

What Should Be the Default SFA Strategy:

Updated Evidence for TASC C or D Femoro popliteal Lesions

Biologic and Mechanical Suppression for Restenosis: Drug-Eluting Stent

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On behalf of the Investigators

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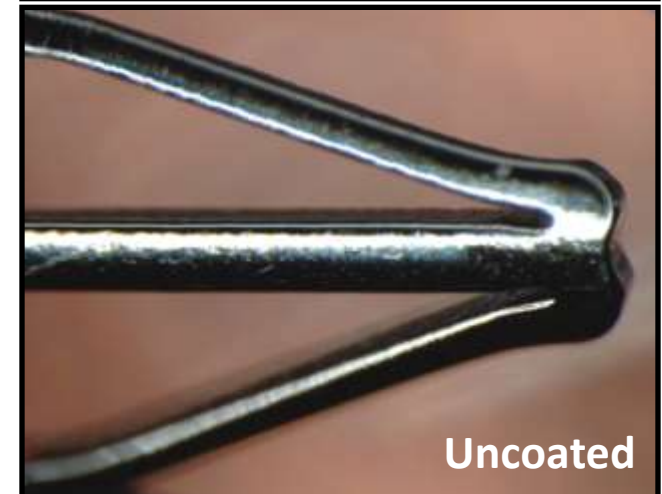
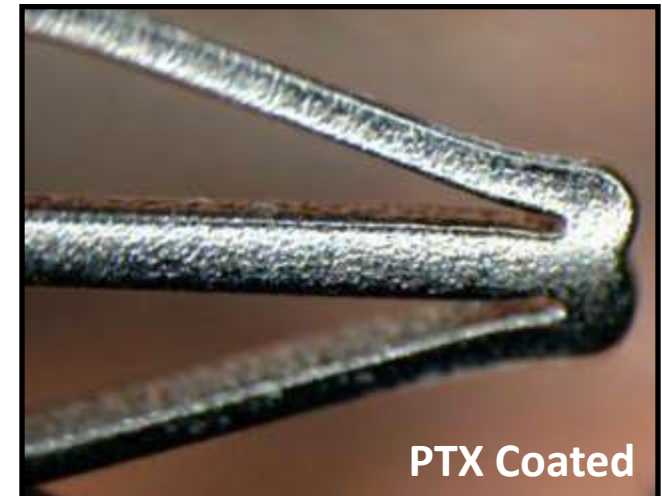
COI Disclosure

First Author : Hiroyoshi Yokoi

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- 8.Affiliation with Endowed Department : none
- 9.Other remuneration such as gifts : none

Zilver PTX Drug-Eluting Stent

- Designed for the SFA
- Available in 50 countries including US, EU and Japan
- Dual therapy
 - **Mechanical scaffold:**
Zilver Flex[®] stent platform
 - **Drug therapy:** Paclitaxel only
 - No polymer or binder
 - 3 $\mu\text{g}/\text{mm}^2$ dose density
- Sponsor: Cook Medical



Japan PMS Compared to RCT and SAS

	Zilver PTX RCT	Zilver PTX SAS	Zilver PTX Japan PMS
Key Study Criteria	No significant untreated inflow tract stenosis		ALL patients treated with Zilver PTX enrolled (up to enrollment limit), NO exclusion criteria
	At least one patent runoff vessel		
	Maximum 2 Zilver PTX stents per lesion	Maximum 4 Zilver PTX stents per patient	
	Lesion length ≤ 14 cm	No exclusions	
	One lesion per limb		
	No prior stent in SFA	In-stent restenosis included	
	Excluded if serum creatinine > 2.0, renal failure, or dialysis	No exclusions	
Antiplatelets	Clopidogrel or ticlopidine recommended for 60 days, aspirin indefinitely		
Follow-up	5 years	2 years	5 years
Patency	Core laboratory analysis	Site analysis	
Stent Integrity	X-ray core laboratory analysis		



Increasingly complex patients and lesions

Leave the *right thing* behind in SFA TASC-C/D lesions

- *Stent Integrity*
- Safety (no increased stent thrombosis)
- Anti-restenosis effect
- Pattern of restenosis

5-year Stent Integrity from RCT

Study Period	Number of New Events	Fracture Rate¹
Enrollment	0	0.0%
1-year	4	0.9%
3-year	3	1.9%
5-year	0	1.9%

¹ Kaplan-Meier estimates

Zilver PTX has excellent durability
in challenging SFA environment

Stent Integrity through 12 months

- 1066 stents were evaluated by sites in Japan PMS
 - 17 total fractures (1.6%)

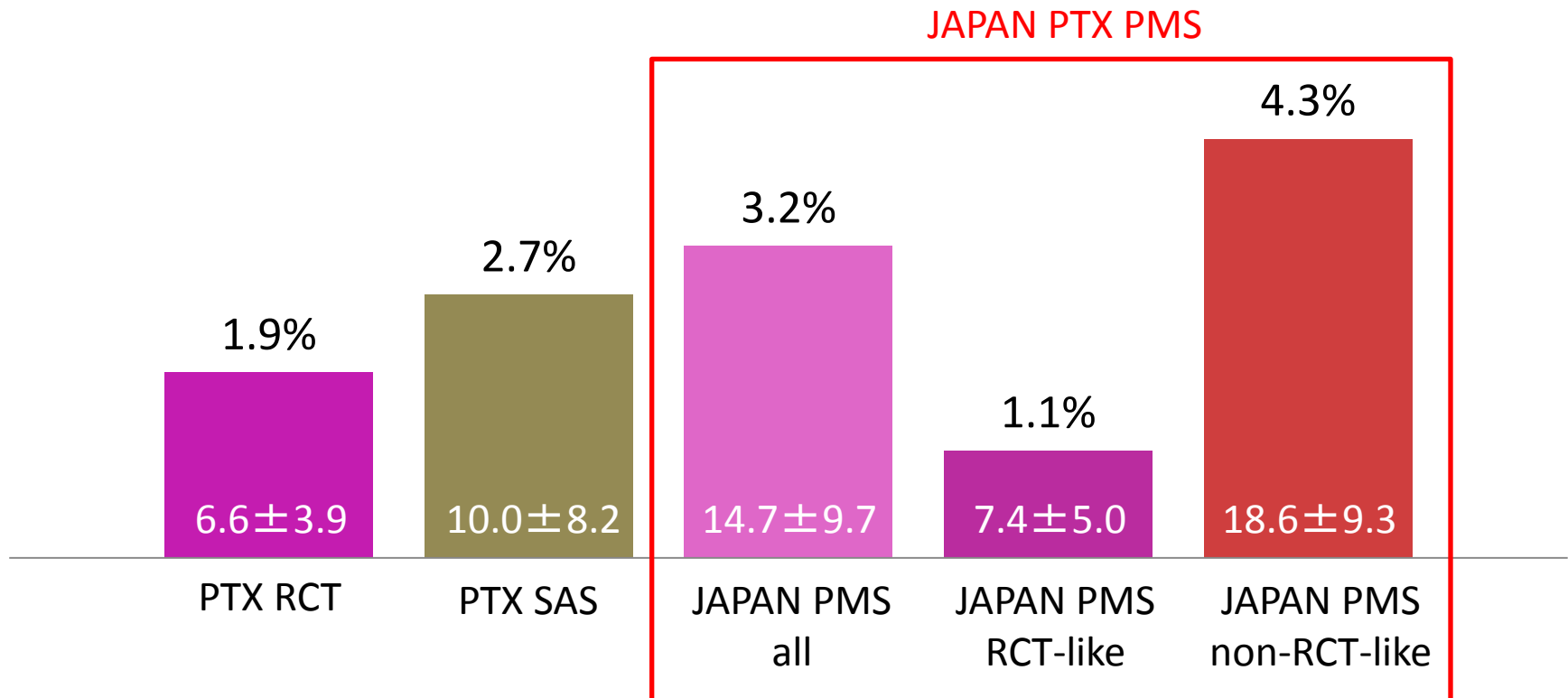
	RCT	SAS	Japan PMS
Fracture Rate	0.9%	1.5%	1.6%
Number of Stents Evaluated	457	1889	1066

Low fracture rate, not significantly greater than in pre-market studies despite more complex lesions (e.g., longer, more ISR, fewer patent runoff vessels)

Leave the *right thing* behind in SFA TASC-C/D lesions

- Stent Integrity
- *Safety (no increased stent thrombosis)*
- Anti-restenosis effect
- Pattern of restenosis

12-Month Stent thrombosis/Occlusion after stent Placement

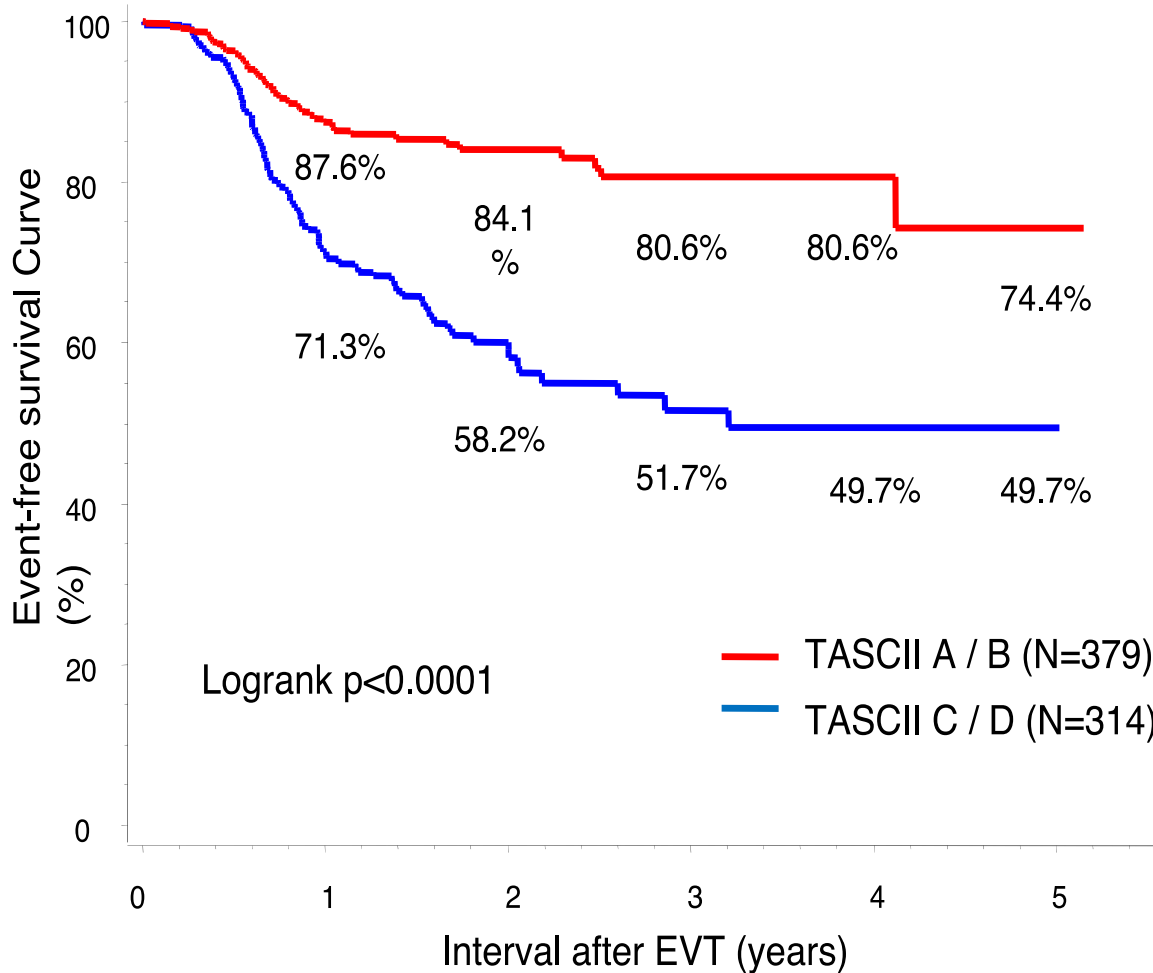


Leave the *right thing* behind in SFA TASC-C/D lesions

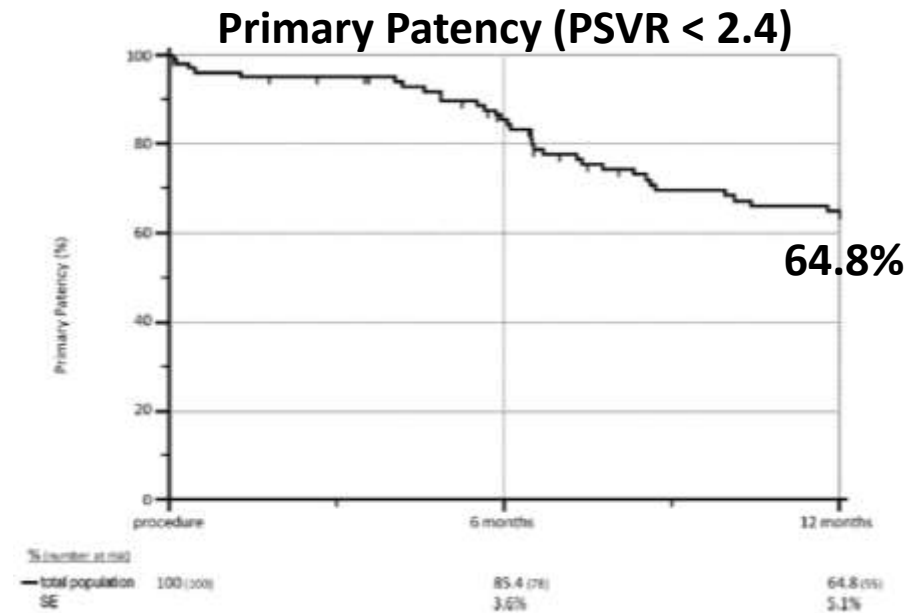
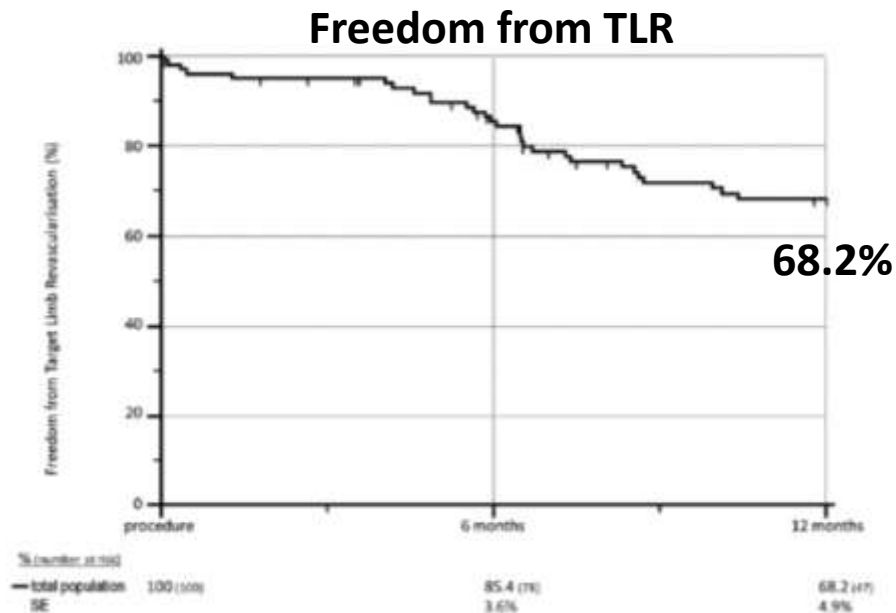
- Stent Integrity
- Safety (no increased stent thrombosis)
- *Anti-restenosis effect*
- Pattern of restenosis

Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent

Primary Patency Rate



Bare Metal Stent Results in Long Lesions - DURABILITY 200 Study Results



5 occurrences of thrombosis reported (5/100, 5%) through 30 days

Patient	Time	Event Description	Treatment
1	In hospital	Occlusion	Successful thrombectomy, PTA and stent
2	Post-discharge	Occlusion	Successful thrombectomy
3	5 days	Acute ischemia	Successful thrombolysis
4	12 days	Thrombosis	Bypass
5	14 days	Claudication	Successful thrombolysis, PTA and stent



Effect of Bare-Metal Nitinol Stent Implantation and Paclitaxel-Eluting Nitinol Stent Implantation on Vascular Response in the Superficial Femoral Artery Lesion Assessed on Intravascular Ultrasound

Kojiro Miki, MD; Kenichi Fujii, MD; Daizo Kawasaki, MD; Masashi Fukunaga, MD; Machiko Nishimura, MD; Tetsuo Horimatsu, MD; Ten Saita, MD; Hiroto Tamaru, MD; Takahiro Imanaka, MD; Masahiko Shibuya, MD; Motomaru Masutani, MD; Mitsumasa Ohyanagi, MD; Tohru Masuyama, MD

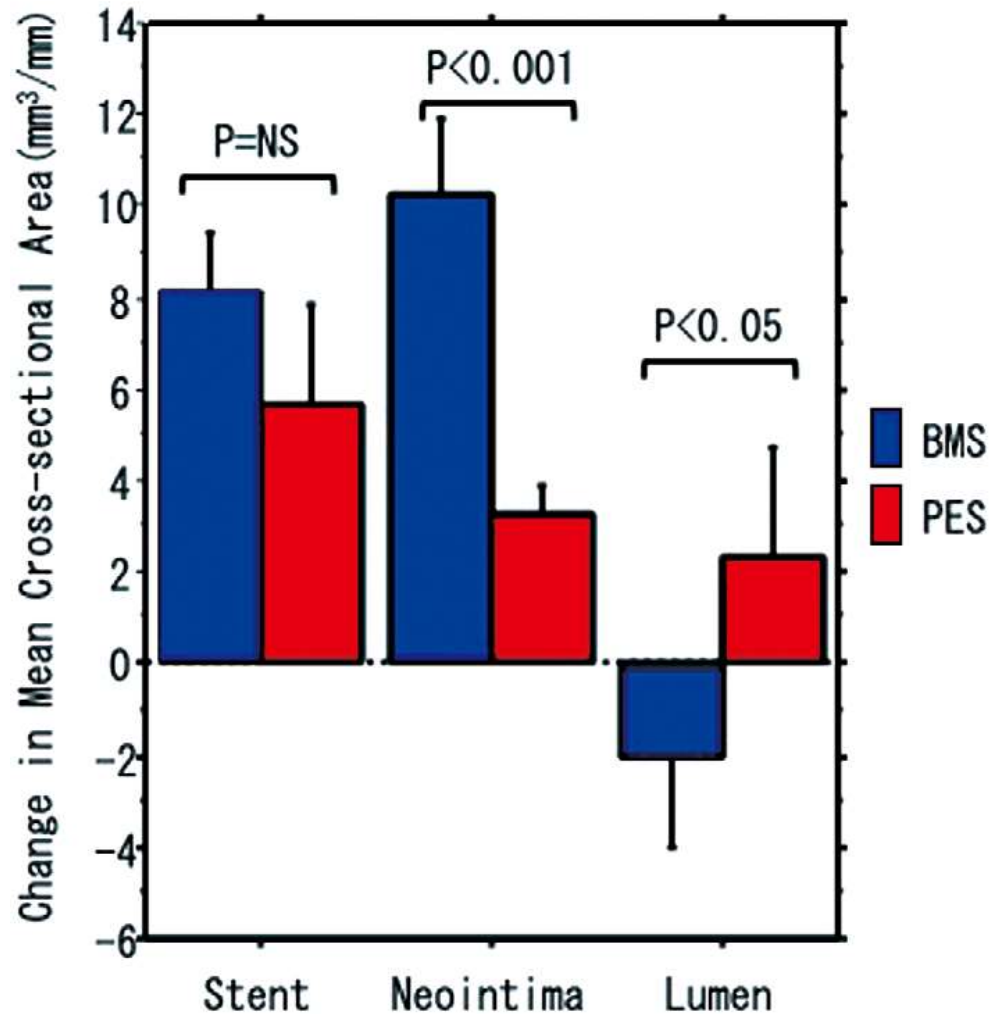
Methods and Results: We retrospectively analyzed 38 de novo SFA lesions from 32 patients who underwent endovascular therapy (EVT) with self-expanding bare-metal nitinol stent (25 lesions; BMS group) or self-expanding paclitaxel-eluting nitinol stents (13 lesions; PES group). At 6 months after EVT, follow-up IVUS was done to evaluate NIH. Serial IVUS volumetric analysis was done after stent deployment and at follow-up. Mean stent, lumen and neointimal areas were calculated as the volume divided by the stent length. The primary endpoint of this study was

NIH. Serial IVUS volumetric analysis was done after stent deployment and at follow-up. Mean stent, lumen and neointimal areas were calculated as the volume divided by the stent length. The primary endpoint of this study was mean late lumen loss at 6-month follow-up. The mean follow-up period was 189 ± 39 days. Mean neointimal area was smaller in the PES group compared to the BMS group ($3.3 \pm 1.0 \text{ mm}^2$ vs. $10.2 \pm 4.1 \text{ mm}^2$, $P < 0.001$). Mean late lumen loss was significantly lower in the PES group compared to the BMS group ($-2.3 \pm 3.7 \text{ mm}^2$ vs. $2.1 \pm 4.7 \text{ mm}^2$, $P < 0.05$).

Conclusions: EVT with DES in SFA lesions might decrease NIH associated with ISR in short-term follow-up. (Circ J 2014; 78: 1451–1458)

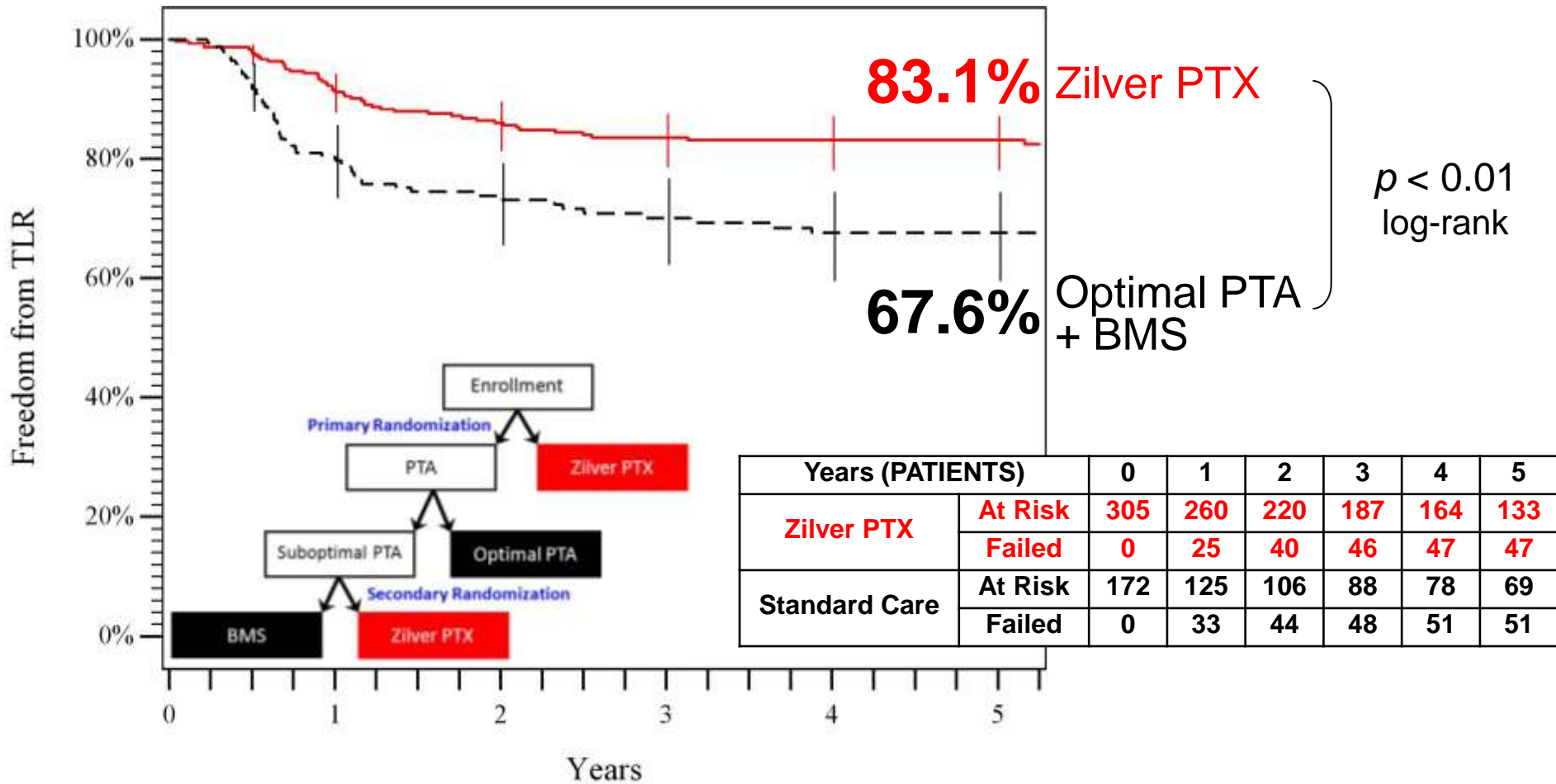
Key Words: Endovascular therapy; Intravascular ultrasound; Paclitaxel-eluting nitinol stent; Restenosis; Superficial femoral artery

Change in Stented Segment



5-year Freedom from TLR

Zilver PTX vs. Standard Care



At 5 years, Zilver PTX demonstrates a 48% reduction in reintervention compared to standard care

12-Month Results with Zilver PTX[®] in Long Femoropopliteal Lesions

Thomas Zeller, M.D.

Clinical and Interventional Angiology

Herz-Zentrum

Bad Krozingen, Germany



Baseline Lesion Characteristics

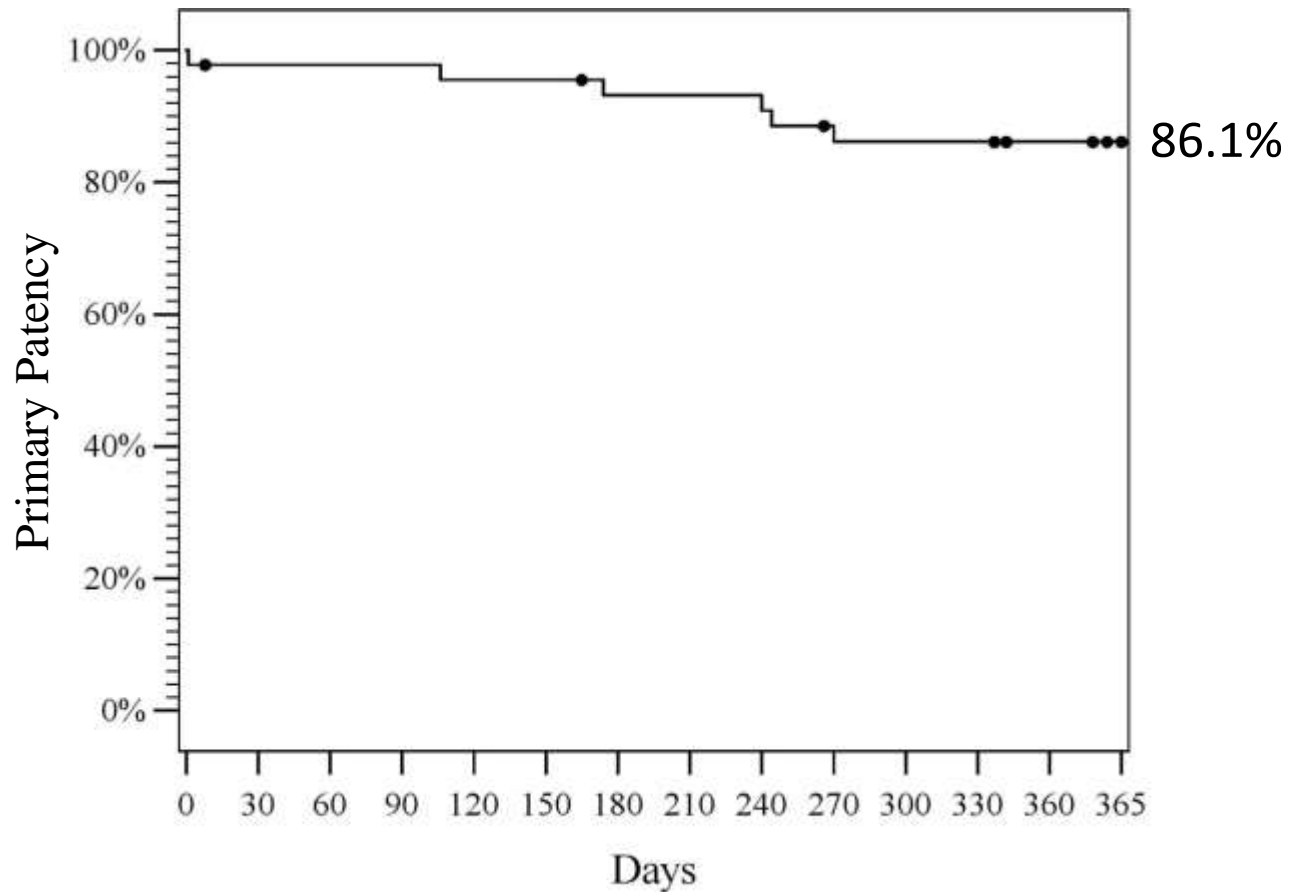
Lesions		45
Lesion length (mm)¹		189.3 ± 91.1
Diameter stenosis (%)¹		95.4 ± 11.1
Total occlusions¹		82.2%
<i>De novo</i> lesions		97.8%
Lesion calcification¹	None	11.1%
	Mild	33.3%
	Moderate	15.6%
	Severe	40.0%

¹ Angiographic core lab assessment

12-Month Safety

- No procedure- or device-related mortality (0/45 patients)
- 86.1% event-free survival (freedom from death, amputation, TLR, worsening Rutherford classification)

12-Month Primary Patency



Similar to 12-month Kaplan-Meier patency estimates in RCT and SAS pre-market studies

Patient Demographics and Comorbidities

	Zilver PTX RCT	JPMS RCT-like	JPMS non-RCT-like	<i>p</i> -value
Patients	236	324	583	-
Age (years)	68 ± 10	73 ± 9	74 ± 8	NS
Male	66%	73%	69%	NS
Diabetes	50%	58%	59%	NS
High cholesterol	76%	59%	62%	NS
Hypertension	89%	86%	85%	NS
Pulmonary disease	19%	8%	8%	NS
Renal disease¹	10%	42%	45%	NS

¹ Of patients with renal disease in the Japan PMS, 82% were in renal failure defined as eGFR < 60 and/or dialysis

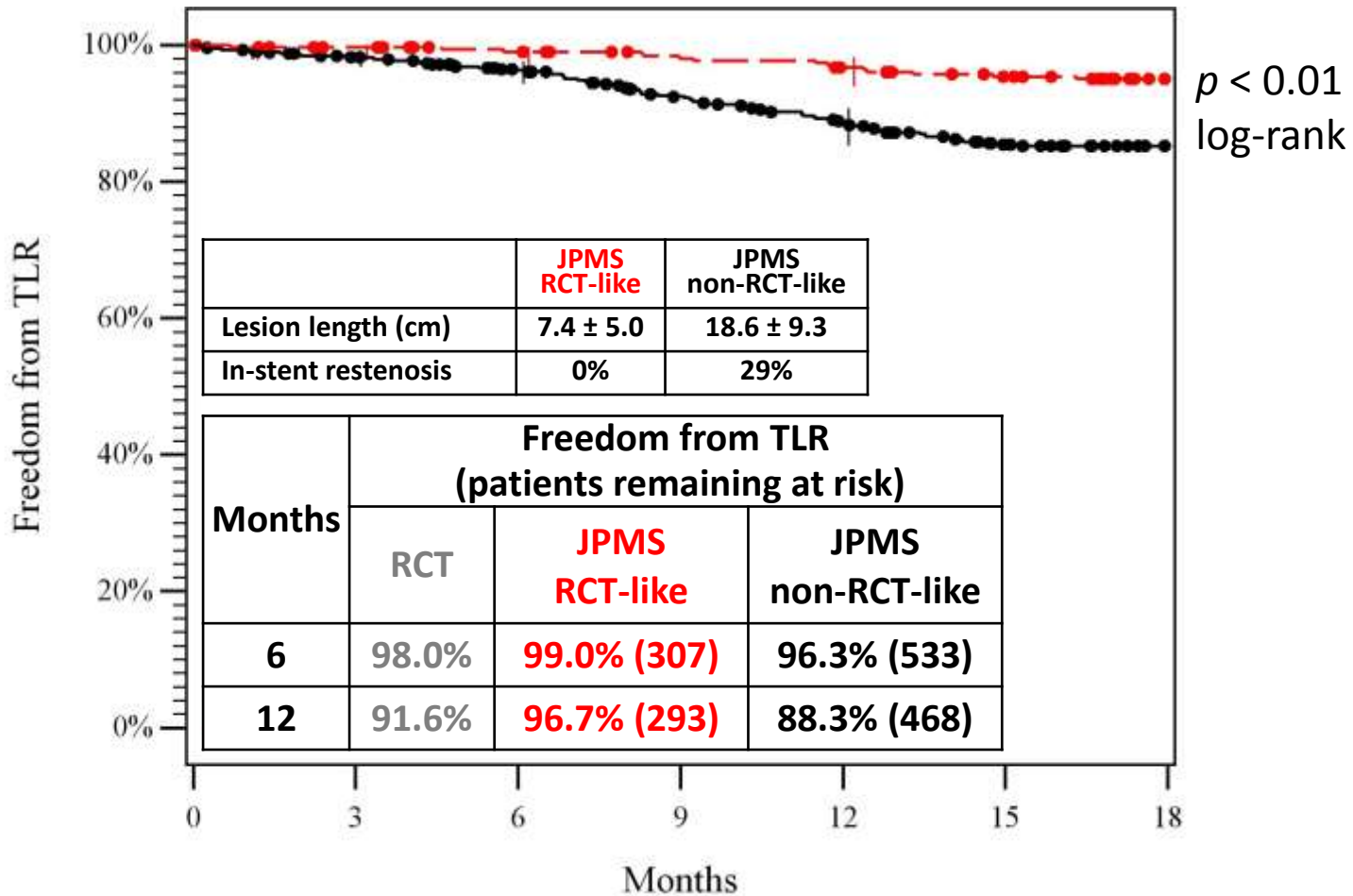
No significant differences between RCT-like and non-RCT-like patients

Baseline Lesion Characteristics

	Zilver PTX RCT	JPMS RCT-like	JPMS non-RCT-like	<i>p</i> -value
Lesions	247	378	703	-
Lesion length (cm)	6.6 ± 3.9	7.4 ± 5.0	18.6 ± 9.3	< 0.001
Diameter stenosis (%)	80 ± 17	89 ± 12	93 ± 9	< 0.001
Total occlusions	30%	28%	49%	< 0.001
In-stent restenosis	0%	0%	29%	< 0.001
Patent runoff vessels	0	0%	0%	< 0.001
	1	22%	29%	
	2	35%	36%	
	3	42%	34%	

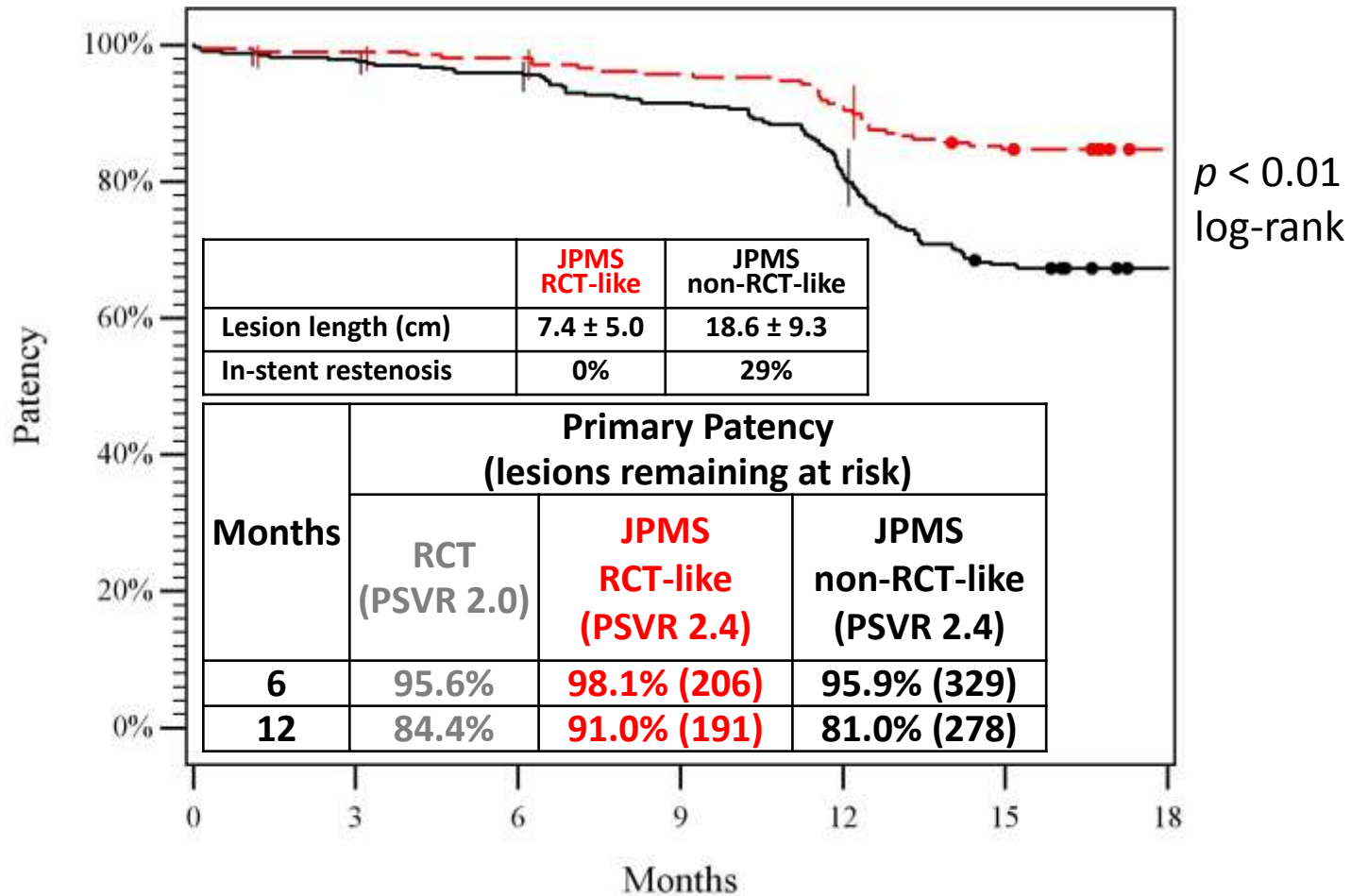
Non-RCT-like lesions are significantly more complex than RCT-like lesions

Freedom from TLR



Freedom from TLR is excellent in complex lesions and slightly lower than in RCT-like lesions

Primary Patency by Duplex Ultrasonography



Primary patency is excellent in complex lesions and slightly lower than in RCT-like lesions

Study Comparison

	Zilver PTX RCT ¹	Zilver PTX SAS ²	Zilver PTX Longer Lesions	Japan PMS RCT-like	Japan PMS non-RCT-like	Durability 200 ⁴
Patients	236	787	45	324	583	100
Lesions	247	900	45	378	703	100
Lesion length (cm)	6.6 ± 3.9	10.0 ± 8.2	18.9 ± 9.1	7.4 ± 5.0	18.6 ± 9.3	24.2
Total occlusions	30%	38%	82.2%	28%	49%	N/A
In-stent restenosis	0%	15%	0%	0%	29%	0%
Study Outcomes						
Thrombosis/Occlusion	1.9% ^a	2.7% ^a	2.2% ^b	1.1% ^a	4.3% ^a	5.0% ^c
1-year Freedom from TLR^a	90.8%	89.3%	86.1%	96.7%	88.3%	68.2%
1-year Primary Patency^a	82.7% (PSVR < 2.0)	82.8% (PSVR < 2.0)	86.1% (PSVR < 2.0)	91.0% (PSVR < 2.4)	81.0% (PSVR < 2.4)	64.8% (PSVR < 2.4)

^a Kaplan Meier estimate at 12 months, ^b 12-month thrombosis rate, ^c 30-day thrombosis rate

Zilver PTX TLR and patency rates in complex lesions from Japan PMS compare favorably to published BMS results in complex lesions.

Thrombosis/occlusion rates in complex lesions appear similar for Zilver PTX and BMS.

1. Dake MD, et al. *Circ Cardiovasc Interv.* 2011;4:495-504.

2. Dake MD, et al. *J Endovasc Ther.* 2011;18:613-23.

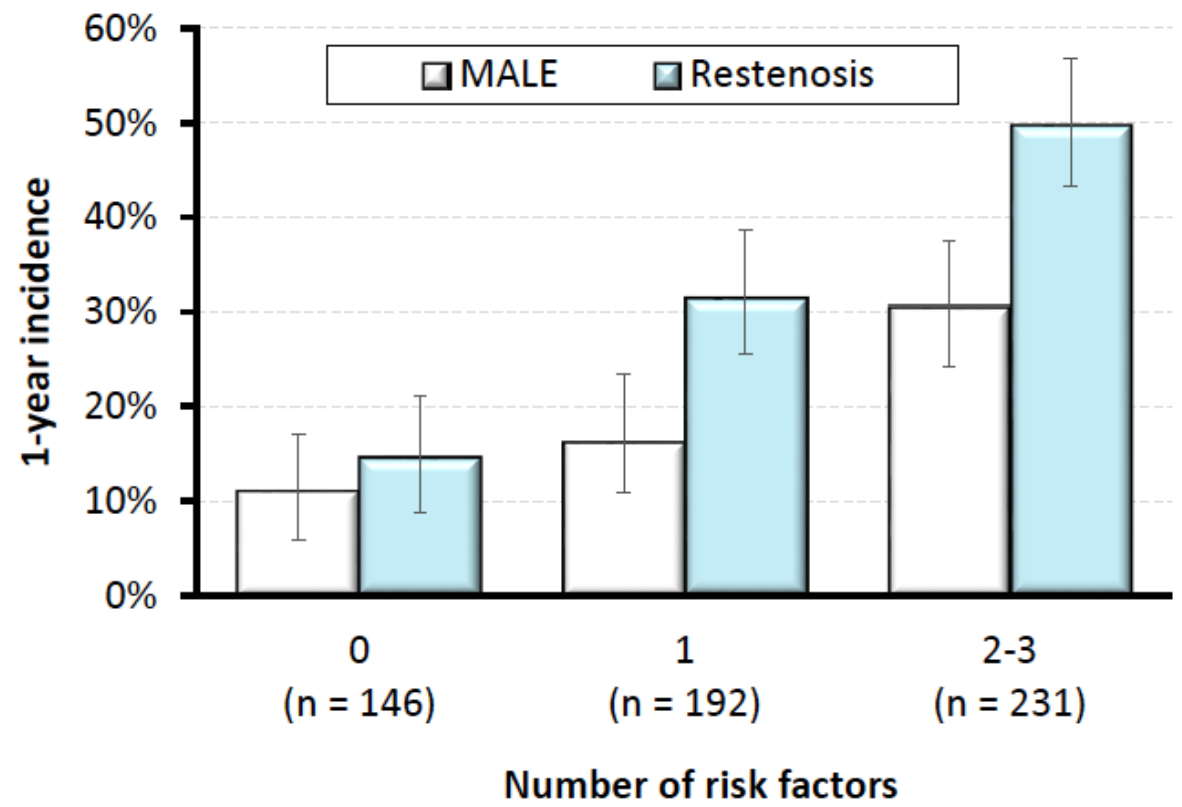
3. Bosiers M, et al. *J Cardiovasc Surg (Torino).* 2013;54:115-22.

4. Bosiers M, et al. *JVS.* 2011;54:1042-1050.



No. of Risk Factors & Restenosis/MALE Incidence

- Risk factors for restenosis**
- 1) lesion length ≥ 16 cm
 - 2) EEM area ≤ 27 mm²
 - 3) MSA ≤ 12 mm²



1-year restenosis rate was as low as 15% in cases with none of these risk factors, whereas it reached 51% in those with ≥ 2 risk factors

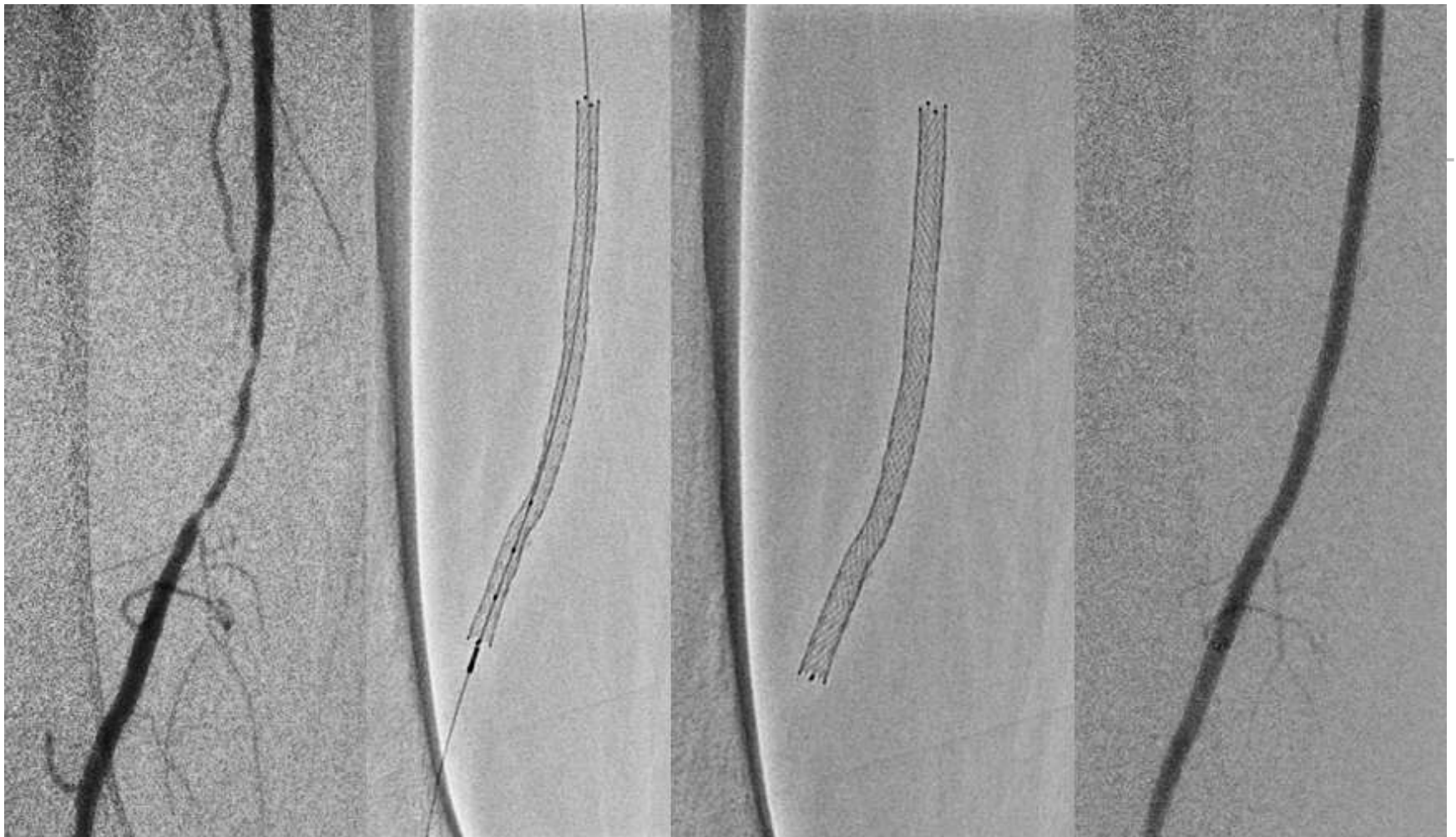
69 y.o male Rt. SFA

Rutherford 3

TASC II : A

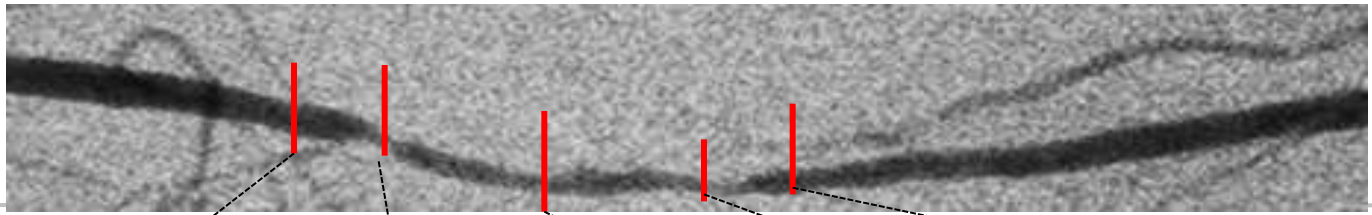
Prior CABG, HTN, DM, SMK



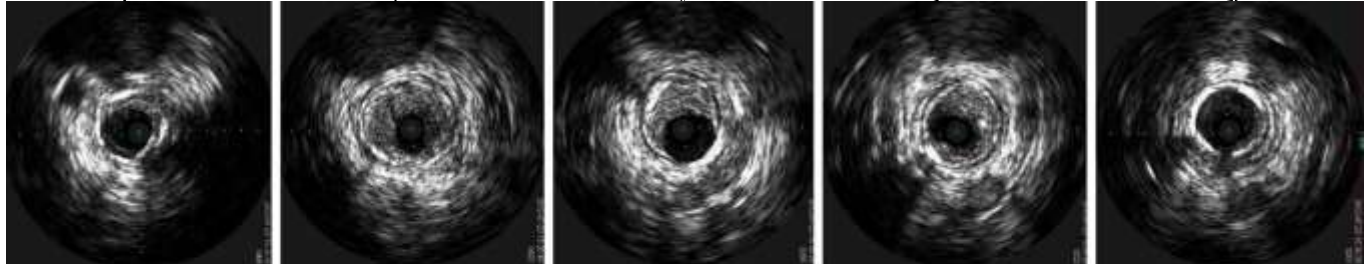


Pre balloon : Shiden 4.0/40mm
STENT : Zilver PTX 6.0/120mm
Post balloon : Senri 5.0

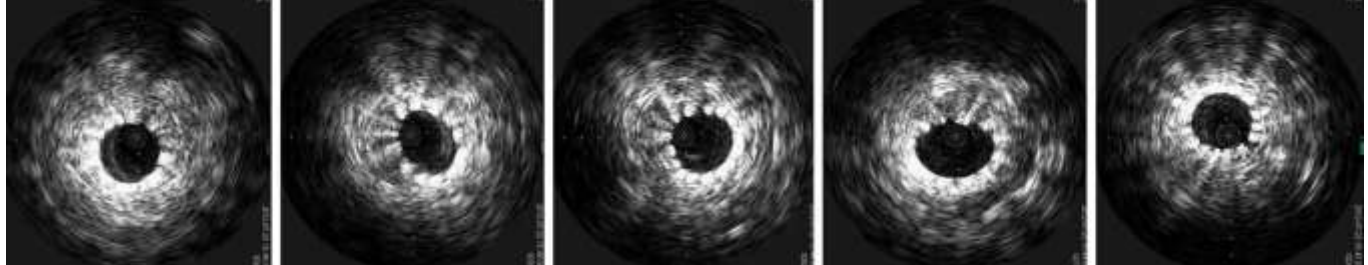
ANGIO



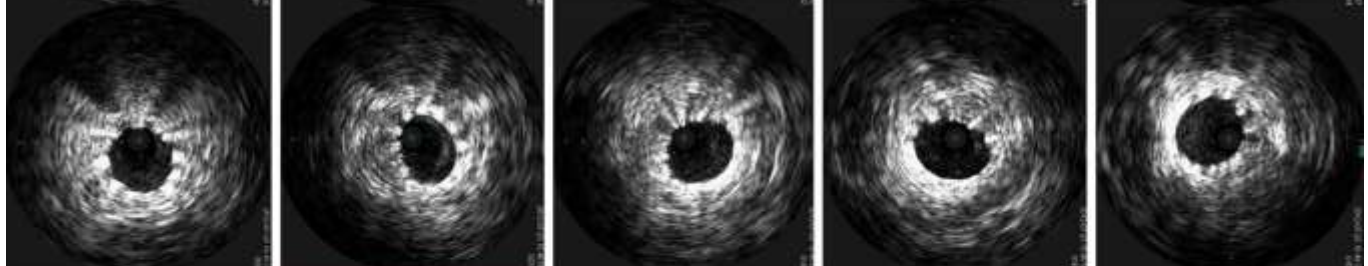
Pre STENT



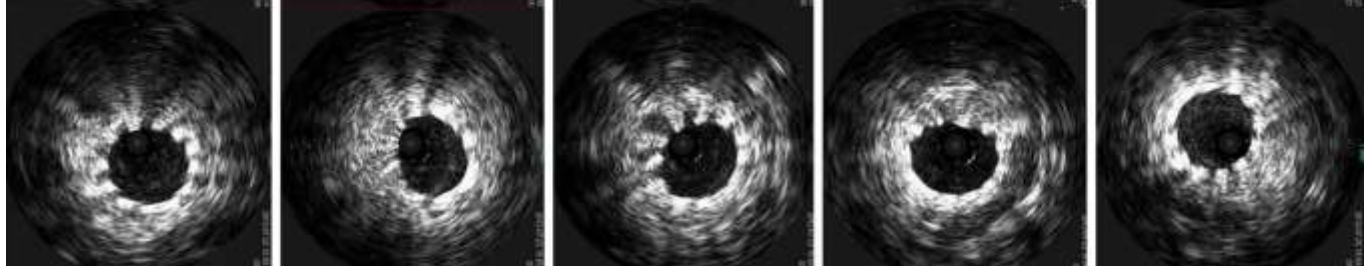
Post STENT



Post 8 atm

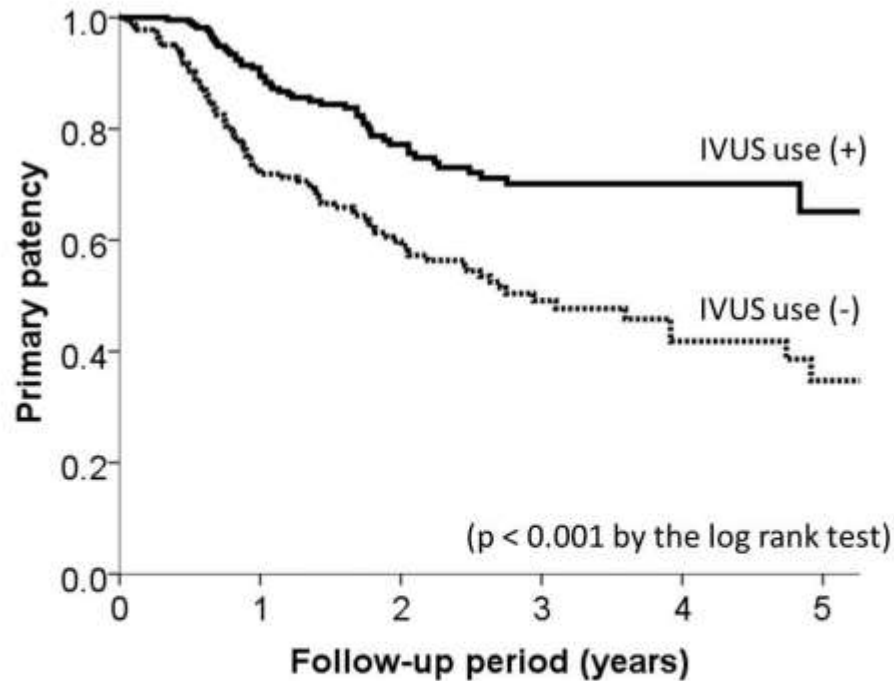


Post 16 atm



The Power of IVUS

Conclusion: IVUS use in femoro-popliteal stenting for TASC II class A to C lesions was associated with a higher rate of primary patency in PAD patients.



		0 yr	1 yr	2 yr	3 yr	4 yr	5 yr
IVUS use(-)	No. at risk	234	126	74	37	20	9
	Rate±SE	100±0%	72±3%	60±4%	49±4%	42±5%	35±6%
IVUS use(+)	No. at risk	234	173	96	58	34	13
	Rate±SE	100±0%	90±2%	77±3%	70±4%	70±4%	65±6%

Advantages of IVUS Guided Intervention

Pre-intervention

- 1) High probability to capture the true lumen
- 2) Identify proximal and distal reference segment landing zones and accurately select stent length
- 3) Accurately measure and lumen size to maximize stent dimensions
- 4) Determine when debulking should be considered

Post-intervention

- 1) Maximize stent CSA relative to reference
- 2) Ensure full lesion coverage
- 3) Recognize, diagnosis and treat complications

80s male, CLI without dialysis



Infective gangrene on 4th toe

Risk factors

Type II DM, Hypertension

Hyperlipidemia

Previous History of

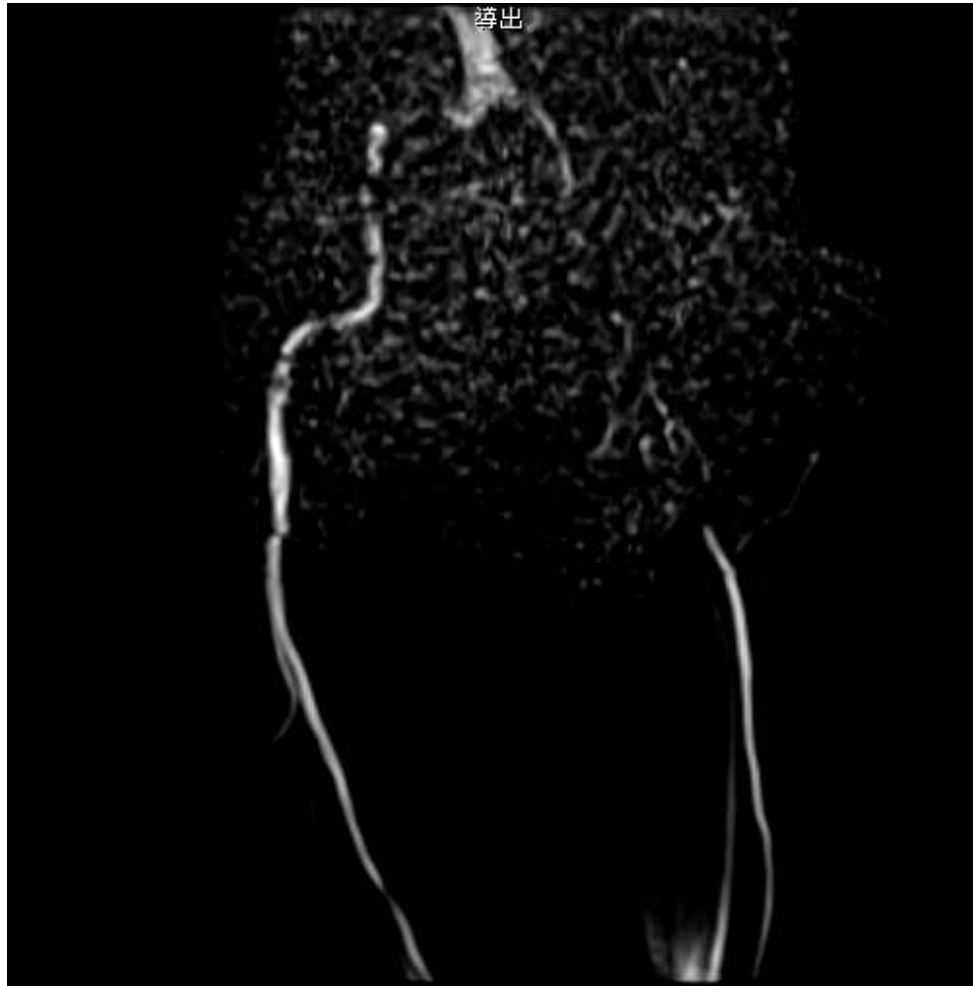
Post CABG

Post CVA

Severe AS



Lower extremities MRA



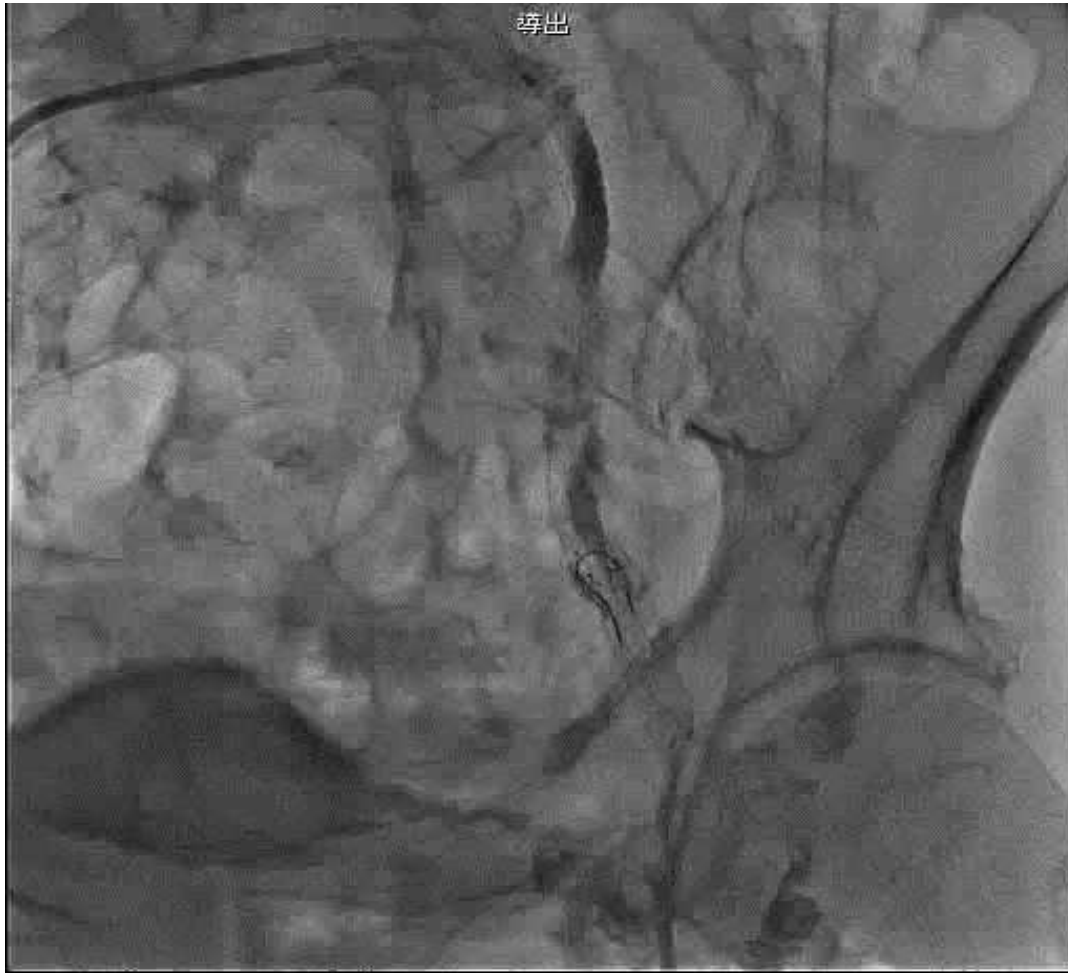
Lt CIA Occusion



Lt SFA Occusion

ABI: Rt 0.72, Lt not measure
SPP: RT 48/32. Lt 15/7

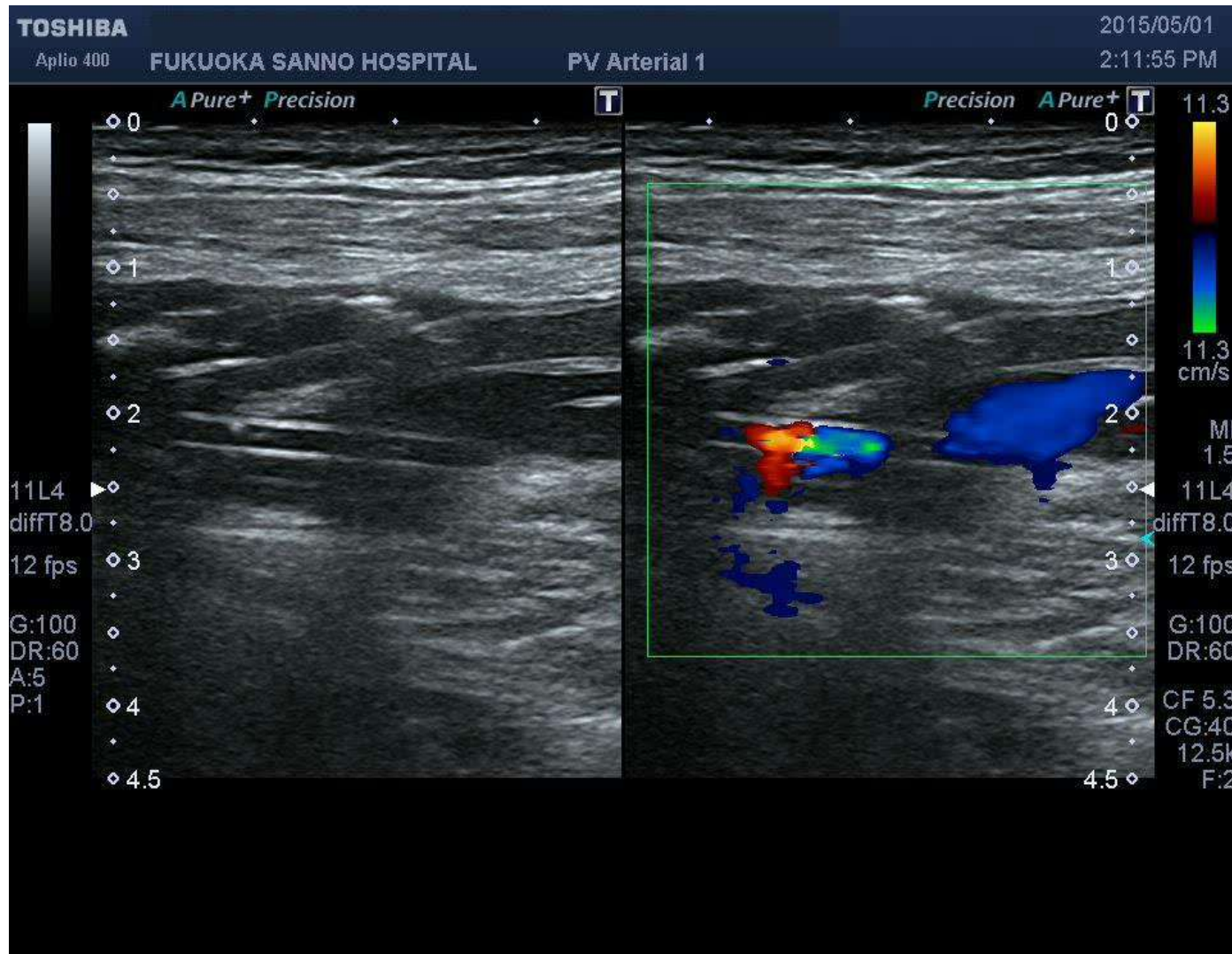
Final Ango (1st session)



0.018 Treasure GW manipulation with 4F CXI catheter through novel side-grooved sheath by surface echo guidance

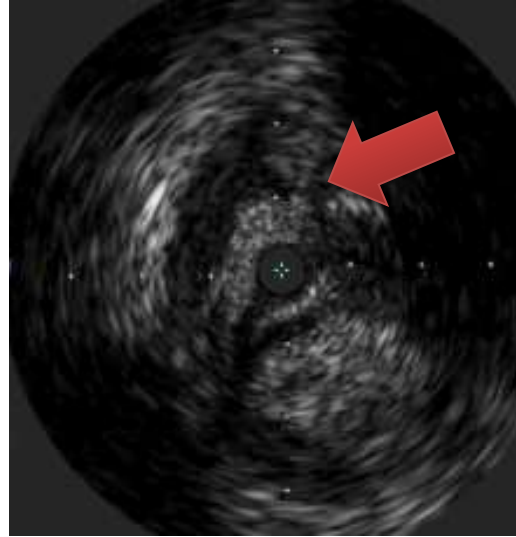


Echo guide (SFA-DFA Bif)

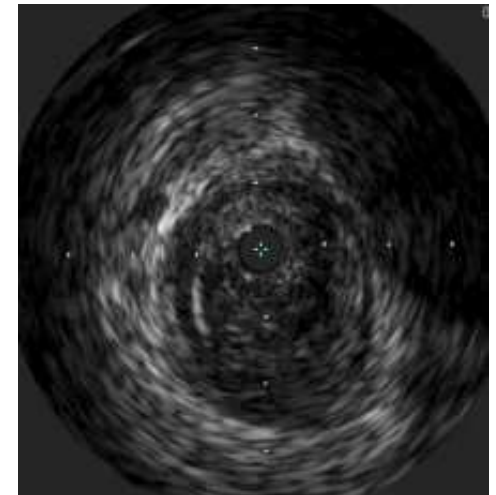
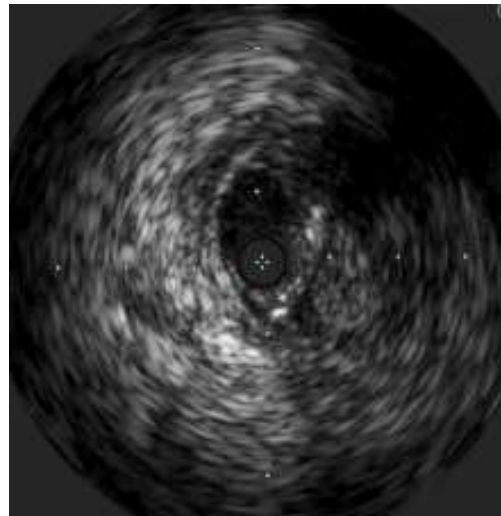
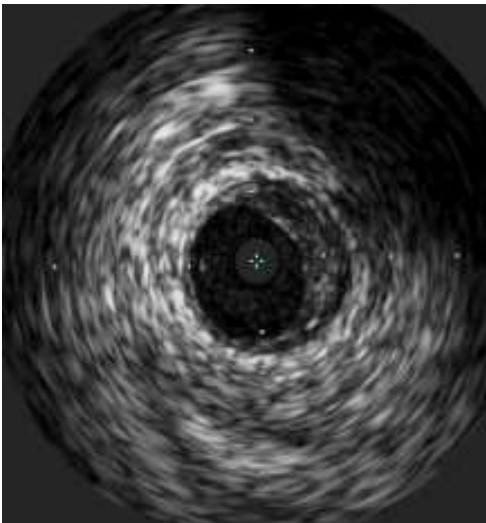


1st IVUS after BA

High probability to capture the true lumen

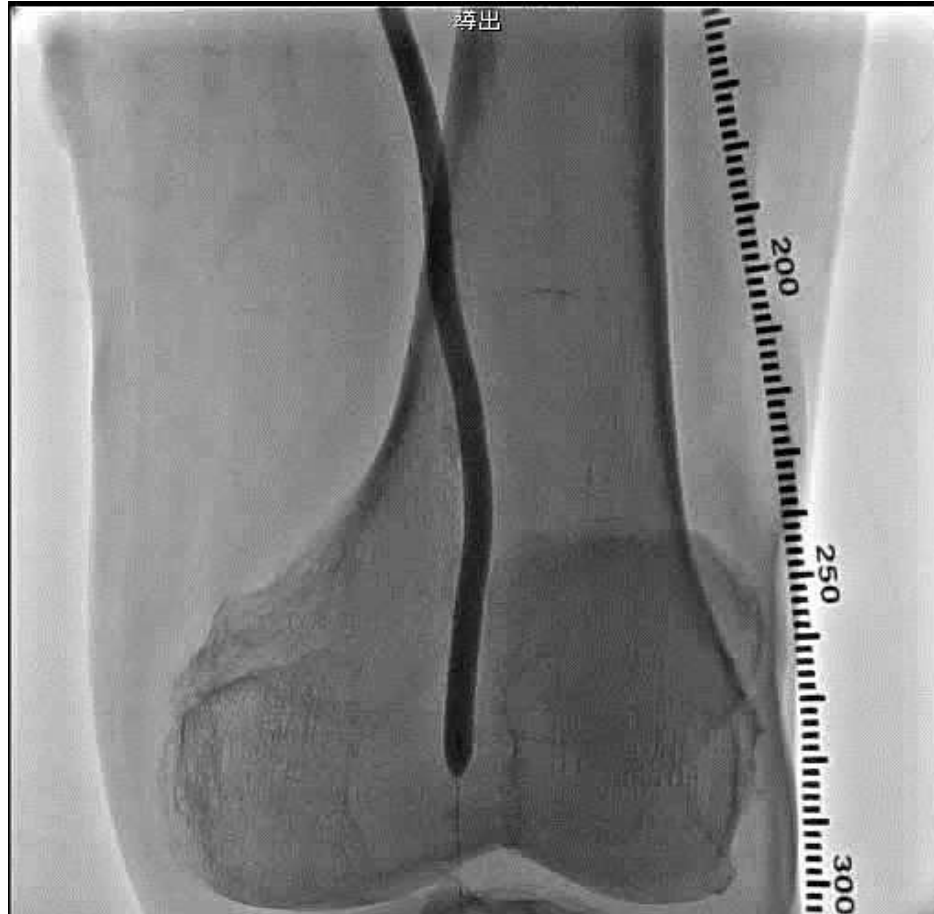


Subintimal Space



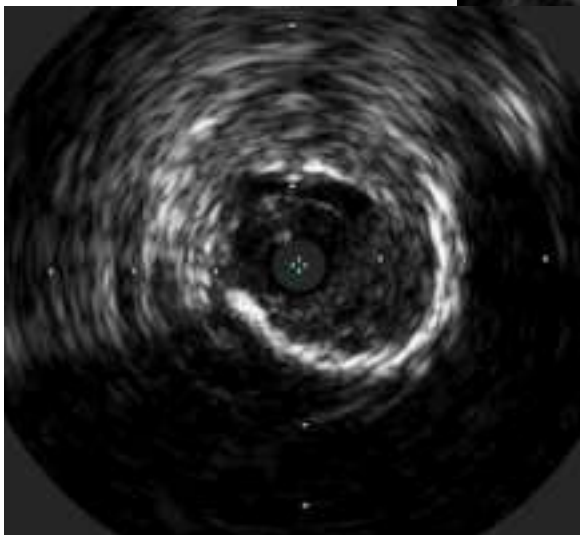
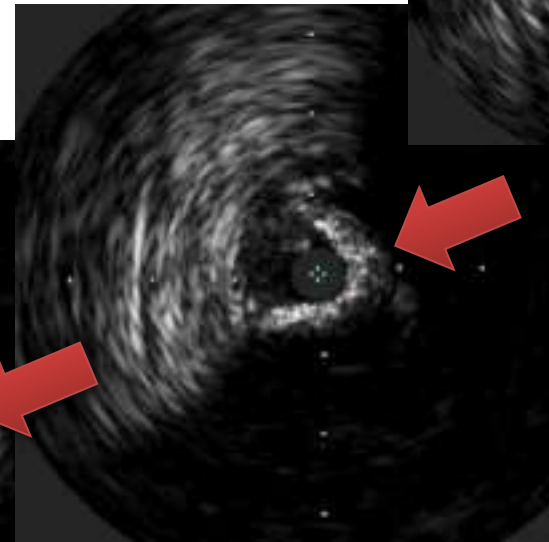
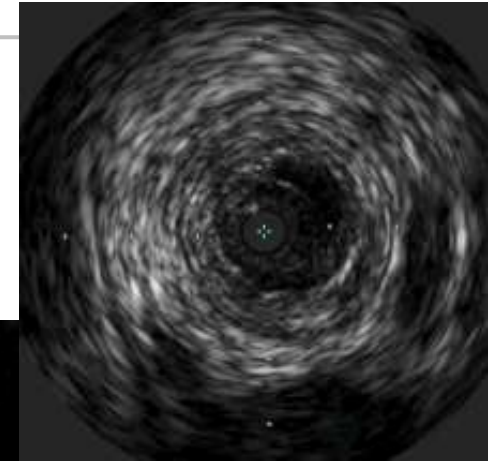
SFA CTO BA 2nd

(Ultraverse : 4.0 × 220mm)



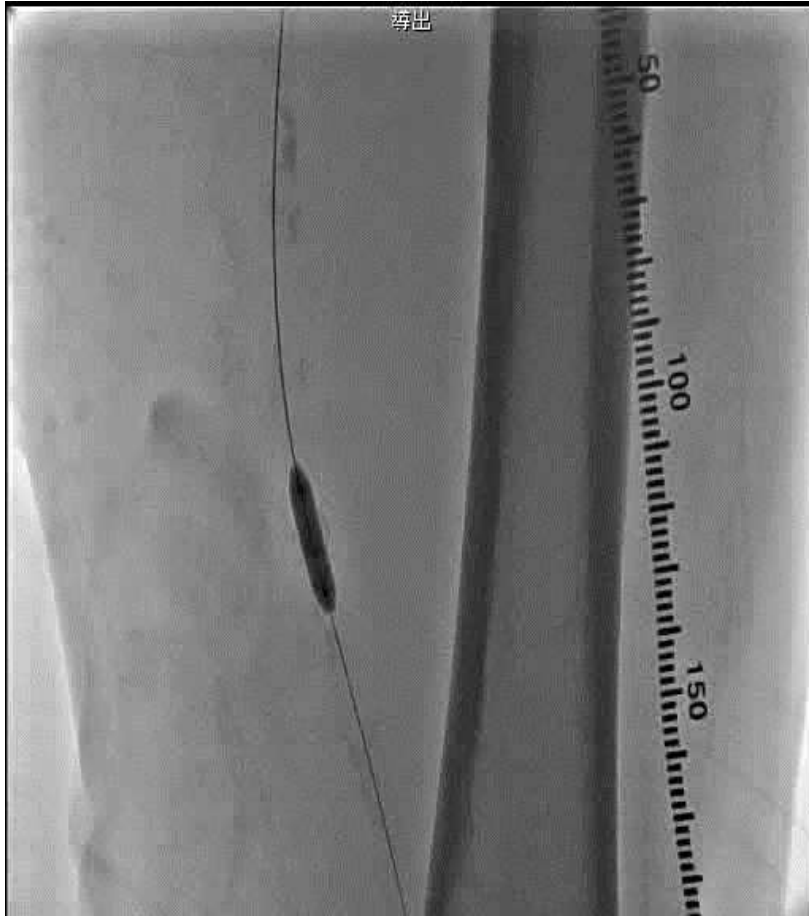
2nd IVUS after BA

Determine when lesion preparation should be considered



270 degree
severe superficial
calcification

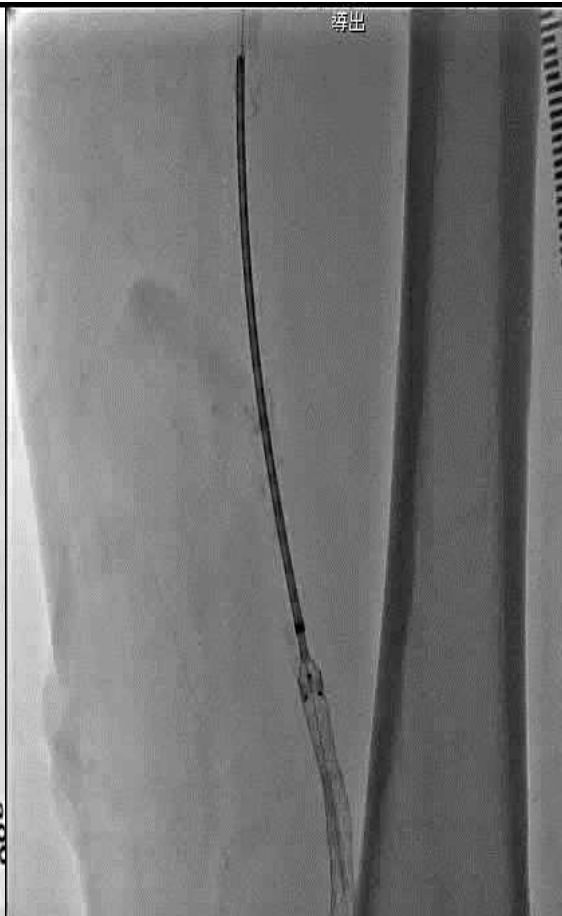
Lesion Preparation (Cutting BA 4.0 × 15mm)



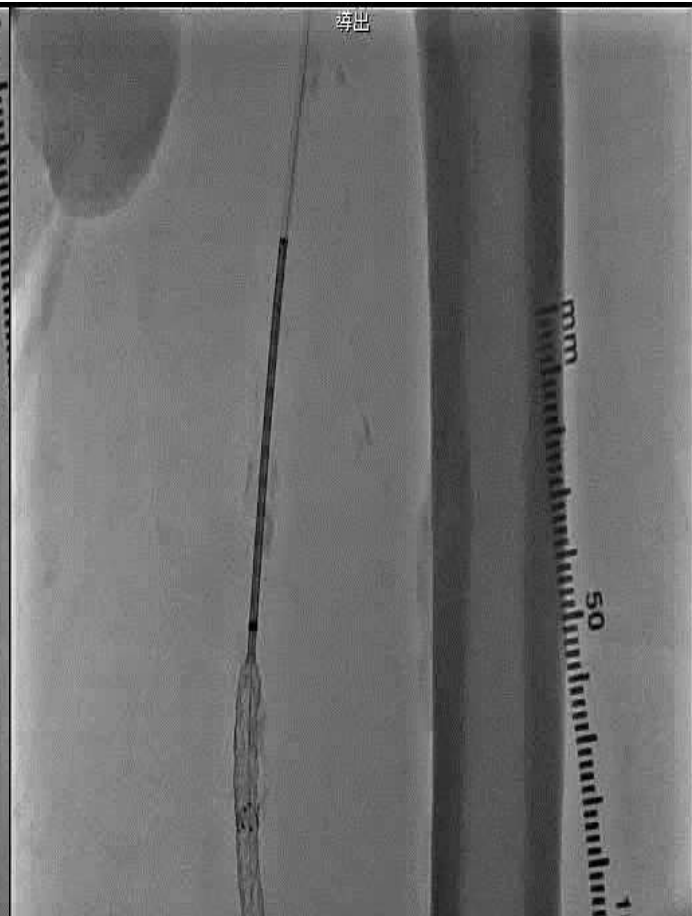
DES Implantation



Zilver PTX
(6.0 × 100mm)

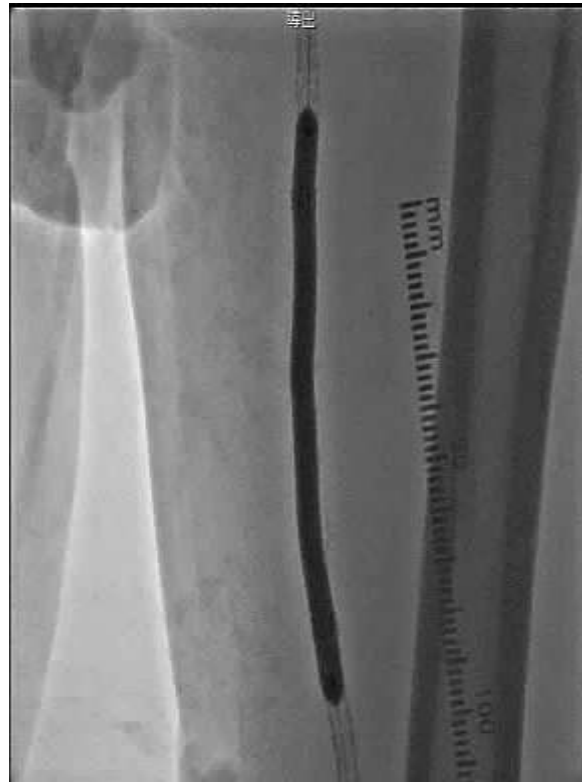
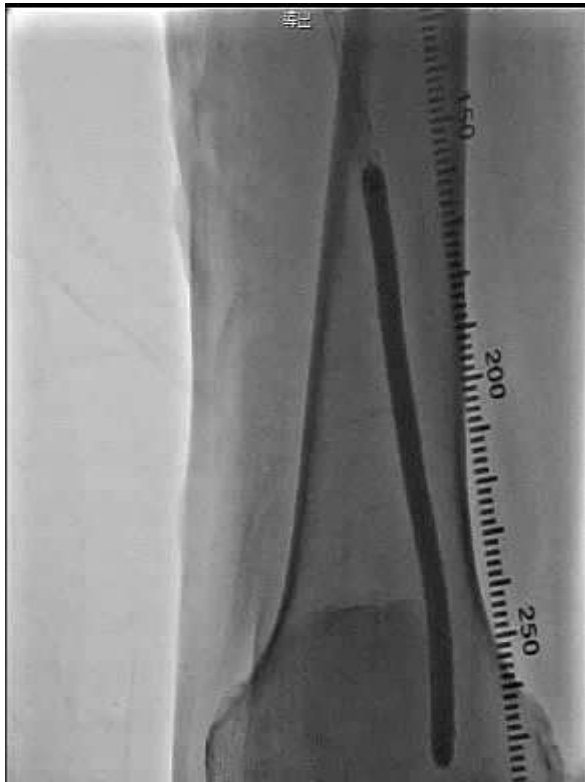


Zilver PTX
(6.0 × 100mm)

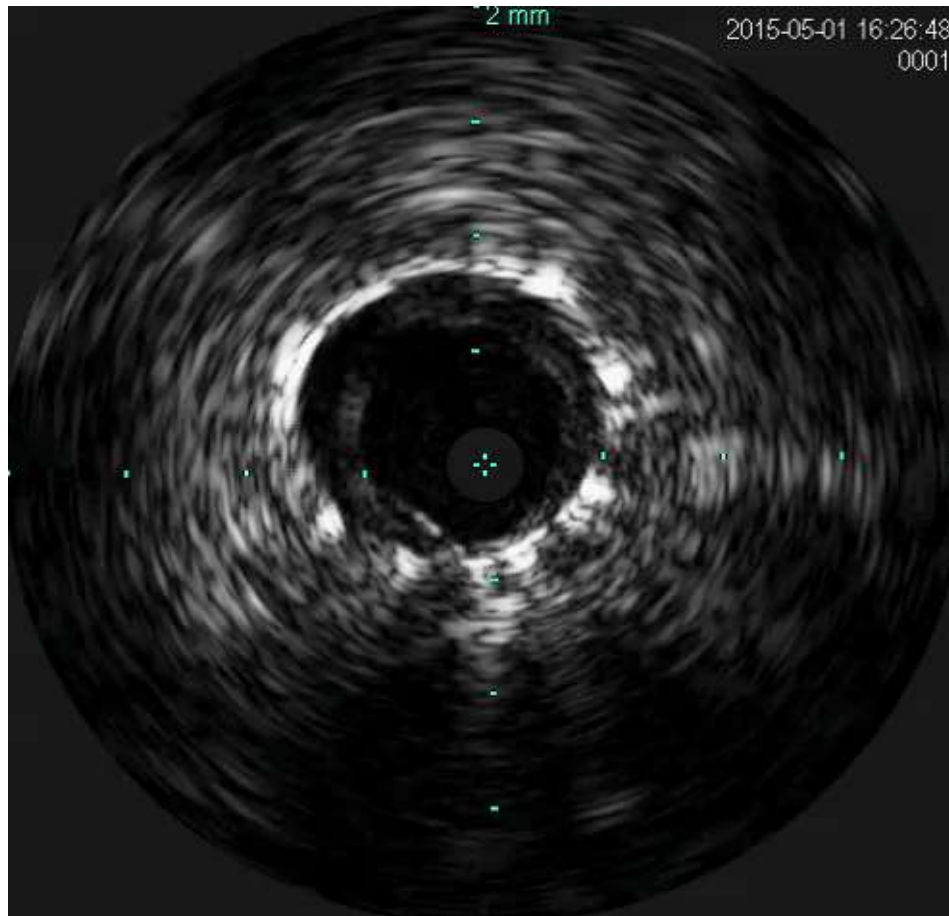


Zilver PTX
(7.0 × 100mm)

Post Stent dilatation with high-pressure (18atm) BA dilatation (5.0 × 100mm)



IVUS (Post BA)



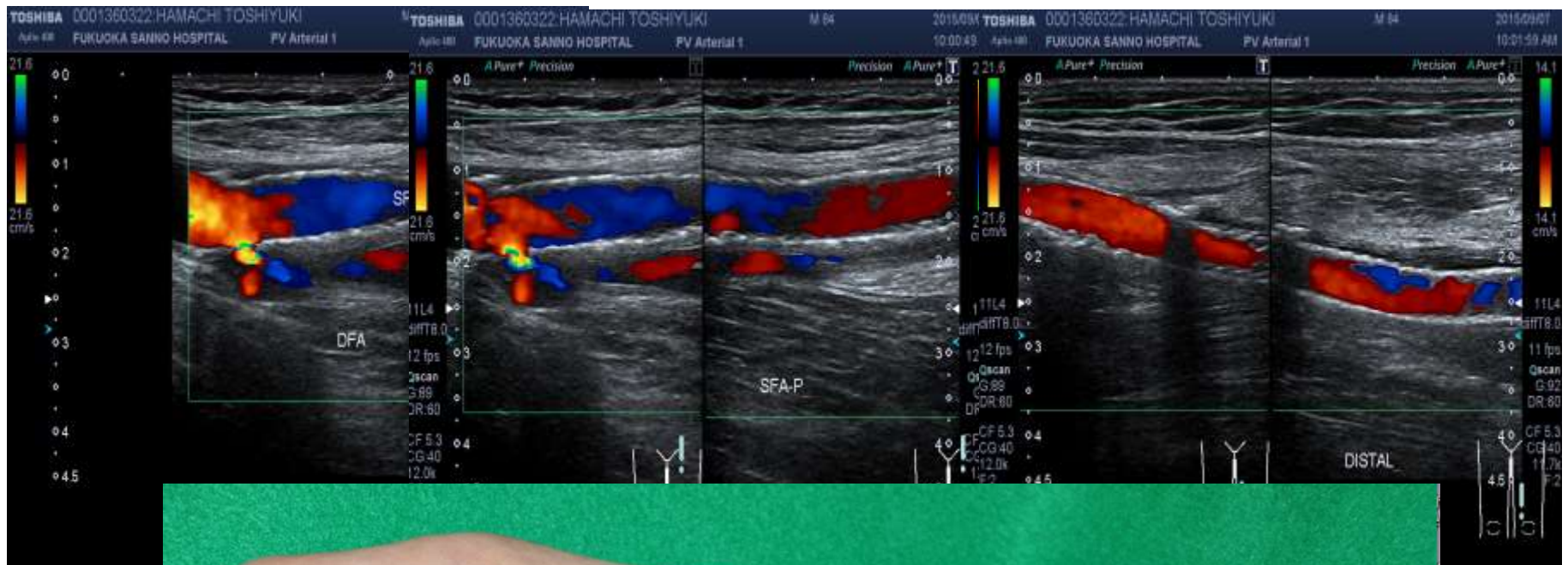
Final Angio



After minor amputation, wound was completely healed



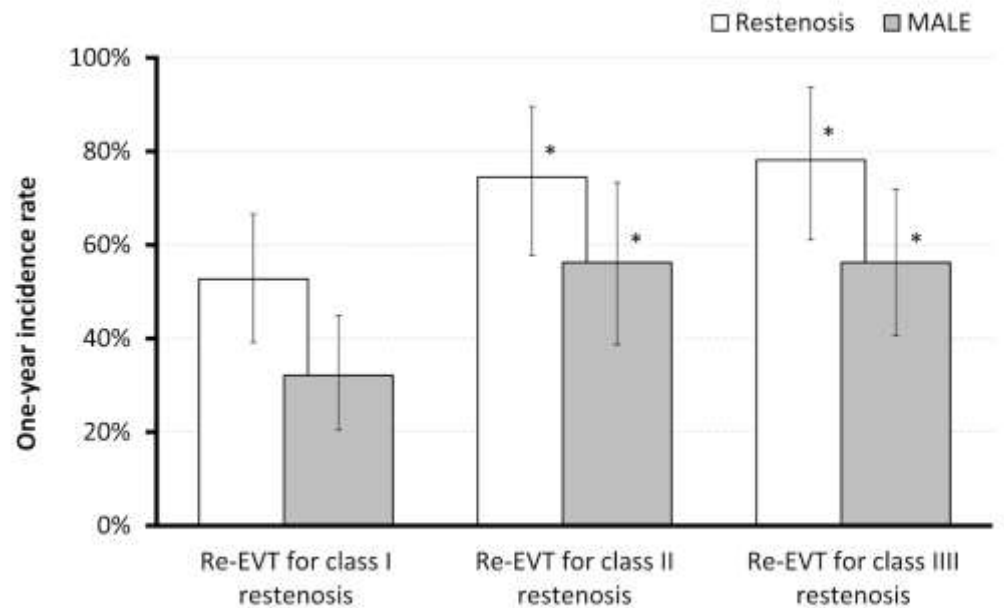
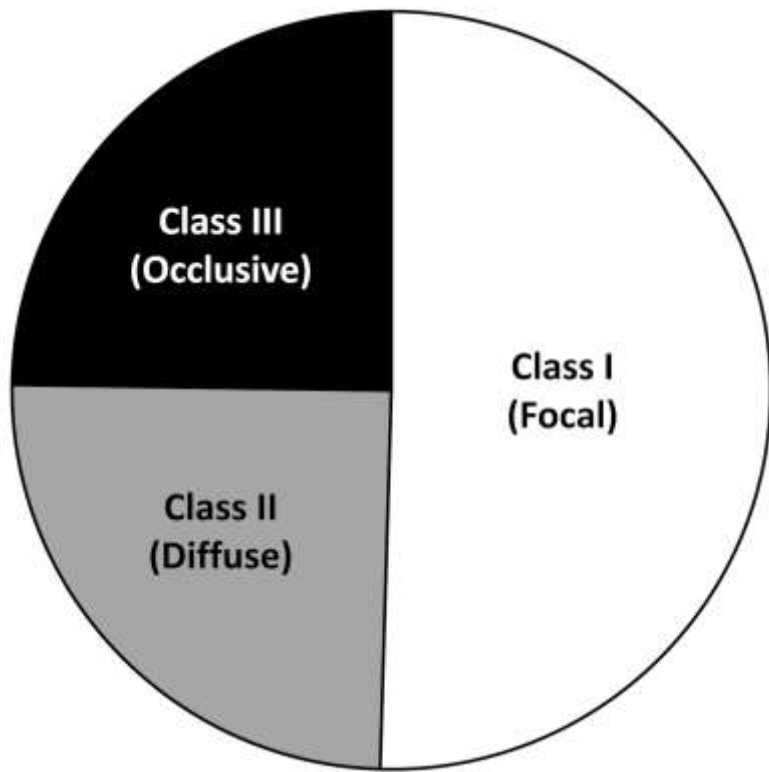
18 months later (No restenosis)



Leave the *right thing* behind in SFA TASC-C/D lesions

- Stent Integrity
- Safety (no increased stent thrombosis)
- Anti-restenosis effect
- *Pattern of restenosis*

The characteristics of in-stent restenosis after drug eluting stent implantation in femoropopliteal lesions and 1-year prognosis after repeat endovascular therapy for these lesions”



Leave the *right thing* behind in SFA TASC-C/D lesions

- Stent Integrity

Very low

- Safety

No increased stent thrombosis

- Anti-restenosis effect

Excellent than BMS in simple & complex lesion

- Pattern of restenosis

Benign



JET

Japan Endovascular Treatment Conference 2018

2018

■Date

2/23 → 25
2018 FRI SUN

■Venue

Knowledge Capital Congress Convention Center,
Grand Front Osaka

■President

Yoshiaki Yokoi

MD, FJCC, FSCAL, FACC
Departments of Cardiology, Kishiwada Tokushukai Hospital