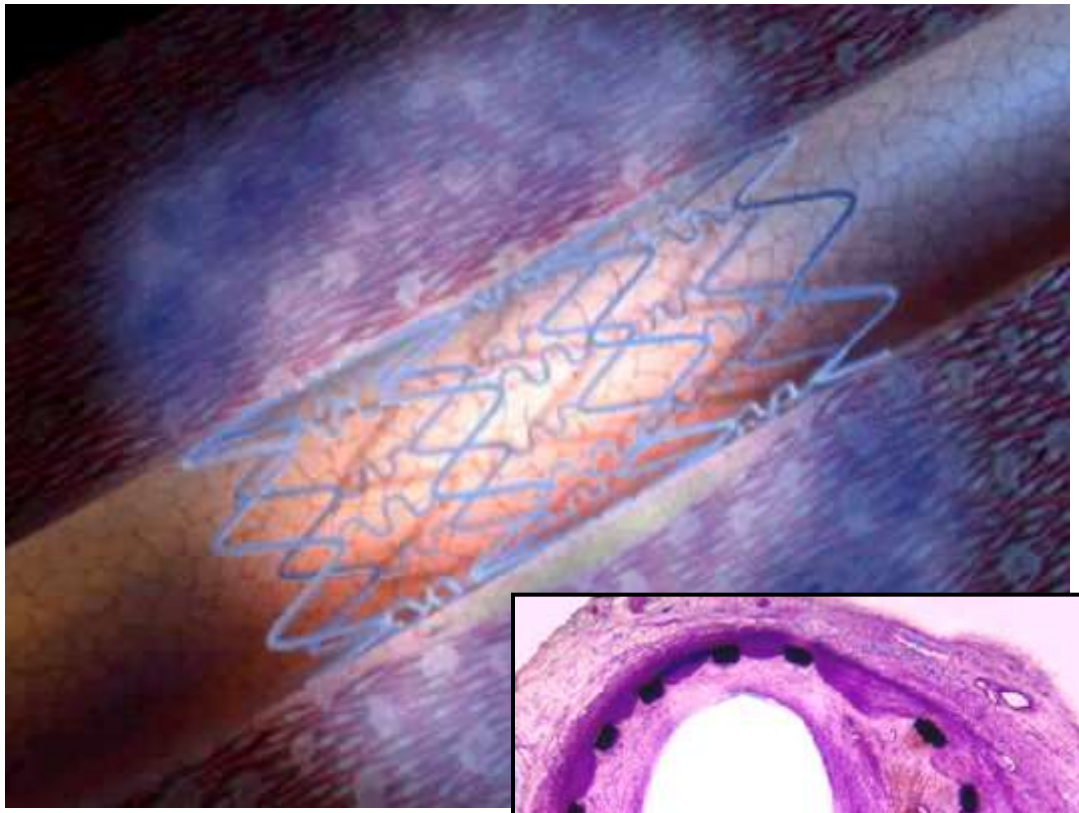


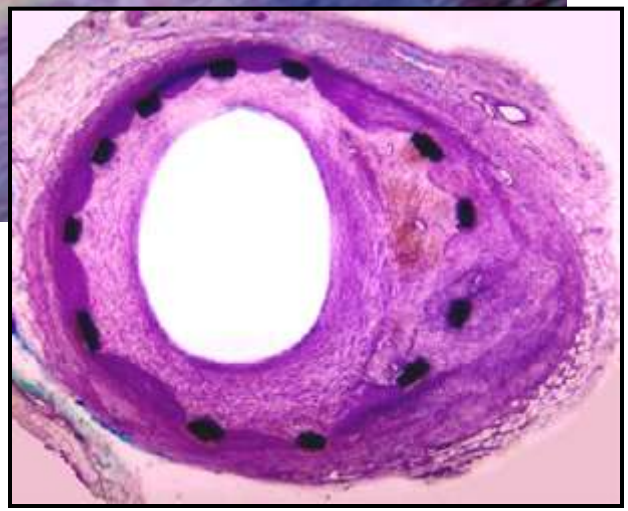


Restenosis
(intimal hyperplasia)

Drug eluting stent for SFA



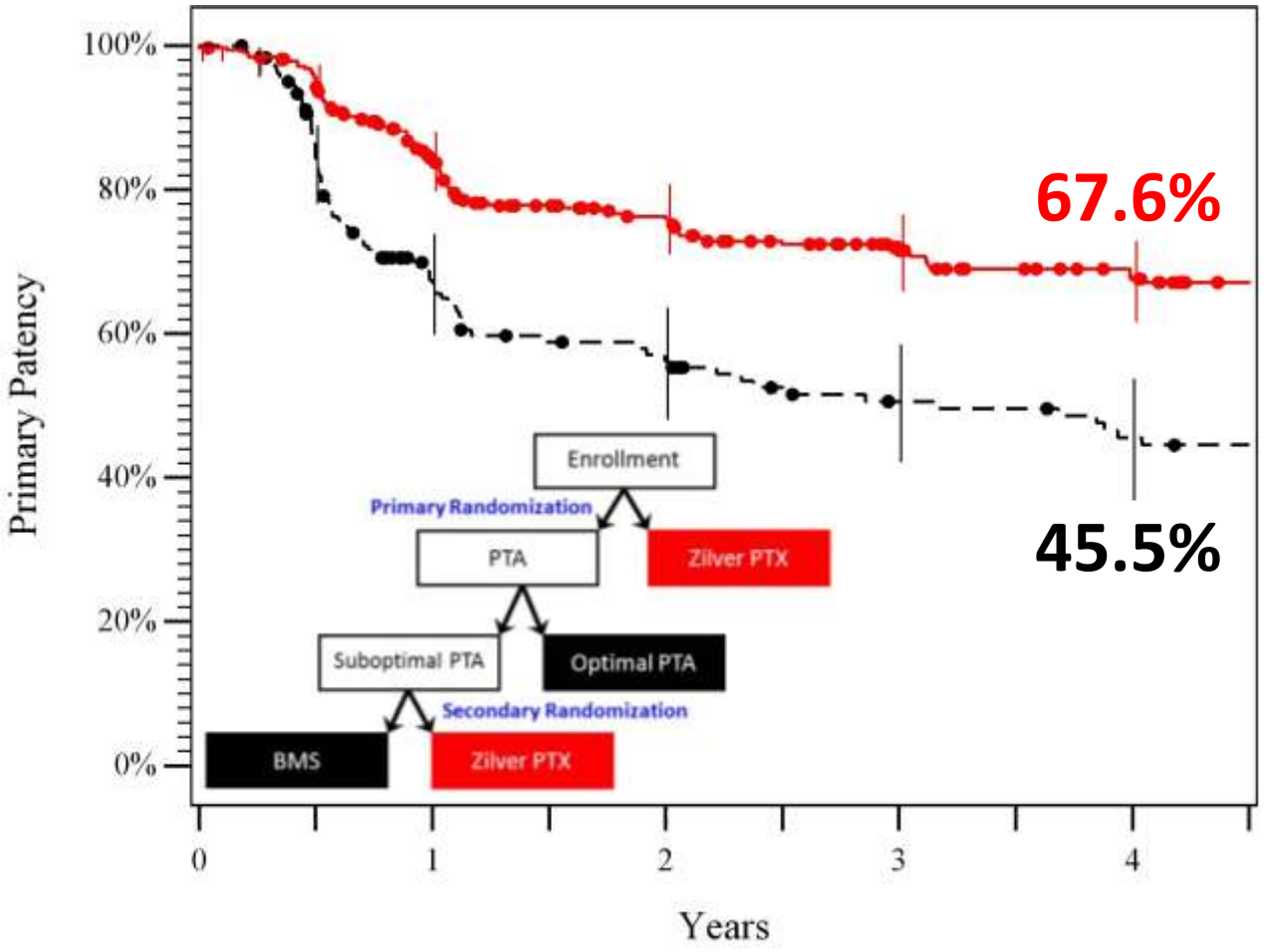




Zilver® PTX® Drug-Eluting Stent

- Designed for the SFA
- PMDA approved
- Paclitaxel only
  - No polymer or binder
  - 3 mg/mm^2 dose density
- Stent Platform: Zilver® Flex™

4-Year Primary Patency (PSVR < 2.0)
Zilver PTX vs. Standard Care – Drug Effect



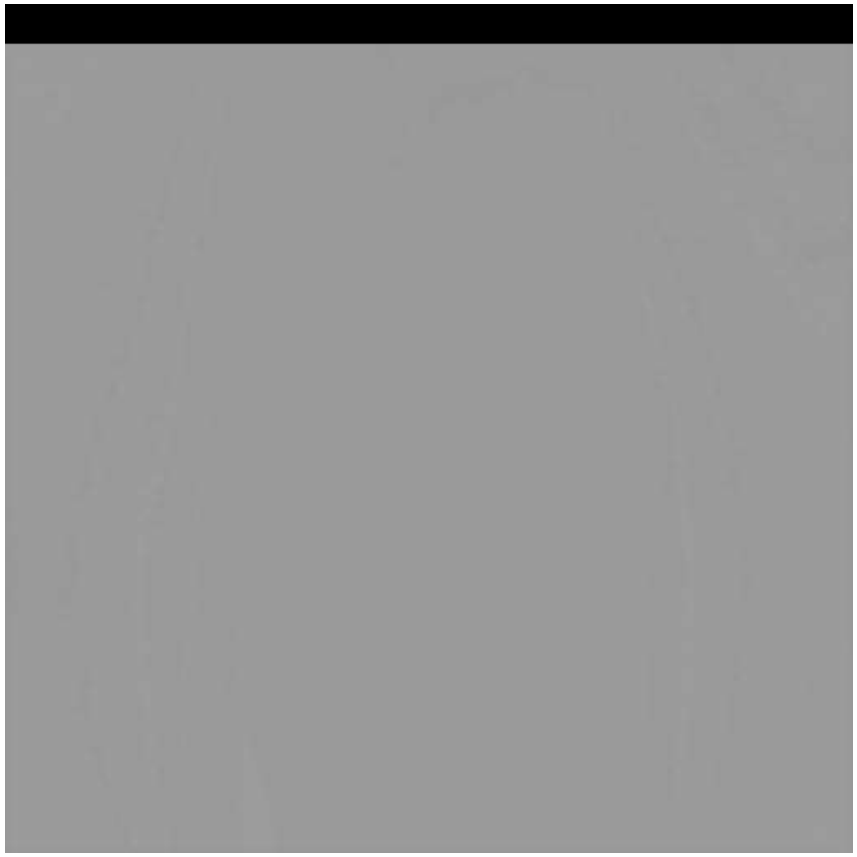
Zilver PTX
(n = 239)
LL: 66±39mm

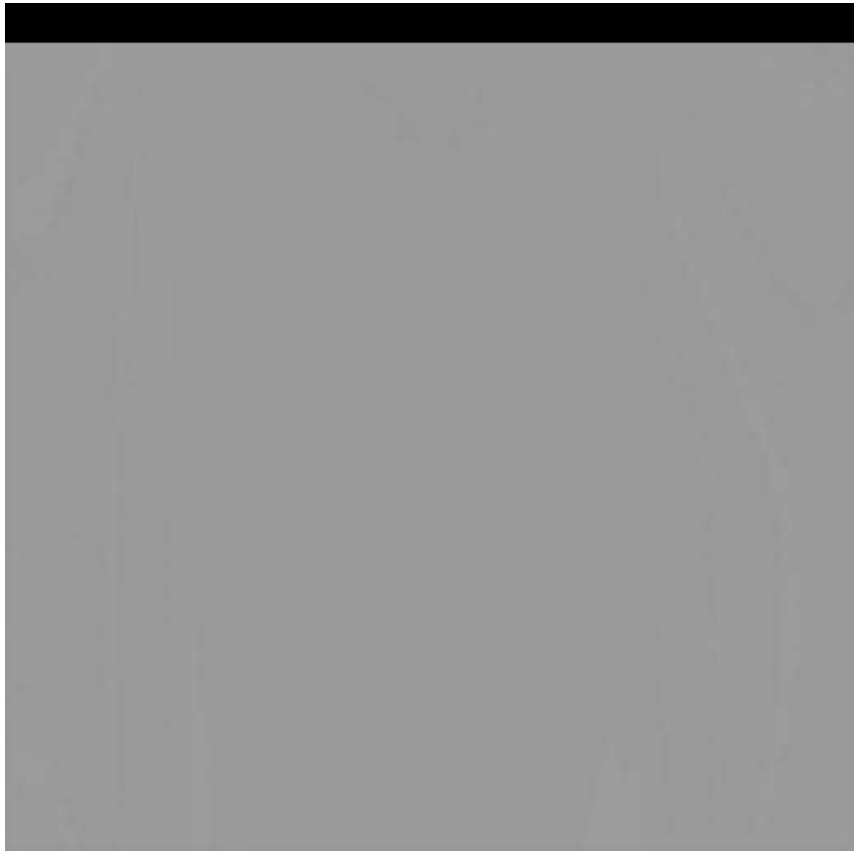
Optimal PTA
+ BMS
(n = 129)
LL: 63±41mm

$p < 0.01$
log-rank

Ansel GM, et al. VIVA 2013

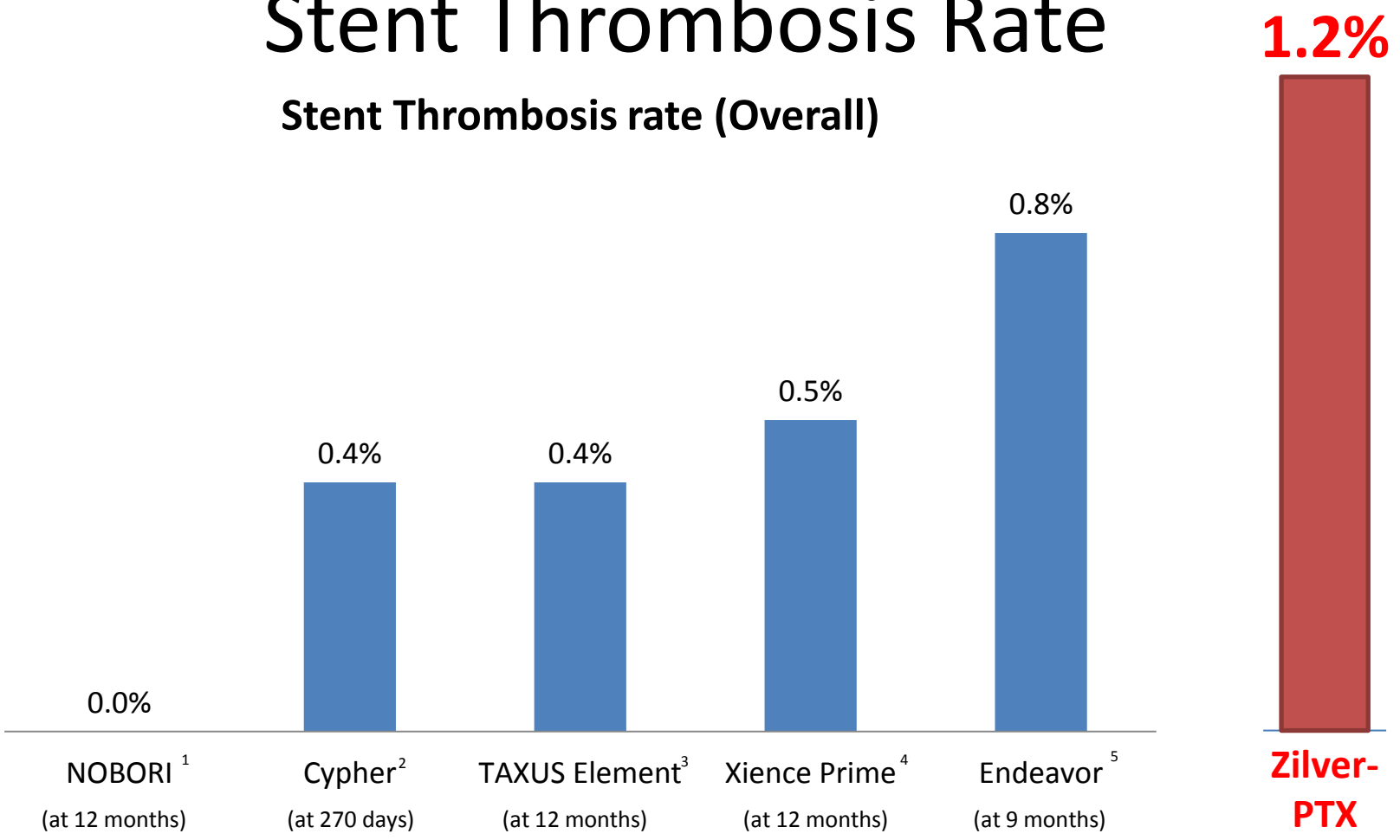
ST (stent thrombosis) after Zilver-PTX implantation





3 days later, acute thrombotic occlusion was occurred
at Rt SFA treated with Zilver-PTX stent (6.0*120mm*3).

Coronary and Peripheral DES Stent Thrombosis Rate



1 Dr. Sigmund Silber Munich, presented at: AHA 2008; No Late and no Very Late Stent Thrombosis with a Drug-Eluting Stent of the Second Generation: 2 Years Results from the Randomized NOBORI-I trial

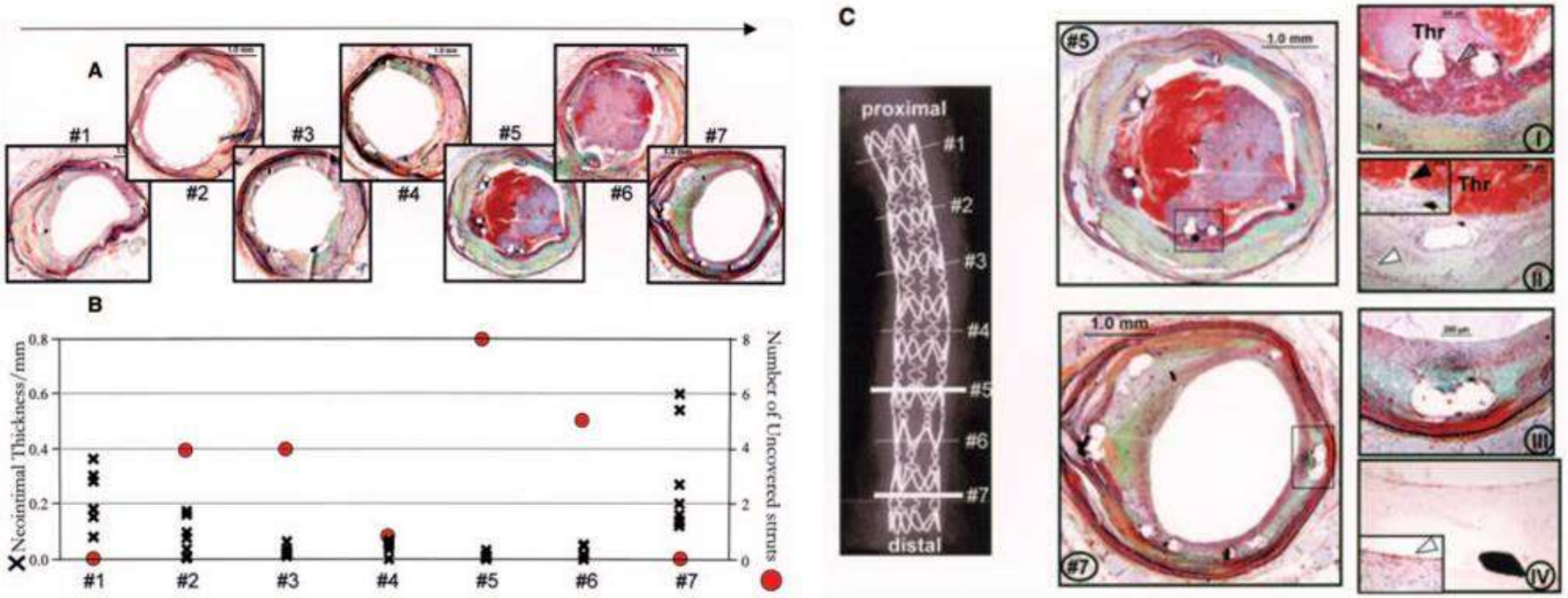
2 Dr.Moses, at al. Sirolimus-Eluting Stents versus Standard Stents in Patients with stenosis in a Native Coronary Artery; New England Journal of Medicine 2003;349:1315-23

3 Dr. Kereiakes, at al. Journal of the American College of Cardiology 2010;56:264-71. Primary Results of the PERSEUS Trial

4 FDA Summary of Safety and Effectiveness Data

5 FDA Summary of Safety and Effectiveness Data

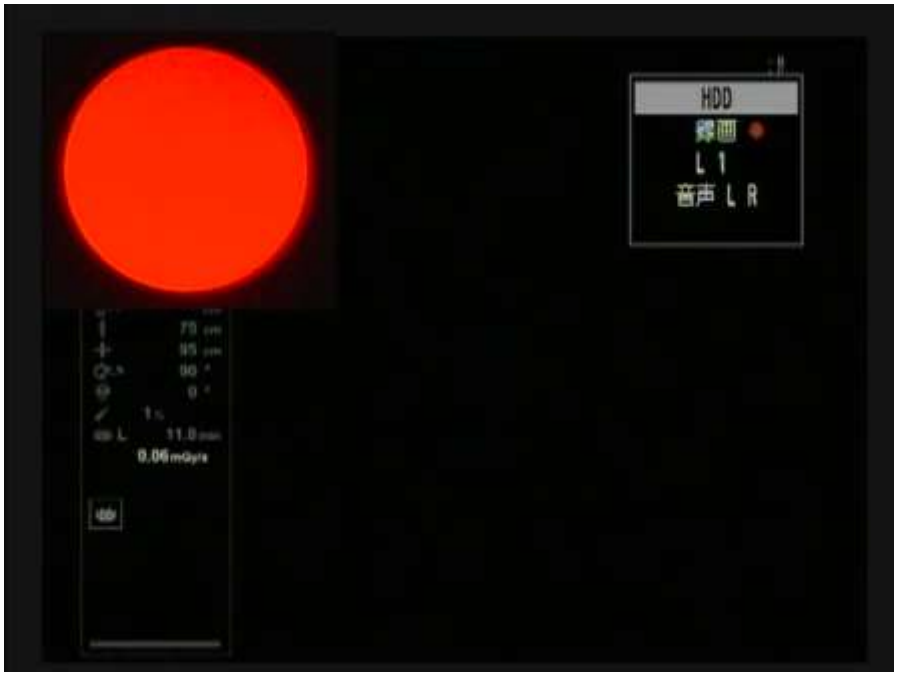
Pathological Correlates of Late Drug-Eluting Stent Thrombosis: Strut Coverage as a Marker of Endothelialization



A univariable logistic generalized estimating equations model of occurrence of thrombus in a stent section vs ratio of uncovered to total stent struts per section demonstrated a marked increase in risk for LST as the number of uncovered struts increased. **The odds ratio for thrombus in a stent with a ratio of uncovered to total stent struts per section >30% is 9.0 (95% CI, 3.5 to 22).**

Finn et al. Circulation. 2007;115:2435-2441.

Angioscopic assessment for arterial repair
BMS (S.M.A.R.T) vs. DES (Zilver-PTX)@2months

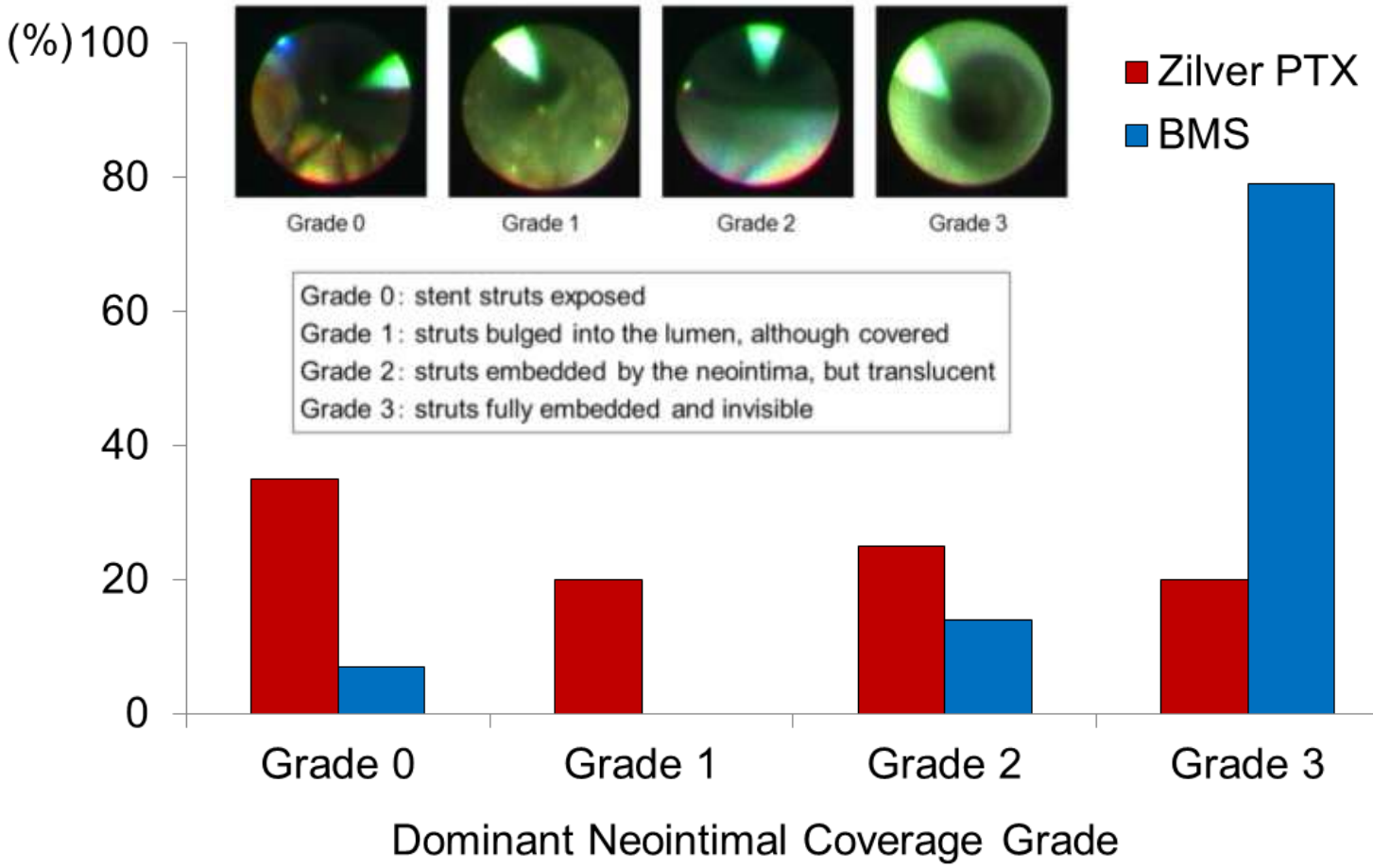


S.M.A.R.T, BMS (7.0*100mm)
*Stent strut fully embedded and invisible (grade 3)

Zilver-PTX, DES (7.0*120mm)
*Stent strut exposed (grade 0)

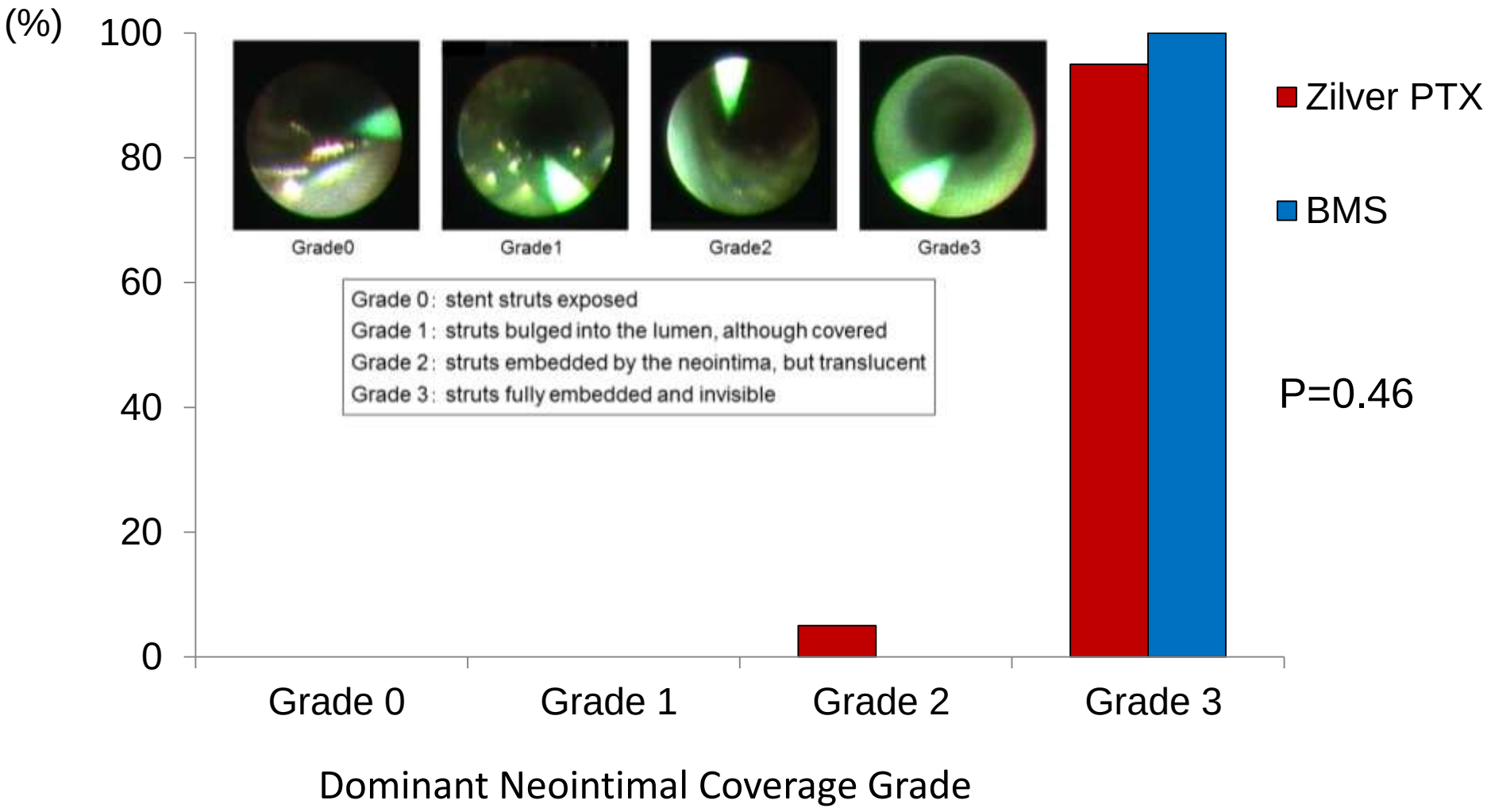
Ishihara T, Iida O, et al. Circ J 2013

Angioscopic assessment for arterial repair
BMS vs. DES @2months

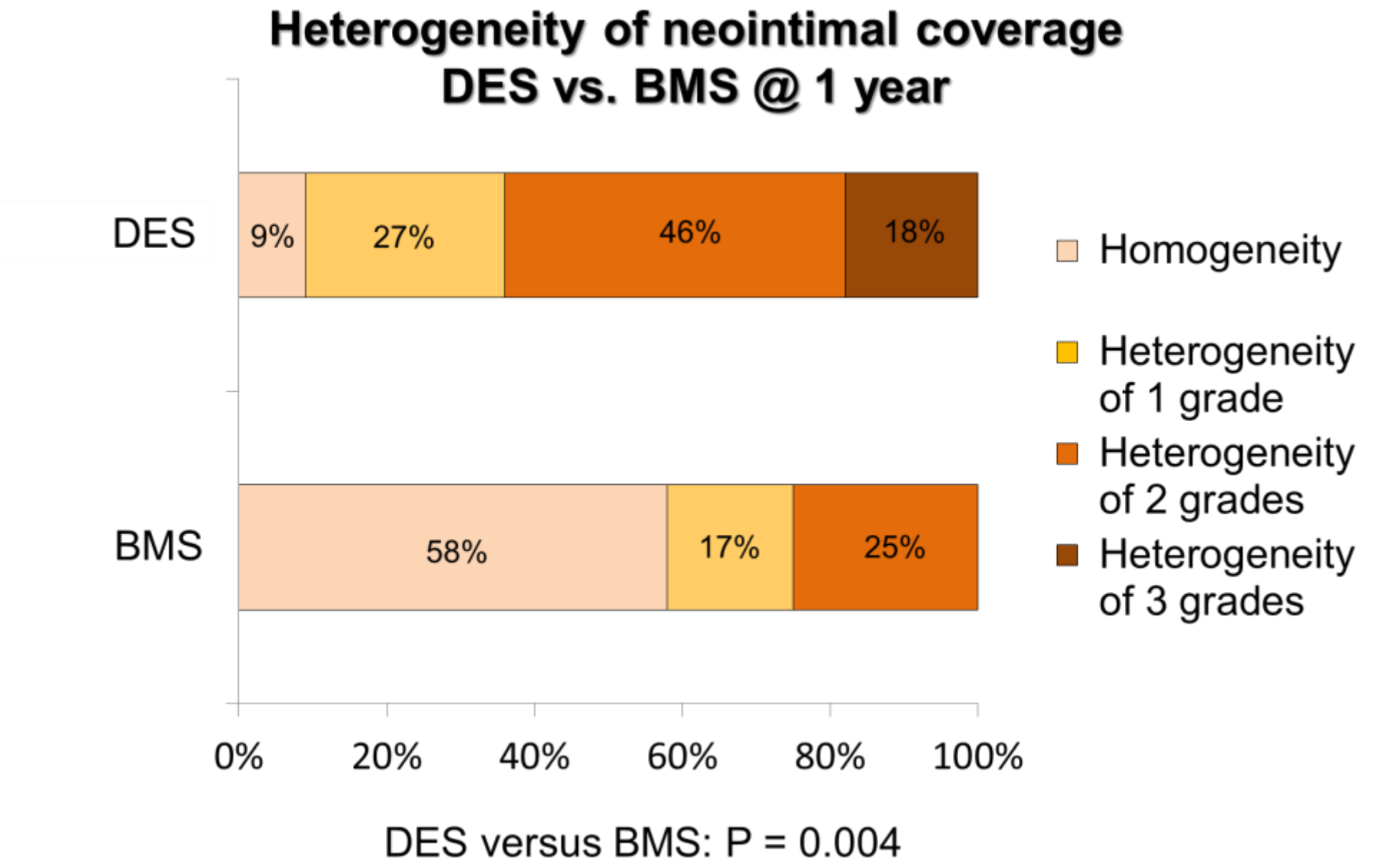


Ishihara T, Iida O, et al. Circ J 2013 inpress

Angioscopic assessment for arterial repair
BMS vs. DES @12months



Ishihara T, Iida O, et al. ACC 2014



Ishihara T, Iida O, et al. ACC 2014

SMART Nitinol Self-Expanding Stent in the Treatment of Obstructive Superficial Femoral Artery Disease:

Three-year Clinical Outcomes from the STROLL Trial

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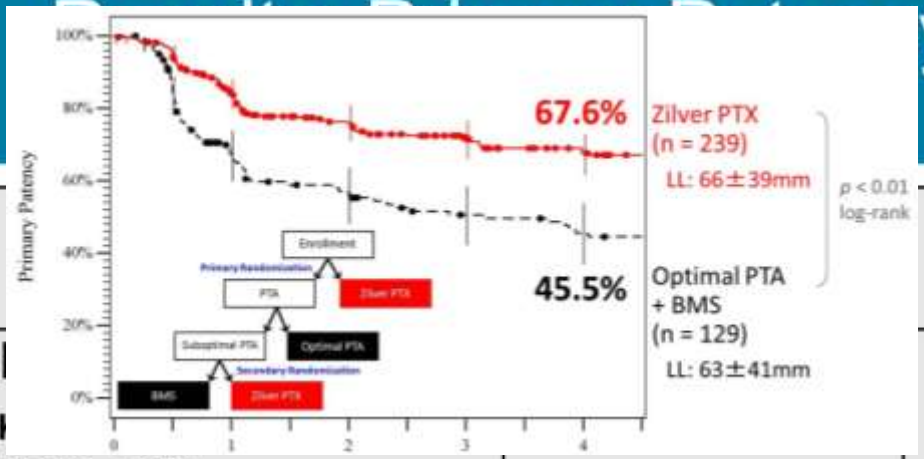
INSTITUTE FOR HEART, VASCULAR AND STROKE CARE

y (LL: 77±31mm)



		24 months	36 months
(PSVR < 2.5)		74.9%	72.7%
DUS Patency (PSVR < 2.5)	81.1% (154/190)	83.5% (132/158)	83.9% (115/137)
Absence of Clinically Driven TLR	87.4% (202/231)	79.0% (173/219)	75.8% (157/207)

Primary Patency: composite endpoint of absence of clinically driven TLR and DUS assessed binary restenosis defined as diameter stenosis >50% (non-patent).

DUS patency: stent non-patency defined as a diameter stenosis >50% with a specific a peak systolic velocity ratio as measured by Duplex Ultrasonography

Clinically driven TLR: any intervention in the stented target lesion following documented recurrent symptomatic leg ischemia by Rutherford/Becker Classification (2,3,4) with a resting or exercise ABI <0.8 and >50% diameter in-lesion stenosis by angiography. Or >70% in-lesion diameter stenosis by angiography in the absence of ischemic signs and symptoms.

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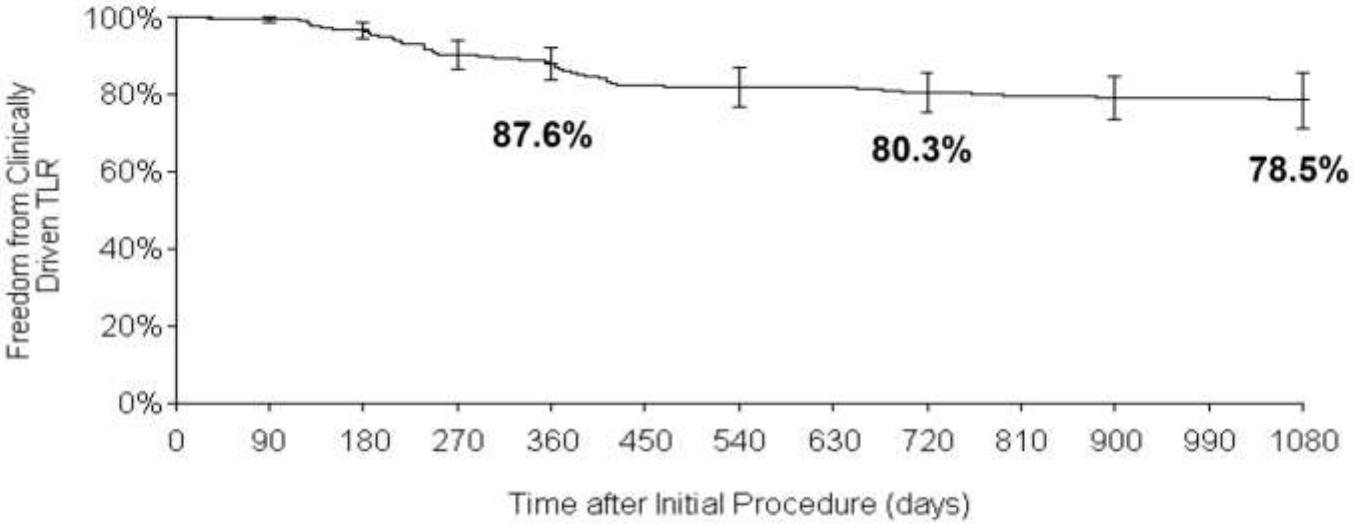
Freedom from Clinically-Driven TLR:1080 days



Clinically Driven TLR	0	30	90	180	270	360	540	720	900	1080
# Entered	250	250	247	244	235	213	206	184	175	161
# Censored	0	3	1	1	5	0	5	4	8	53
# Incomplete	0	0	1	1	2	1	3	2	3	7
# At Risk	250	249	246	243	232	213	202	181	170	131
# Events	0	0	1	7	15	6	14	3	3	1
# Events/Month	--	0.0	0.5	2.3	5.0	2.0	2.3	0.5	0.5	0.2
% Survived	100.00%	100.00%	99.60%	96.73%	90.47%	87.91%	81.87%	80.50%	79.07%	78.50%
SE	0.00%	0.00%	0.41%	1.15%	1.92%	2.14%	2.57%	2.69%	2.85%	3.64%

Cumulative stent fracture rate

Stent Fracture	6-month	12-month	24-Month	36-Month
Type I	1.49% (3/202)	2.03% (4/197)	2.3% (4/177)	3.6% (6/169)
Type II	0.0% (0/202)	0.0% (0/197)	0.0% (0/177)	0.0% (0/169)
Type III	0.0% (0/202)	0.0% (0/197)	0.0% (0/177)	0.0% (0/169)
Type IV	0.0% (0/202)	0.0% (0/197)	0.0% (0/177)	0.0% (0/169)
Type V	0.0% (0/202)	0.0% (0/197)	0.0% (0/177)	0.0% (0/169)
Any Stent Fracture	1.49% (3/202)	2.03% (4/197)	2.3% (4/177)	3.6% (6/169)

Only Type I Fractures

Type I Single Strut fracture
Type II Multiple single Strut fracture
Type III Complete transverse linear separation without stent displacement
Type IV Complete transverse linear fracture with stent displacement
Type V Spiral dissection of stent

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Position of S.M.A.R.T stent in recent endovascular era

Aorto-iliac lesions

・The durability of S.M.A.R.T. stent was superior to that of the other stents. The particular design characteristics of the S.M.A.R.T. stent may have accounted for the better results in AI lesions.

Femoropopliteal lesions

・Primary patency rate with S.M.A.R.T stent is 81.7% at 12 months, 74.9% at 24 months and 72.7% at 36 months, respectively.

・Balance of safety and efficacy (DES versus BMS) is clinically important decision making of stent use.

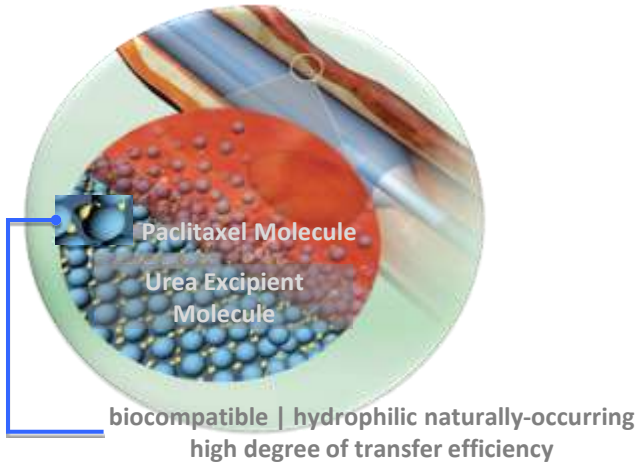
S.M.A.R.T could be still first line tehrapy and well work in recent endovascular era because of its truth and result.

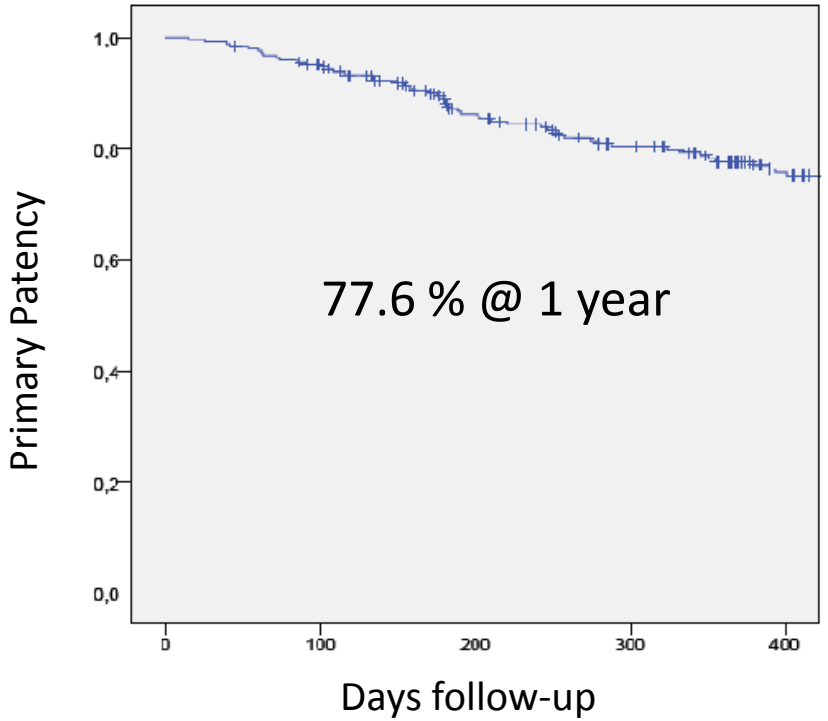
Real-World Registry DEB for Extensive Femoropopliteal Lesions

Single center registry of femoropopliteal lesions

288 limbs treated, All-comers, Rutherford 2-6

Lesion-length:	**24.0 ± 10.1 cm**
Stenosis / occlusion	34.7 % / **65.3 %**
De-novo:	51.7 %
Restenosis:	11.1 %
In-stent restenosis (ISR):	**37.2 %**



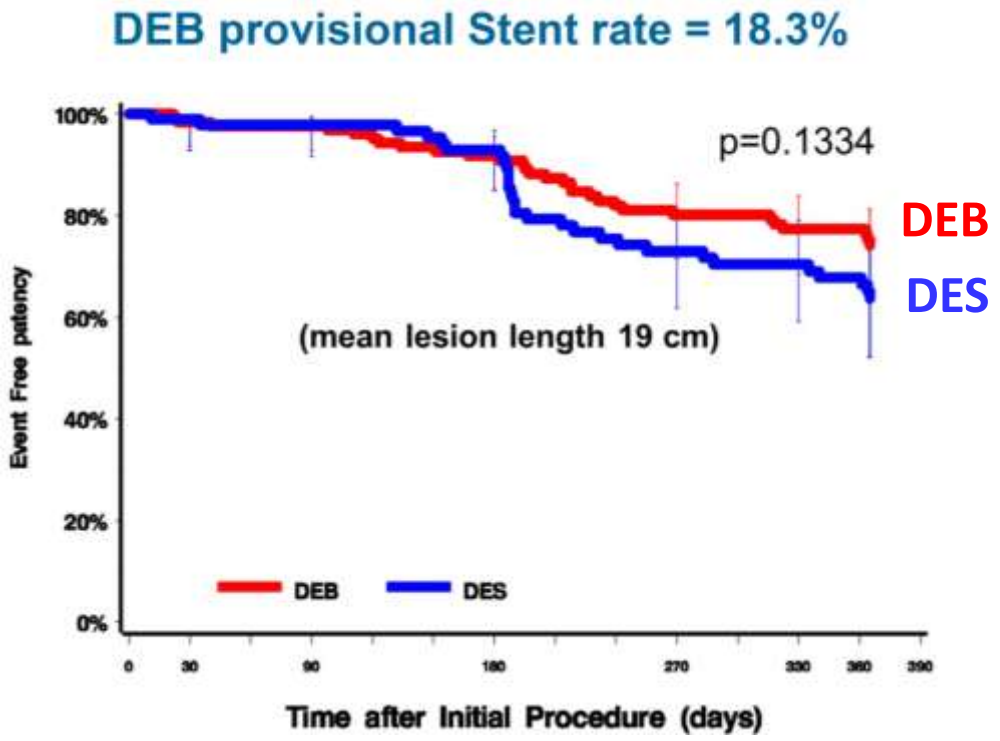


Days	0	90	180	270	360
Number at risk	249	236	195	163	137

Schmidt A @ LINC 2013

DEB vs. DES in Long SFA lesions

- ✓ Single Center
- ✓ Retrospective with propensity score analysis
- ✓ IN.PACT DEB vs. Zilver PTX
- ✓ 228 patients
- ✓ Mean lesion length = 19 cm

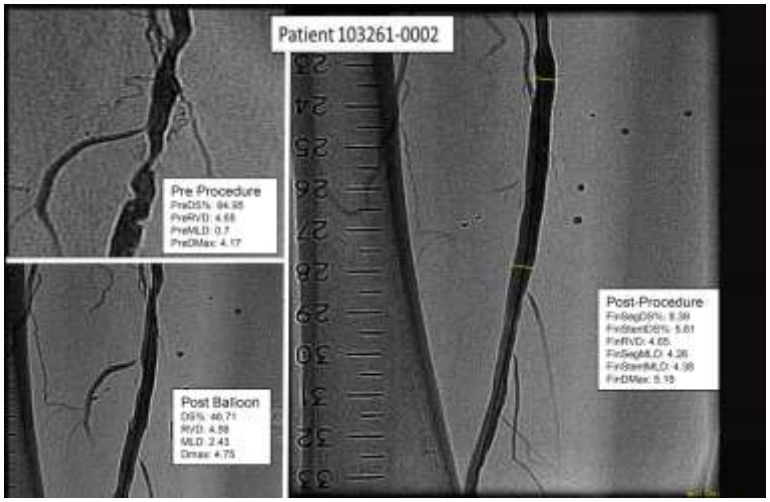


Major Adverse Events	IN.PACT (DEB)	Zilver PTX (DES)	p	adjusted p
n	131	97		
Any TLR	19.3% (21/109)	21.5% (17/79)	0.705	0.55
Clinical-driven TLR	15.6% (17/109)	19.0% (15/79)	0.543	0.572
Loss of Patency	23.9% (26/109)	30.4% (24/79)	0.319	0.372

Zeller T@CX 2013

ESPRIT I Trial

Evaluation of **E**sprit BVS in the Treatment of Patients With Occlusive Vascular Disease of the SFA, CIA and EIA

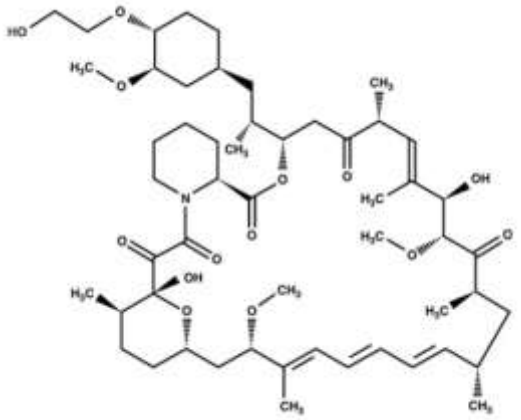


Lesion Characteristics	
External Iliac (%)	11.4
SFA (%)	**88.6**
Target lesion length (mm)	**35.5**
Occlusion length (mm)	22.9
Total occlusions (%)	30.6

Duplex Ultrasound Results to 12 Months

	1-Month	6-Month	12-Month
TLR rate	1.26	1.26	**8.8%**
Restenosis	**0%**	**0%**	**12.9%**

MAJESTIC Trial To Study Self-Expanding DES System Designed To Treat Superficial Femoral Artery (SFA) Lesions



Platform: Innova™, Drug: Paclitaxel, Polymer: Fluorocopolymer

*Boston Scientific Begins Clinical Trial Of Innova™ Peripheral Vascular Drug-Eluting Stent System. The trial is projected to enroll **55** patients across **15** centers in Europe, Australia, and New Zealand. The first implantation in the MAJESTIC trial was performed by **Andrew Holden, MD**, who is Director of Interventional Radiology at Auckland City Hospital in Auckland, New Zealand.