How to Maximize DCB Outcomes and Lutonix DCB BTK Registry

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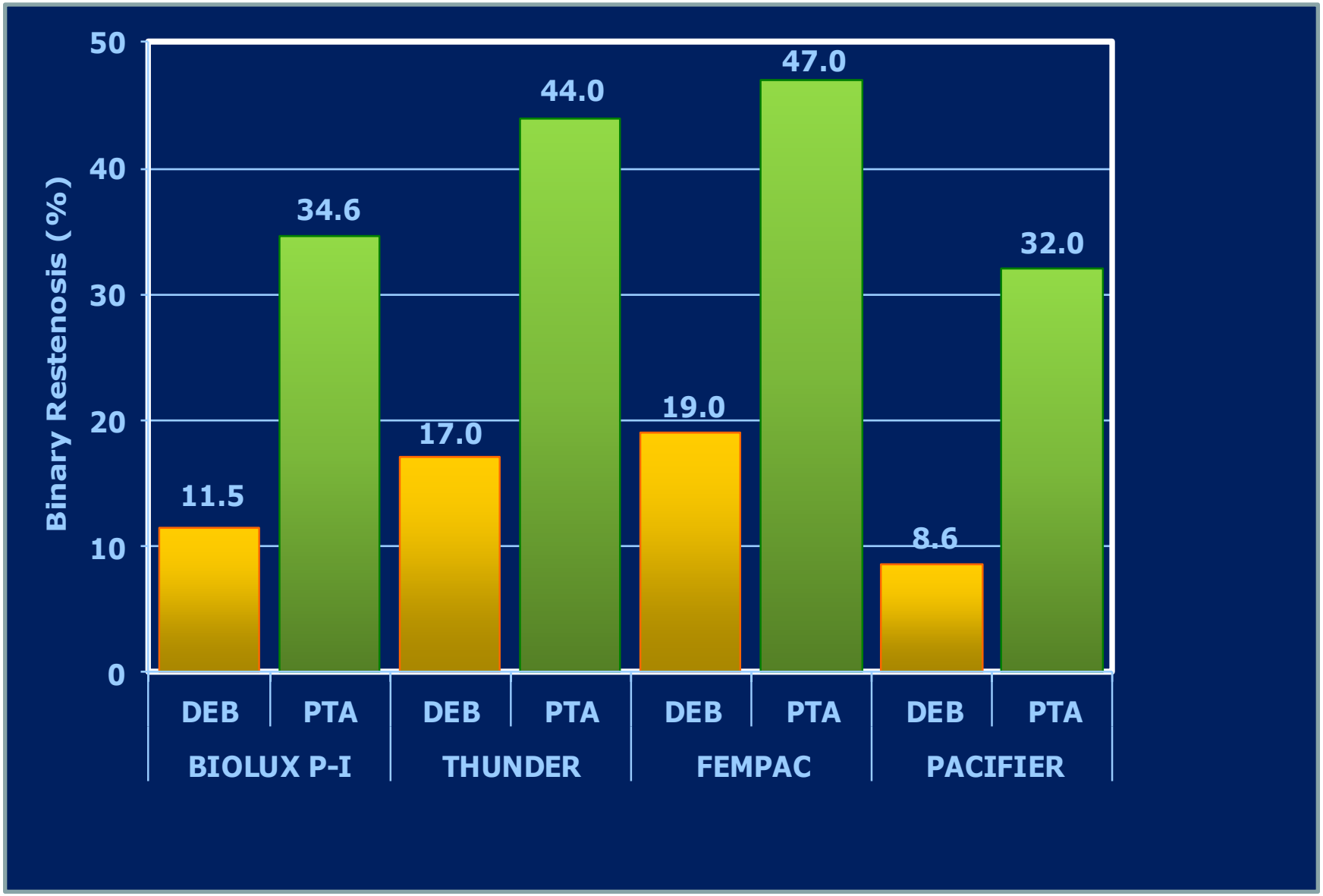
Lesion preparation before DCB ?

Drug Eluting (Coated) Balloon

6 Months Binary Restenosis



Metanalysis DCB vs. POBA

euro PCR 2012

Secondary outcomes

A. Binary restenosis

Study or Subgroup	PCB Events	PCB Total	UCB Events	UCB Total	Weight	Odds Ratio M-H, Random, 95% CI
THUNDER	7	41	21	48	38.8%	0.26 [0.10, 0.71]
FemPac	10	31	22	34	36.1%	0.26 [0.09, 0.73]
PACIFIER	4	40	12	39	25.1%	0.25 [0.07, 0.86]
Total (95% CI)		**112**		**121**	**100.0%**	**0.26 [0.14, 0.48]**
Total events	21		55			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.01$, df = 2 (P = 1.00); $I^2 = 0\%$
Test for overall effect: Z = 4.27 (P < 0.0001)
Heterogeneity$_{(exact)}$: $Chi^2 = 0.004$, df = 2 (P = 0.99)
Test for overall effect$_{(exact)}$: P < 0.00001

Odds Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
PCB Better UCB Better

B. Late lumen loss

Study or Subgroup	PCB Mean	PCB SD	PCB Total	UCB Mean	UCB SD	UCB Total	Weight	Mean Difference IV, Random, 95% CI
THUNDER	0.4	1.2	41	1.7	1.8	48	19.6%	-1.30 [-1.93, -0.67]
FemPac	0.5	1.1	31	1	1.1	34	25.2%	-0.50 [-1.04, 0.04]
LEVANT I	0.4	1.1	39	1.09	1	35	29.7%	-0.69 [-1.17, -0.21]
PACIFIER	-0.05	1.1	40	0.61	1.3	39	25.5%	-0.66 [-1.19, -0.13]
Total (95% CI)			**151**			**156**	**100.0%**	**-0.75 [-1.06, -0.45]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 3.95$, df = 3 (P = 0.27); $I^2 = 24\%$
Test for overall effect: Z = 4.78 (P < 0.00001)

Mean Difference IV, Random, 95% CI
-2 -1 0 1 2
PCB Better UCB Better

C. Death

Study or Subgroup	PCB Events	PCB Total	UCB Events	UCB Total	Weight	Odds Ratio M-H, Random, 95% CI
THUNDER	2	48	1	54	19.4%	2.30 [0.20, 26.25]
FemPac	6	45	3	42	46.6%	2.00 [0.47, 8.57]
LEVANT I	1	48	3	49	21.5%	0.33 [0.03, 3.25]
PACIFIER	0	41	2	41	12.5%	0.19 [0.01, 4.09]
Total (95% CI)		**182**		**186**	**100.0%**	**1.04 [0.34, 3.18]**
Total events	9		9			

Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 3.37$, df = 3 (P = 0.34); $I^2 = 11\%$
Test for overall effect: Z = 0.06 (P = 0.95)
Heterogeneity$_{(exact)}$: $Chi^2 = 4.37$, df = 3 (P = 0.22)
Test for overall effect$_{(exact)}$: P = 0.98

Odds Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
PCB Better UCB Better

Absolute risk reduction of binary restenosis with PCB therapy = 26.7% [15.2%, 38.1%]

What drives restenosis development after DCB angioplasty?

- **Early and late recoil**
- **Insufficient drug penetration into the adventitia**
  - Calcium
  - Plaque burden
  - Eccentric plaque
- **Natural course of the disease**

DCB in Calcified Lesions

THUNDER

Subgroup Results

Group n=129	Control [mm]	Paclitaxel on balloon [mm]	Paclitaxel in contrast agent [mm]	Control minus paclitaxel on balloon [mm]
Total	1.7 ± 1.8	0.4 ± 1.2	2.2 ± 1.6	**1.3**

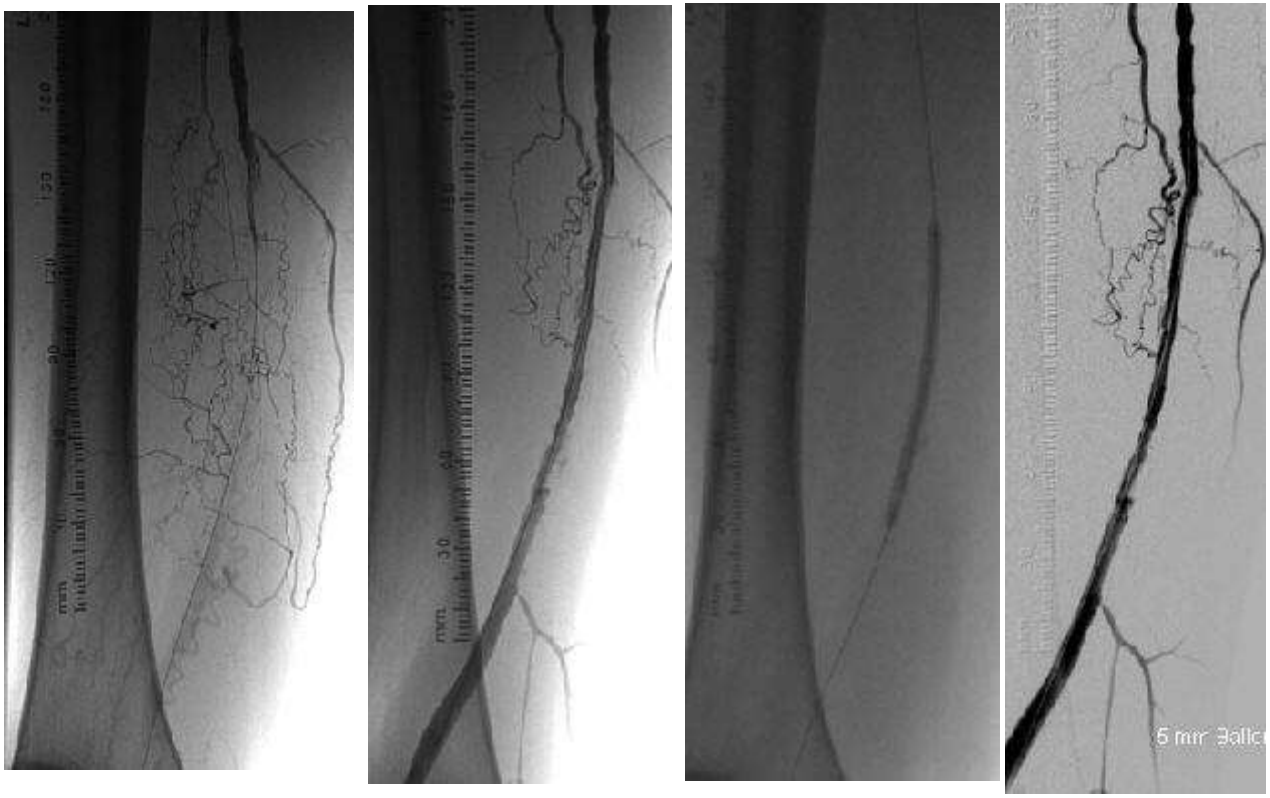
Late lumen loss (mm of diameter) 6 month post PTA

DCB: Large benefit in all subgroups

Subgroup **n control/ n DCB**		LLL (mm) Control minus DCB	LLL (%) DCB/ Control
Diabetes	**21/14**	**1.2**	33
Restenotic lesion	**14/12**	**1.5**	21
Calcification	**18/16**	1.2	**25**
> 10 cm	**5 / 8**	**1.3**	50
Pop. involvement	**13/11**	**1.5**	29

Tepe, Zeller, Albrecht et al. NEJM 2008

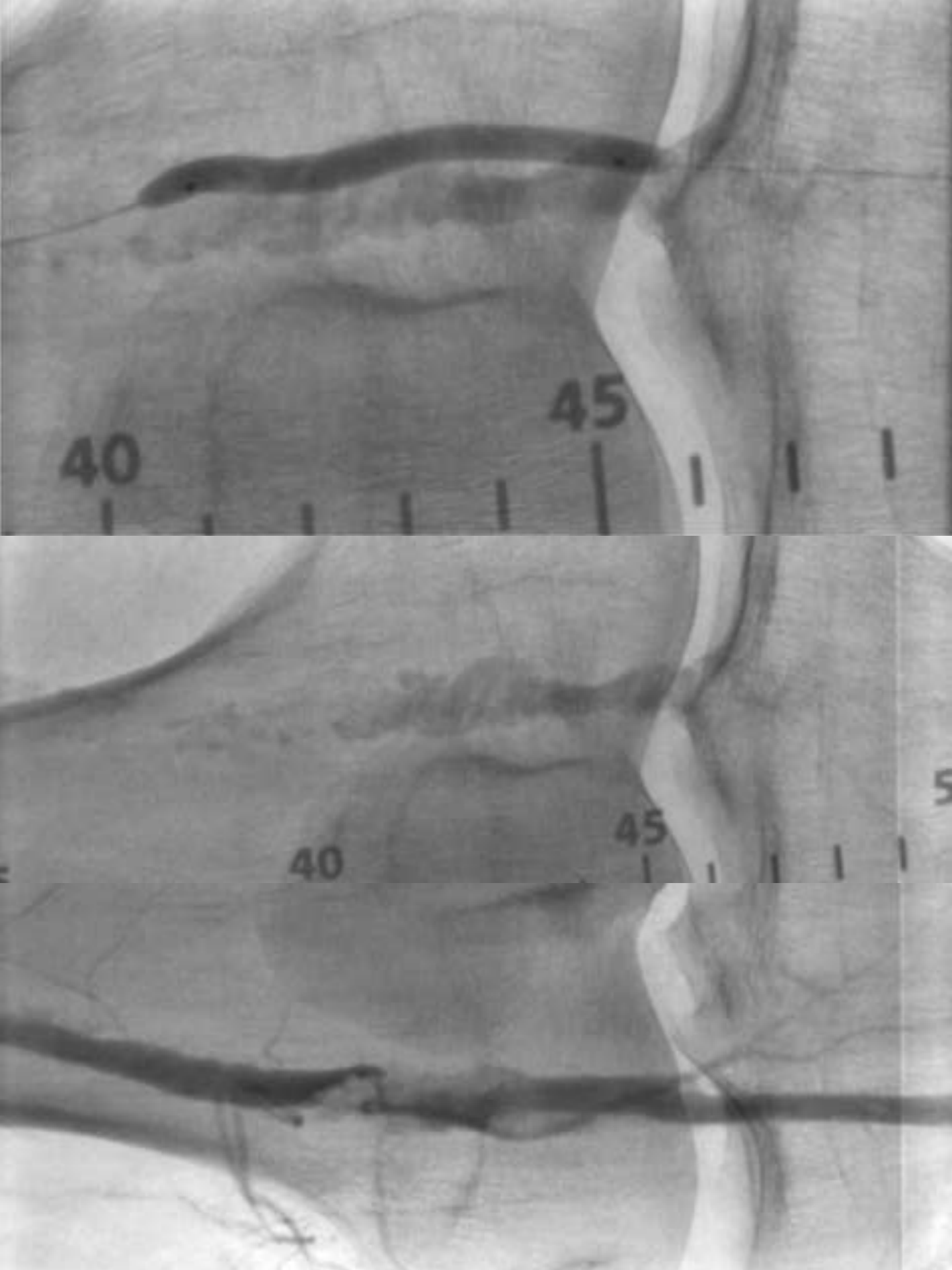
Sample case of restenosis following DCB administration



- CTO with significant calcium burden
- Efforts were made to avoid bail-out stenting, despite sub-optimal acute results

- Further progression at later time points, especially around calcified segment

Angiograms Courtesy of Gunnar Tepe, MD

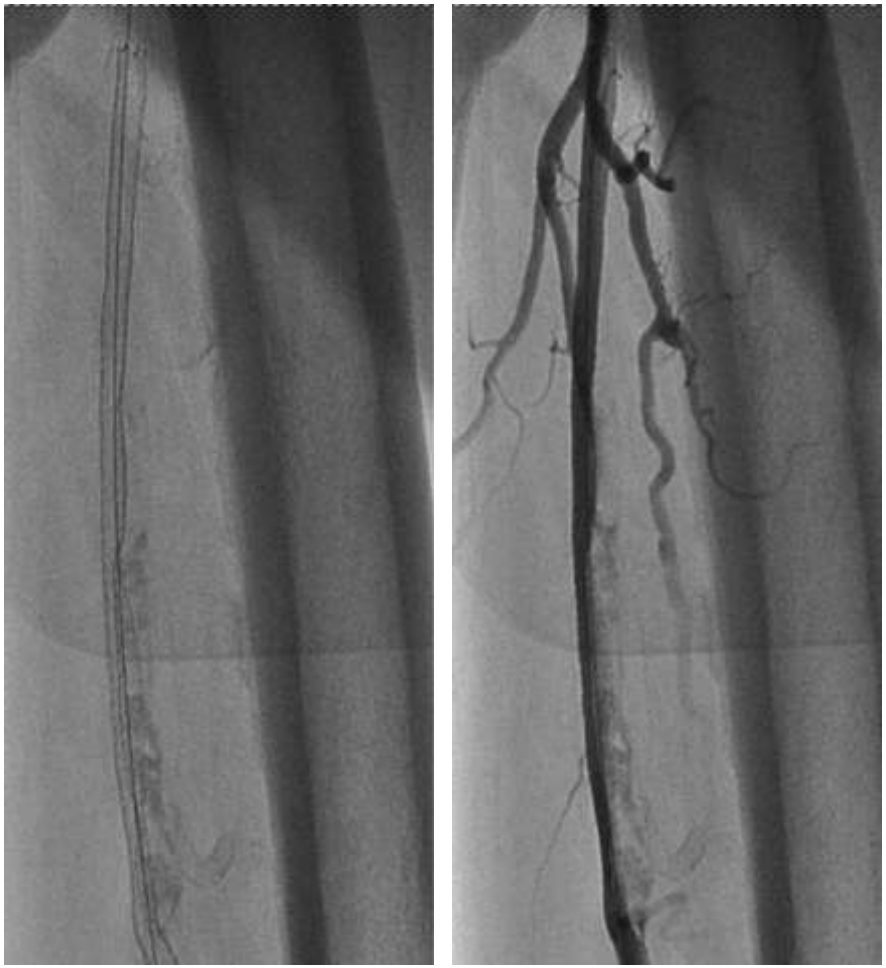

40
45
40
45

SFA-Stent Deployment Evaluation
Stent Compression - Leipzig Data

Angio AP projection

% MLD 15%

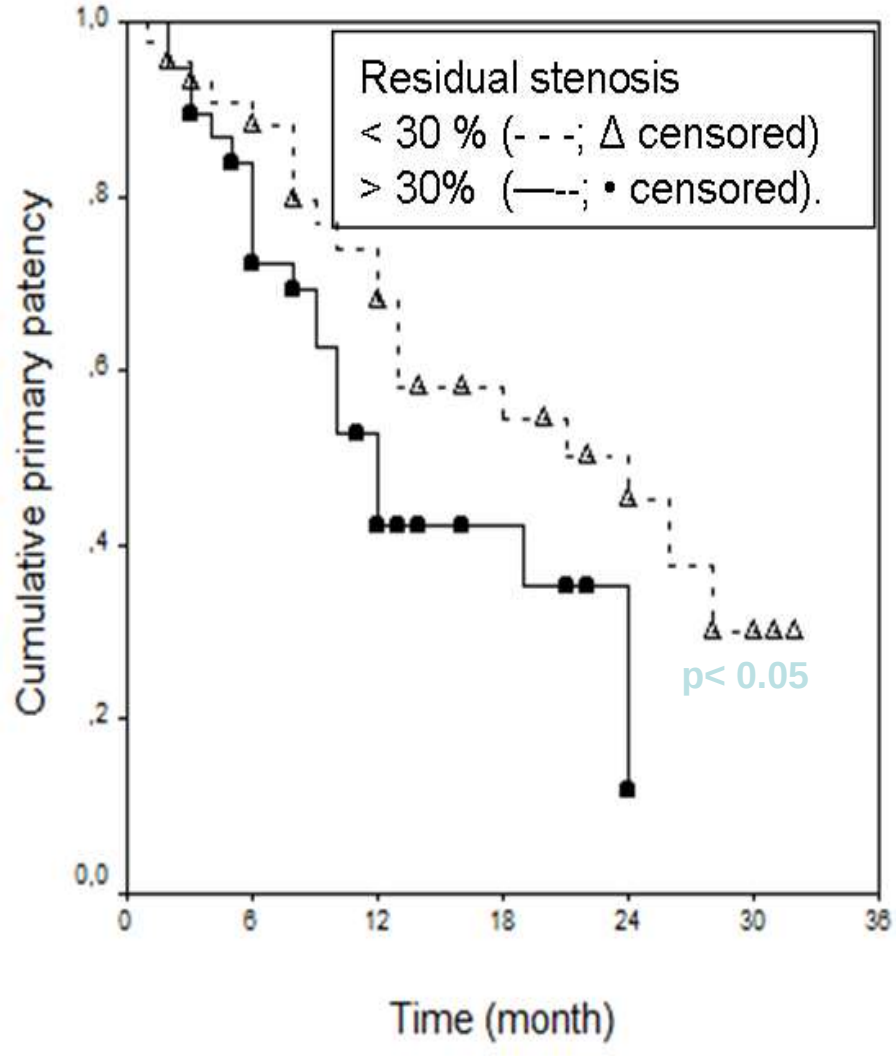
Angio LAO projection



% MLD 42%

Calcified Lesions

Impaired Primary Patency due to Residual Stenosis



Calcification as a barrier ?

DCB in calcified SFA Lesions

- Lack of standardized assessment and quantification methods
- Difficult to detect (needs proper imaging and / or «empiric» assessment via pre-dilatation)
- Frequently observed in long lesions and occlusions as a results of the natural course of disease chronicization
- Diffuse calcification frequently observed in elderly patients, diabetes and chronic renal failure
- Severly calcified lesions constitutes a typical exclusion criterion in most Trials

- Generate false negative ABI
- "Incompressibility", lesion resistance, recoil, dissections, embolism, ...
- Cause of stent malapposition and sub optimal expansion
- Risk factor for Stent fractures

Typical treatment modalities

1. Endovascular:
   - Optimal lesion preparation
     - Aggressive pre-dilat. or
     - Scoring balloon or
     - Debulking
   - Elective Stenting
2. Surgical

IS THERE A ROLE FOR DEB IN CALCIFIED ARTERIES ?

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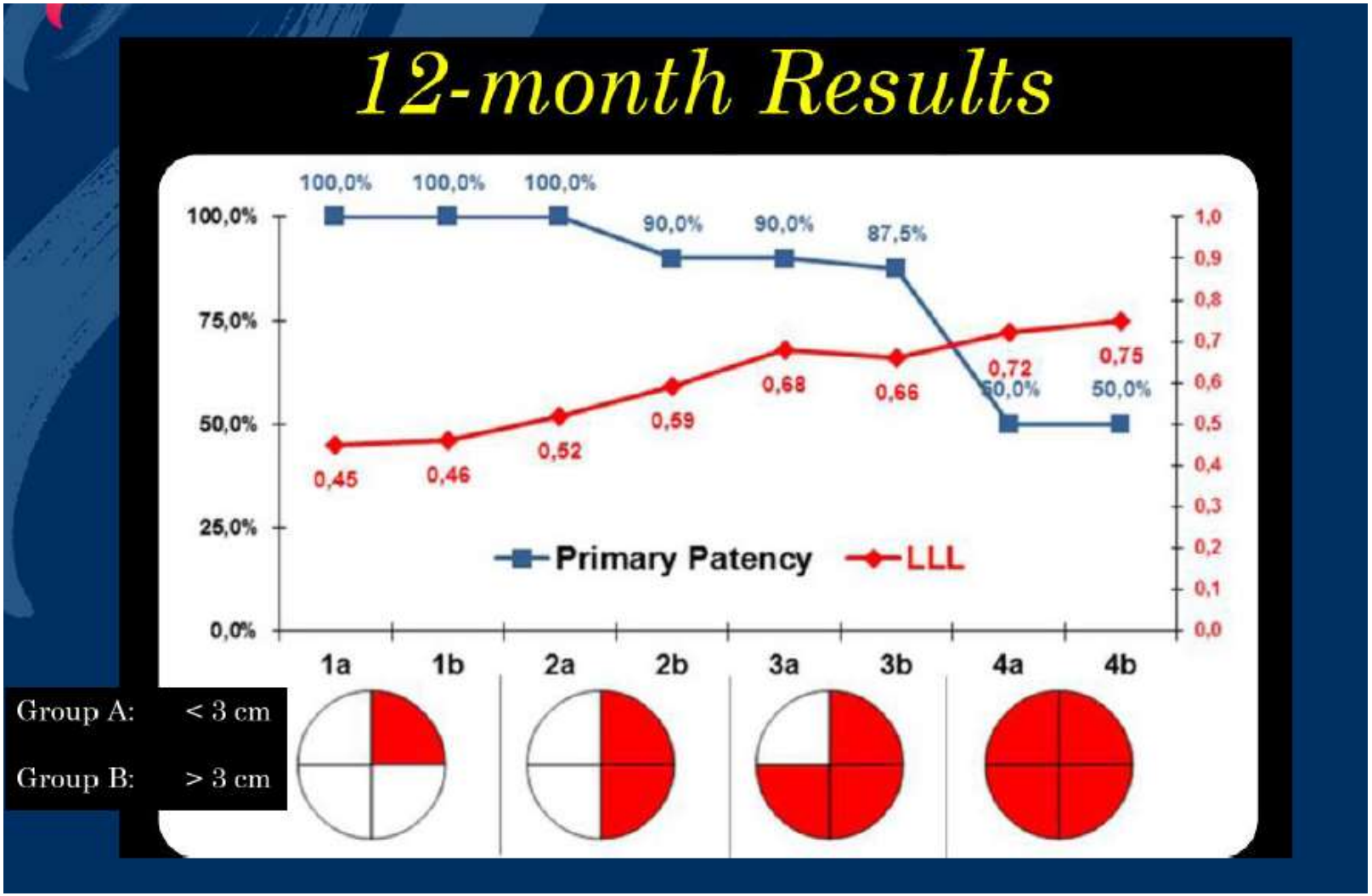
SAPIENZA
UNIVERSITÀ DI ROMA

DCB Use in Calcified Lesions



CT-Angiography Circumferential Distribution

CONCLUSION: DCB and Calcium

- **Calcium is a natural biological barrier for DCB Technology**
- **Worst outcome of DCB efficacy in complete circumferentially calcified lesions**
- **No Impact of occlusion type on DCB efficacy**
- **Effects of debulkng prior DCB are unclear so far**

DCB vs. Existing Modalities for SFA/Pop Interventions

Supera works well in the challenging clinical scenarios of calcium, acute recoil, and long lesions.

	DCB		Supera 	
Severe Calcification	–	Excluded from and/or low rates of in trials[1,2]; calcium represents a barrier to optimal drug absorption.[3]	+	5% TLR* in Severe Calcium at 1 year in SUPERB[4]
Acute Recoil or Dissections	–	Stent/Implant needed to treat. (Flow-limiting dissections can occur up to 40% of time[6])	+	>4x the compression resistance of SNS[5]
Long Lesions	–	Data not yet available in US	+	High freedom from restenosis is consistent across all lesion lengths in SUPERB[4]

1 Lutonix FDA Executive Summary
2 IN.PACT Admiral Summary of Safety and Effectiveness Data
3 Fanelli, F. Calcium Burden Assessment and Impact on Drug-Eluting Balloons in Peripheral Arterial Disease. Cardiovasc Intervent Radiol. 2014 May 9.
4 SUPERB 3 Year Garcia VIVA 2014
5 Data on file at Abbott Vascular.
6 Granada, J. Current Landscape, Opportunities and Challenges for DCB Technologies. TCT 2013.

DCB image courtesy of http://www.medgadget.com/

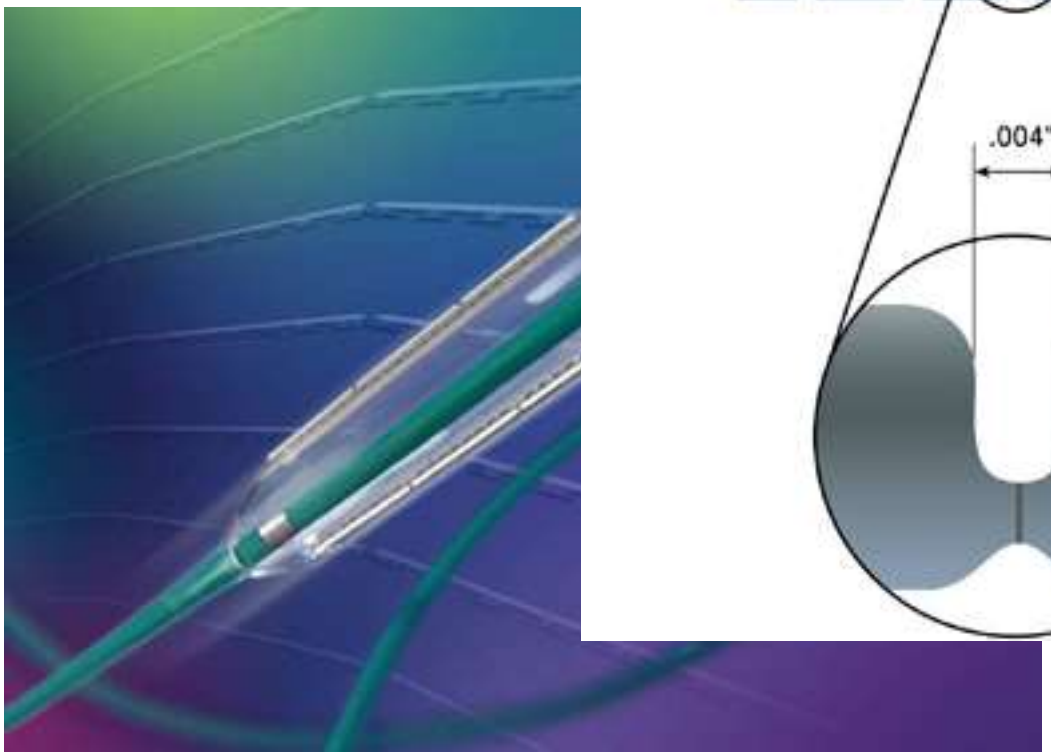
Supera image: Photo on file at Abbott Vascular

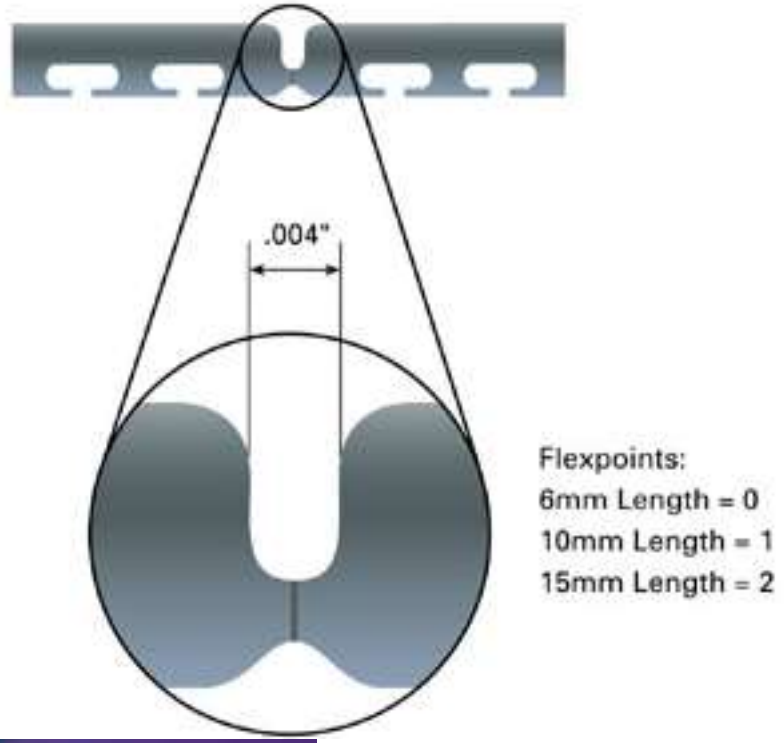
*TLR by KM

Lesion preparation with scoring technology ????

Monorail Scoring Balloon Catheter

Flextome Cutting Balloon (Boston Scientific)





Flextome® Cutting Balloon®: Boston Scientific

- Diameter……..5, 5.5 , 6, 7, 8 mm
- Atherotome……..1 cm
- Wire……0.018”, OTW
- Sheath……...7F
- Shaft Length……50,90,135 cm
- RBP……...10 atm
- Nominal Inflation Pressure……...6 atm

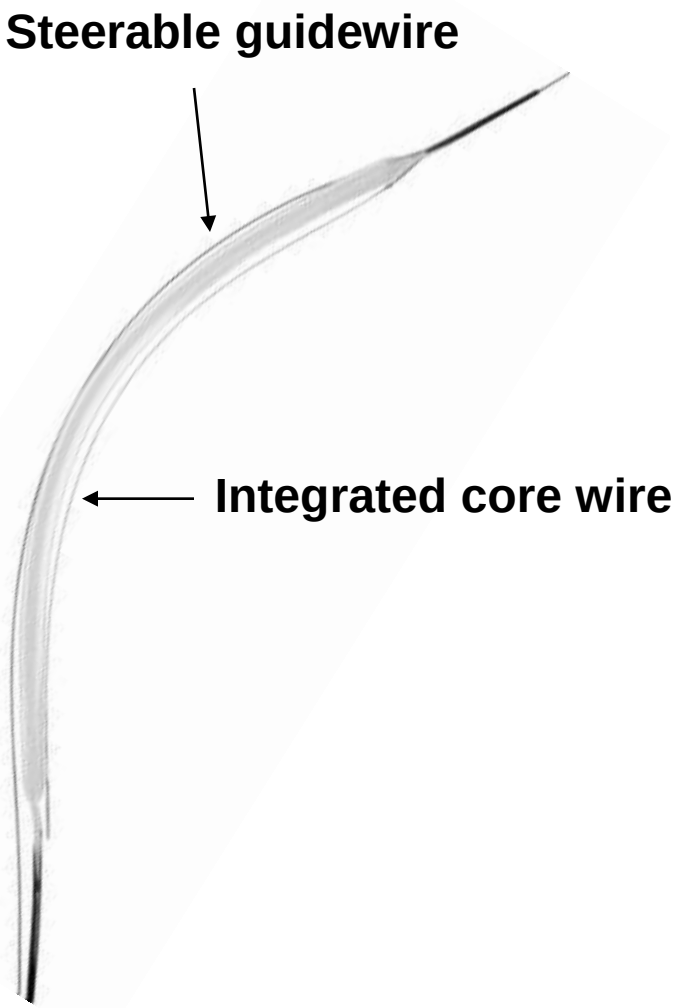
1 cm Device

Monorail Scoring Balloon Catheter

VascuTrak (Bard)

VascuTrak; Key Characteristics

- **Focused Force PTA Catheter**
- **Two wires focus balloon inflation force**
  - Standard 0.014” or 0.018”
  - Integrated 0.010” Wire
- **Short Rapid Exchange**

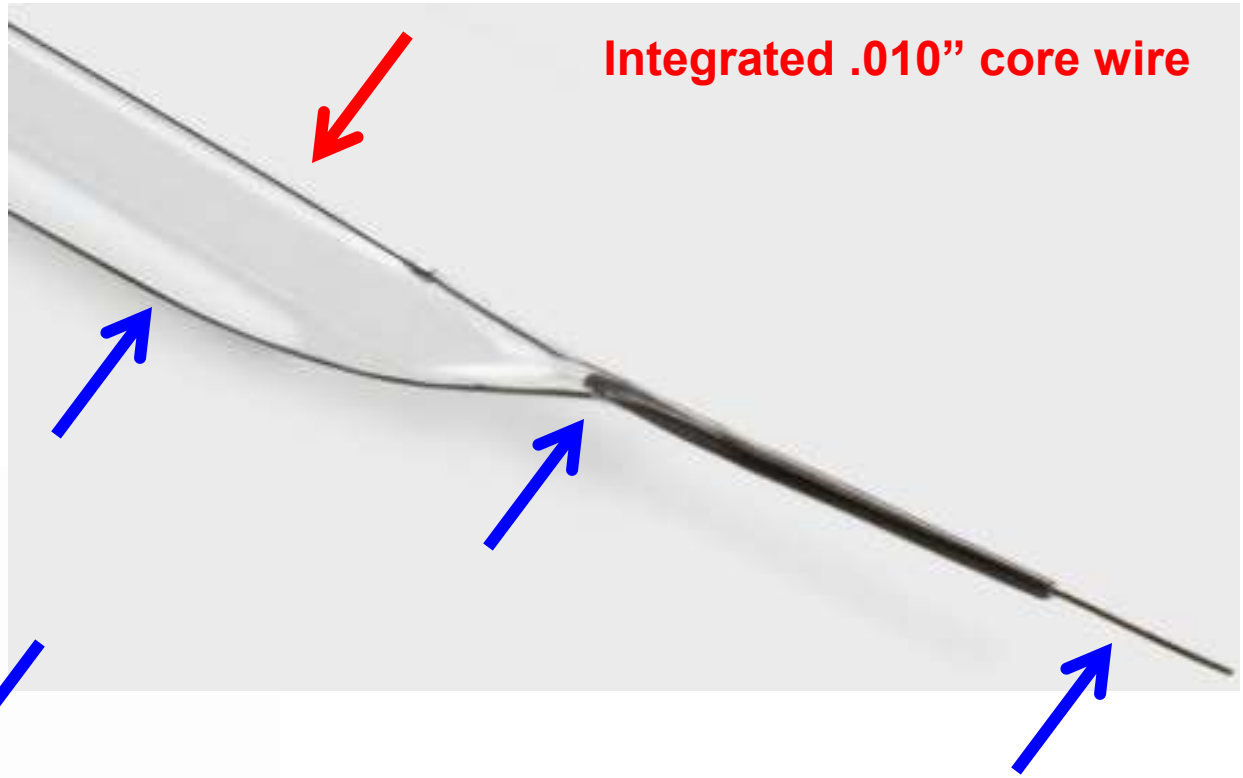


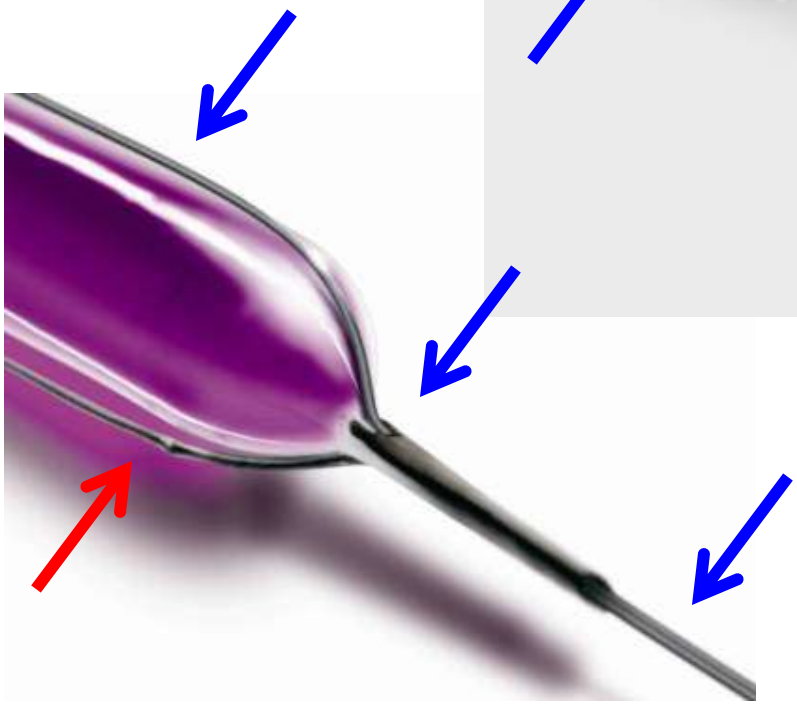
Short Rapid Exchange Technology

Advantages

–Focused force

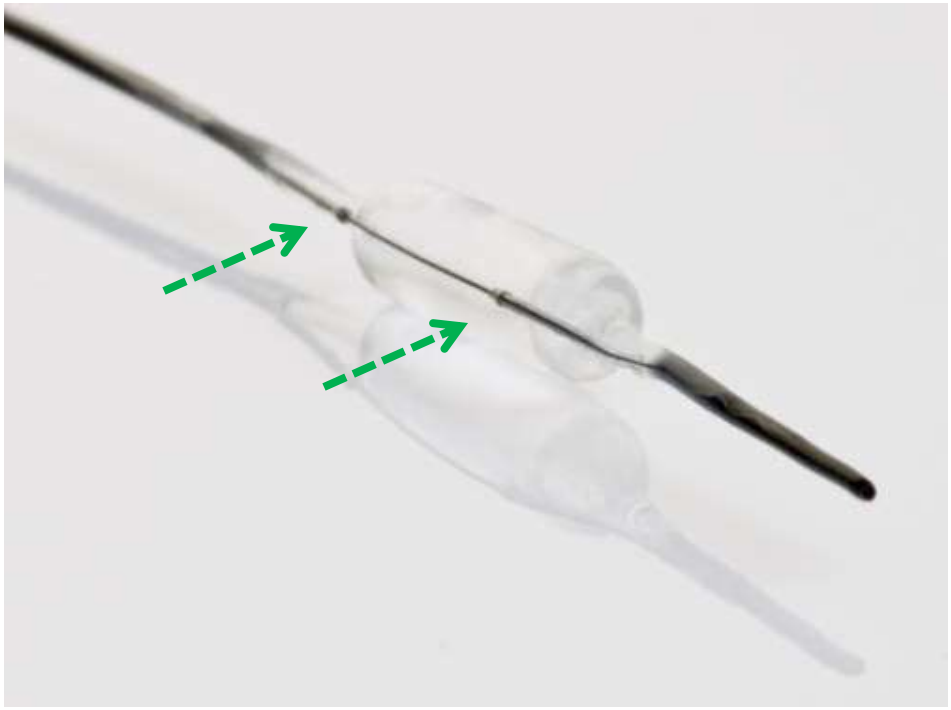
–Enables use of shorter wires

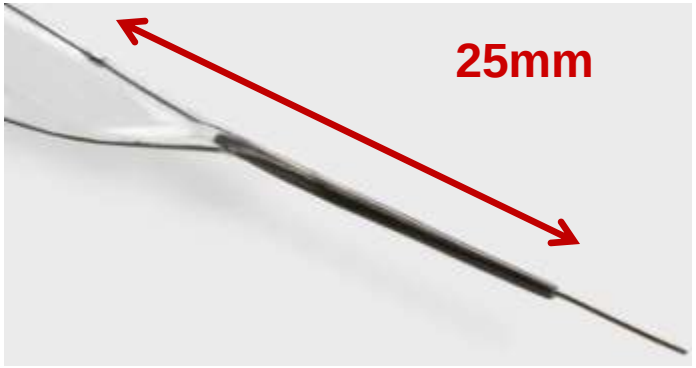




Steerable guidewire: .014” or .018”

Integrated .010” Wire

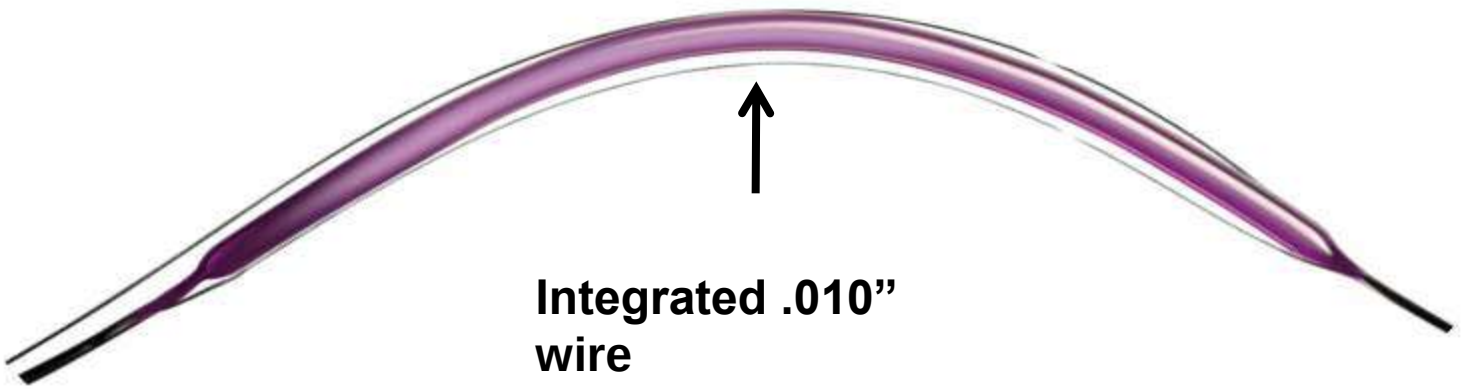




2 radiopaque (platinum) markers on the integrated core wire delineate the working length of the balloon

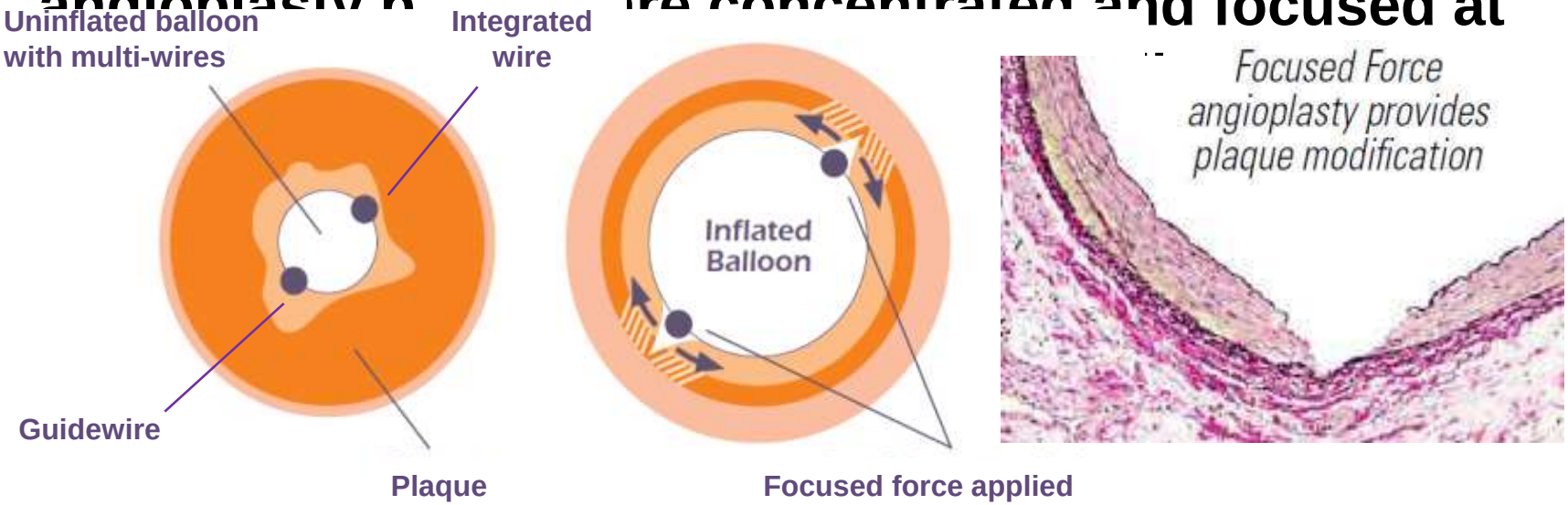
Focused Force Angioplasty

- **VascuTrak™ ➡ <u>Designed to deliver longitudinal focused force for controlled plaque modification</u>**
  - Via integrated wire and the working wire of choice
  - To long diffuse lesions on straight or curved vessels through tortuous anatomy



Mechanism of Action

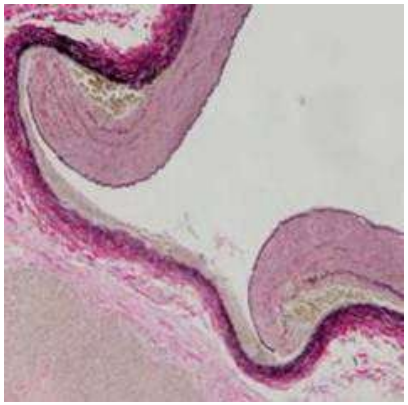
- **Focused Force Angioplasty (FFA) is a technique in which the forces resulting from inflating an angioplasty b[illegible]re concentrated and focused at**



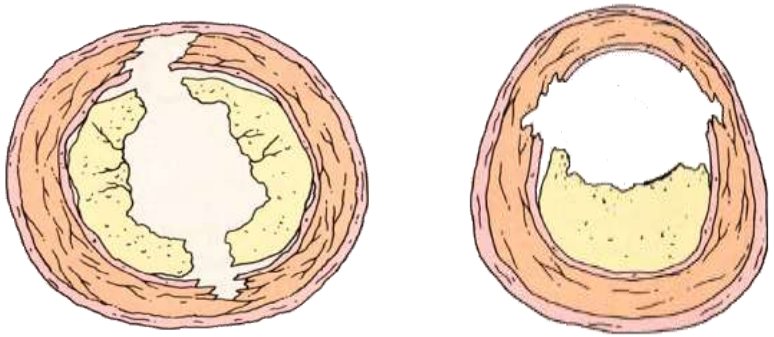
- **External wires focus balloon inflation force**

Clinical Need

- **Plaque and arterial resistance often prevent the lumen and/or a stent from reaching its expected size, despite high pressure balloon inflations**
- **POBA causes plaque to fracture at high pressures producing rapid stretching of the vessel wall**
- **Rapid stretching of the vessel wall generates trauma and recoil which may lead to re-stenosis and prevents lumen enlargement**



POBA Dissection



Atlas of interventional radiology. - C. Cope et al, Gower Medical Publisging, New York, 1990

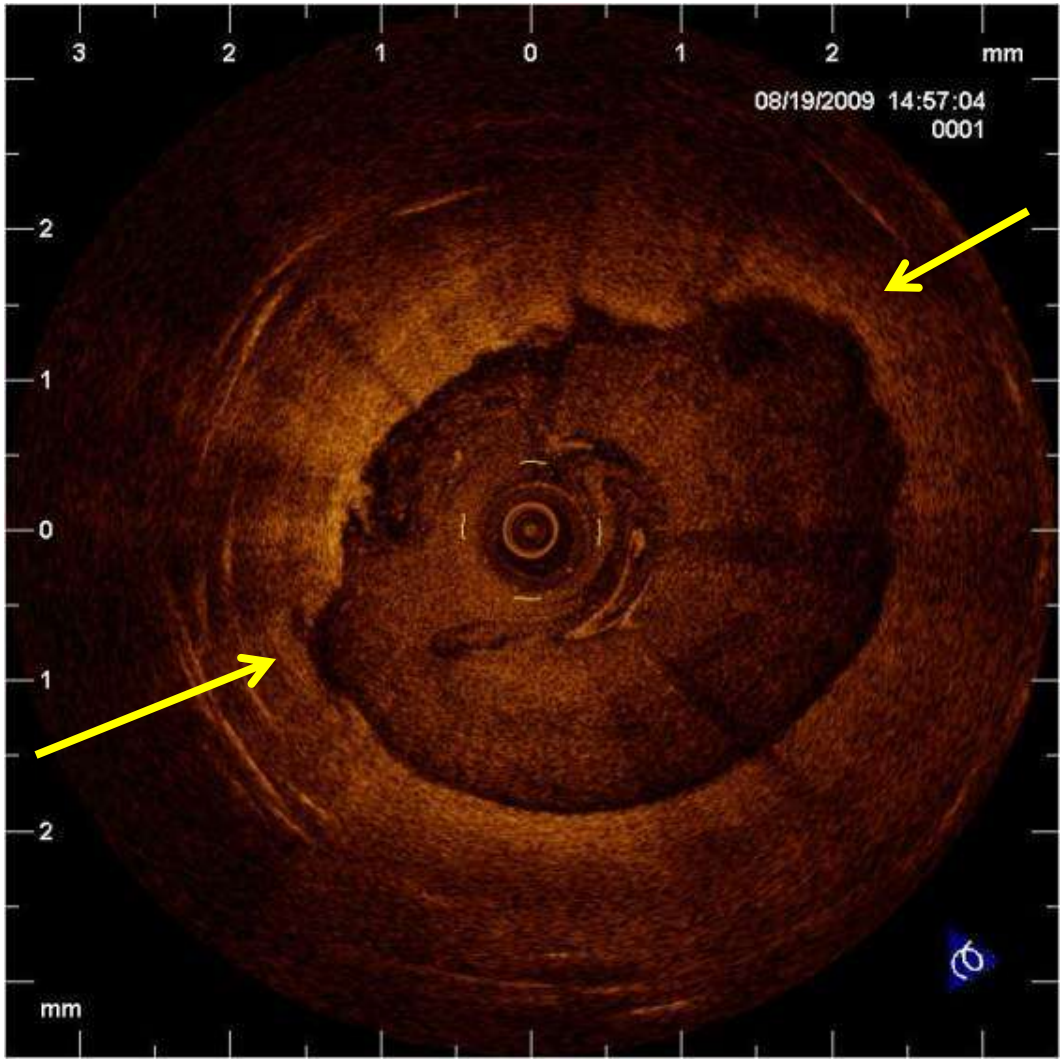
Clinical Challenges

- **Small vessels with long diffuse disease**
- **Resistant lesions**
- **Highly calcified lesions**
- **Plaque shift in bifurcations**
- **High restenosis rates**

- **“... In patients with CLI, the infrapopliteal disease is usually multilevel, multisegmented, and frequently involves the SFA, popliteal, and infrapopliteal vessels.”**

  – V. Nair, 2007

Focused Force Angioplasty (OCT image)



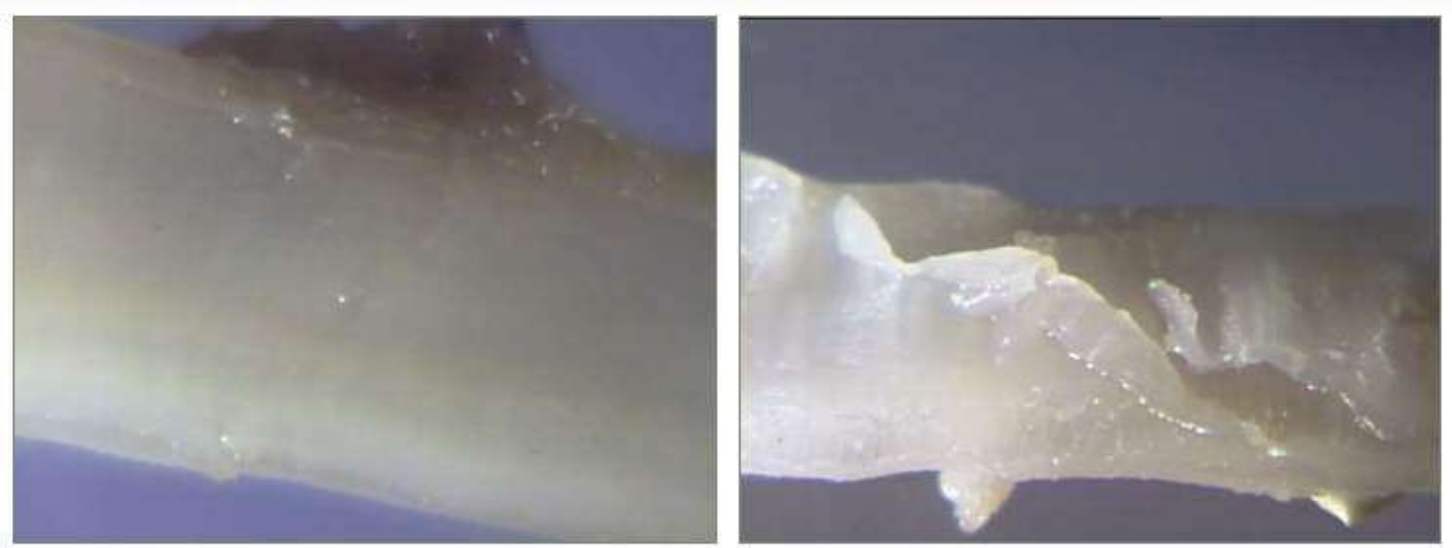
.018” guide wire

.010” integrated wire

OCT: Opthical Coherence Tomography

Source: 32

Slow vs. Fast Inflation



Gradual versus rapid balloon inflation

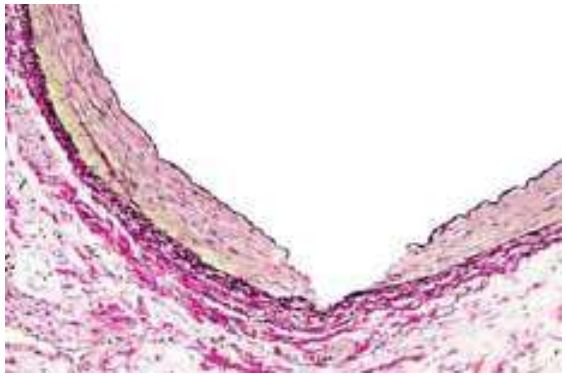
- **"The dissection rate was higher in patients with rapid inflation, 59% vs. 36%, p<0.01."**
- **"The collective complication rate was higher in patients with rapid inflation, 19% vs. 6%, p<0.03."**
  - **R. Ilia, 1993**

Source: 14

VascuTrak™ Mechanism of Action

- **Unique Focused Force design that concentrates the force of the balloon along 2 external longitudinal wires**

- **Focused Force, combined with the utilisation of a slower inflation rate (= slower vessel stretching), provides controlled plaque modification**



Tips for a Successful Procedure

1. Size the nominal balloon diameter 1:1 to the diameter of the vessel being treated.
2. **Do not flush** the balloon.
3. Use a **contrast/saline ratio of 25/75%** for faster inflation and deflation times.
4. **Activate the hydrophilic coating** by wetting the balloon and catheter shaft.
5. Back load the catheter onto the guide wire through the **Short Rapid Exchange** tip.
6. Insert the catheter through the introducer sheath and over the wire **using short advances**.
7. Position the balloon and slowly inflate **1 ATM every 30 seconds** to enable the Focused Force wires to modify the plaque.
8. Once nominal diameter is achieved, initial studies have shown that **prolonged inflation** times may be beneficial.
9. **Slowly apply negative pressure** to deflate the balloon.

Proper Inflation Technique

Key aspects of VascuTrak™ inflation technique:

LOW & SLOW

- **1 Atm every 30 seconds**
  - Allows external wires to contact the lesion first, prior to the remainder of the balloon ➡ longitudinal focused force along the lesion
  - Advantages:
    - Mostl lesions will be effaced before RBP is reached
    - Cracking the plaque first before modifying it

- **Proper balloon sizing; diameter and length**
  - RVD (Reference Vessel Diameter)
  - Use balloon length that covers the entire diseased segment with a single inflation

Proper Inflation Technique

Step-by-step:

- **1 Atm every 30 seconds**
- **Continue up to nominal pressure**
  - Even if plaque has already cracked
  - Nominal pressure is required to reach nominal size of balloon
- **Hold 2 minutes at nominal pressure (= nominal Ø)**
  - To minimise vessel recoil by overcoming the vessel stress rate
- **If lesion doesn't yield after 2 minutes at nominal pressure**
  - Continue with 1 Atm every 30 seconds up to RBP
    - Never go over RBP !!
  - Once lesion yields; keep inflation for 2 minutes

Overcome plaque resistance first,
then the vessel stress (elasticity)

Reimbursement in Korea

- **Cutting PTA balloon Catheter**

코드	품명	수입업소	상한금액	적용일자
J8074068	VASCUTRAK PTA Cathter	바드코리아㈜	461,100	2017-04-01

- **Peripheral Cutting Balloon Catheter**의 급여기준

1. 적응증 (Indication)

가. **동정맥루(Arteriovenous fistula, AVF)**의 협착 및 폐색시 : 혈관크기에 적합한 고식적 풍선(conventional balloon)의 사용에도 불구하고 잔여협착으로 인하여 최대압력시 **풍선직경의 70% 이상 확장되지 않은** 경우 (Residual stenosis>30%)

나. **대퇴동맥(femoral artery)**이하 **동맥**의 협착 및 폐색시 (**내경 70% 이상의 협착**)
- **석회화**가 심한 경우(혈관벽의 50% 이상 석회화; Calcification >50%)
- 혈관우회술 후 문합 부위에 발생한 협착 (Stenosis in anastomosis site)
- **슬와동맥**의 협착 (Popliteal stenosis)

2. 인정개수 (Number): 1개

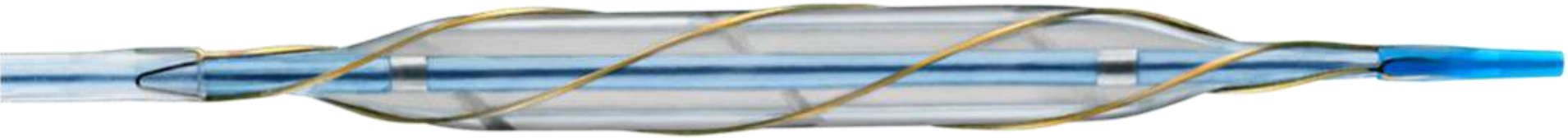
BTK Scoring Catheter Balloon

Chocolate (TriReme Medical)

Scoring Balloon Catheter

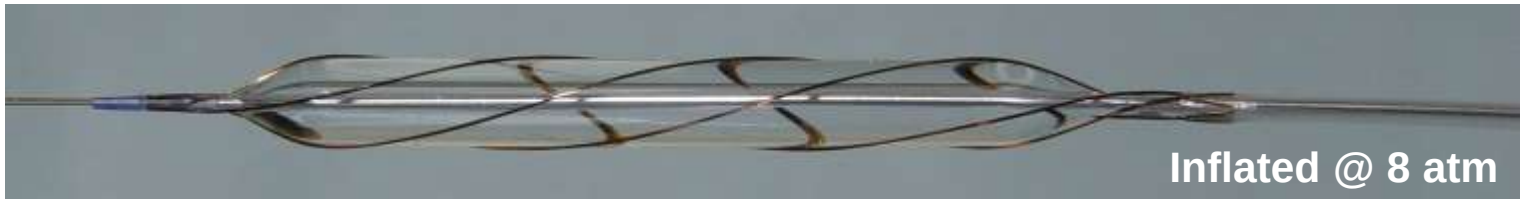
AngioSculpt® PTA

Semi-compliant Nylon Balloon



“Floating” Scoring Element

- **Diameter 2-6 mm, balloon length 20-100 mm**
- **4 Scoring wires 0.007“**
- **0.018“ guide-wire compatibel up to 40 mm length**
- **0.014“ guide-wire compatibel for 100 mm length**
- **Sheath: 5 F (<4 mm) 6F (>4 mm)**



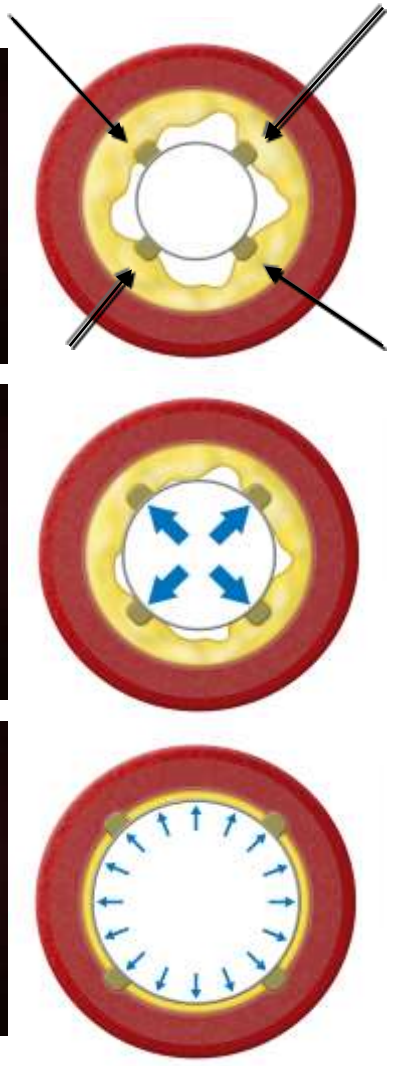
Mechanism of Action

A. As the balloon inflates, ***radial forces concentrate along the edges of the nitinol scoring element***

B. The circumferential forces score the plaque, aiming to a ***more complete luminal expansion*** and a ***more precise and predictable outcome***

No significant device slippage means less risk of damage to healthy tissue[1,2]

C. Reduced dissection rates and elastic recoil mean better final luminal dimensions[3]



1.Kiesz RS, Scheinert D, Peeters PJ, Bosiers M, et al. J AM COll Cardiol. 2008:51;10 (suppl. B); 75
2.Scheinert D, Peeters P, Bosiers M, et al. *Catheter Cardiovasc. Interv*. 2007;70:1034–1039.
3.Costa J, Mintz G, et al. J Am Coll Cardiol. 2007;100:812–817

FeMoropopliteal AngioSculpt sCoring BallOon CaTheter Study

MASCOT Trial

- Prospective, multi-center, non-randomized
- Enrollment period: March 2008 – July 2008
- Rutherford 2&3 (intermittent caludicatio)
- Rutherford 4 (rest pain)
- Rutherford 5 (non-healing wounds)
- Lesion: <80mm
- Diameter: 4.5-6mm

Patrick Peeters, Dierk Scheinert, Gary Gershony, Marc Bosiers

FeMoropopliteal AngioSculpt SCoring BallOon CaTheter Study

MASCOT Trial

- Safety endpoint: complication free survival 1 month post procedure

- Efficacy endpoint: primary patency rate 12 months post procedure (duplex)

Patrick Peeters, Dierk Scheinert, Gary Gershony, Marc Bosiers

MASCOT Acute Procedural Outcome

(N=50)

Successful scoring	**50**	**100%**
Stand-alone treatment	**29**	**58%**
Additional stents used	**21**	**42%**
Distal embolization (successfully treated by immediate PTA with 3.0 x 60 mm balloon)	**1**	**2%**

Most patients were treated with the AngioSculpt balloon alone

MASCOT Study Endpoint Results

Safety endpoint:

Complication Free Survival at 1 month: **96%**

→ 1 death due to COPD on day 6

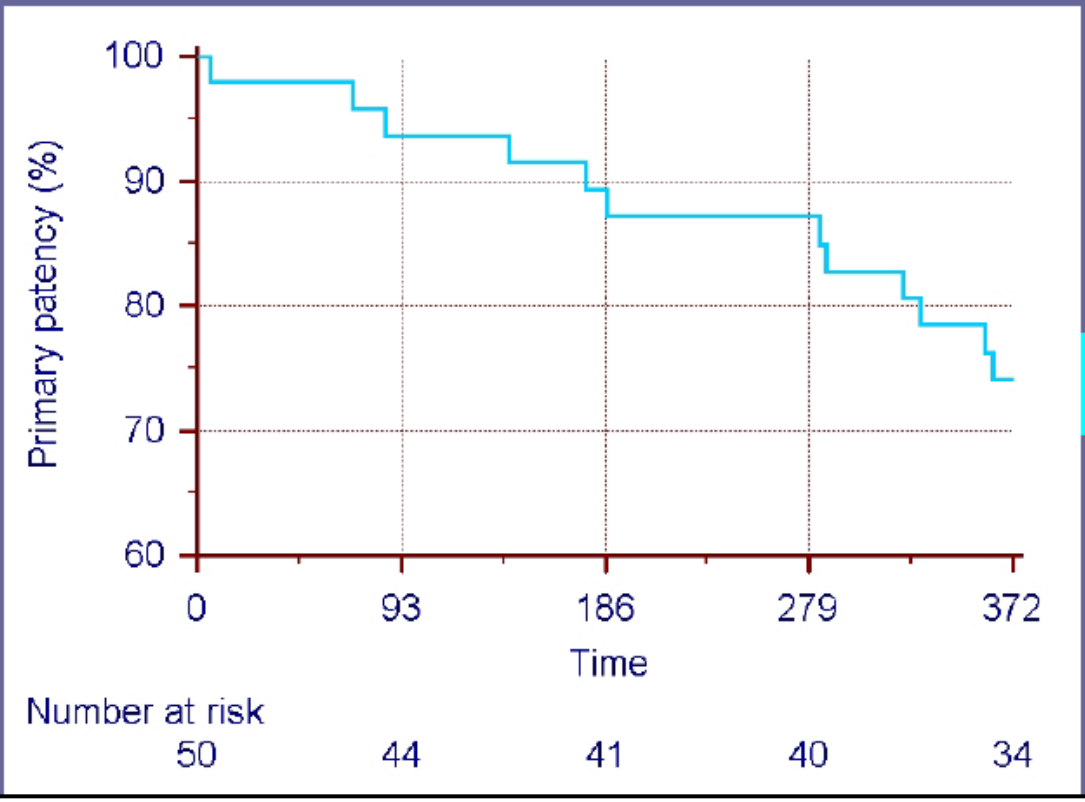
→ 1 endovascular re-intervention on day 7

Emergency PTA of left popliteal artery (study limb) after motor vehicle accident

Efficacy endpoint: Primary patency at 12 months on duplex scan

MASCOT Study Endpoint Results

Efficacy endpoint :
Primary patency at 12 months on duplex



74.1%

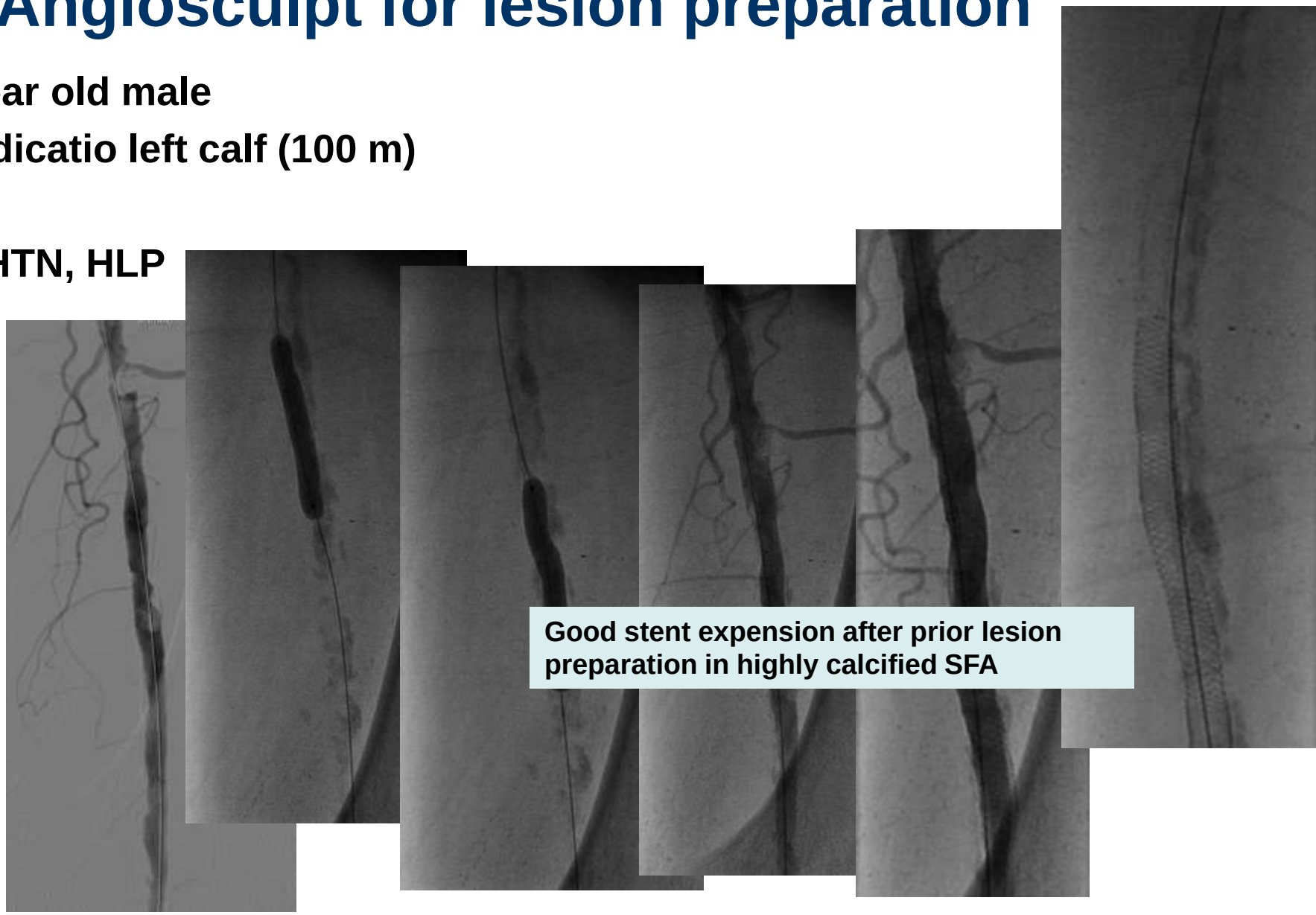
1. Angiosculpt for lesion preparation

82 year old male

Claudicatio left calf (100 m)

CAD

Art. HTN, HLP



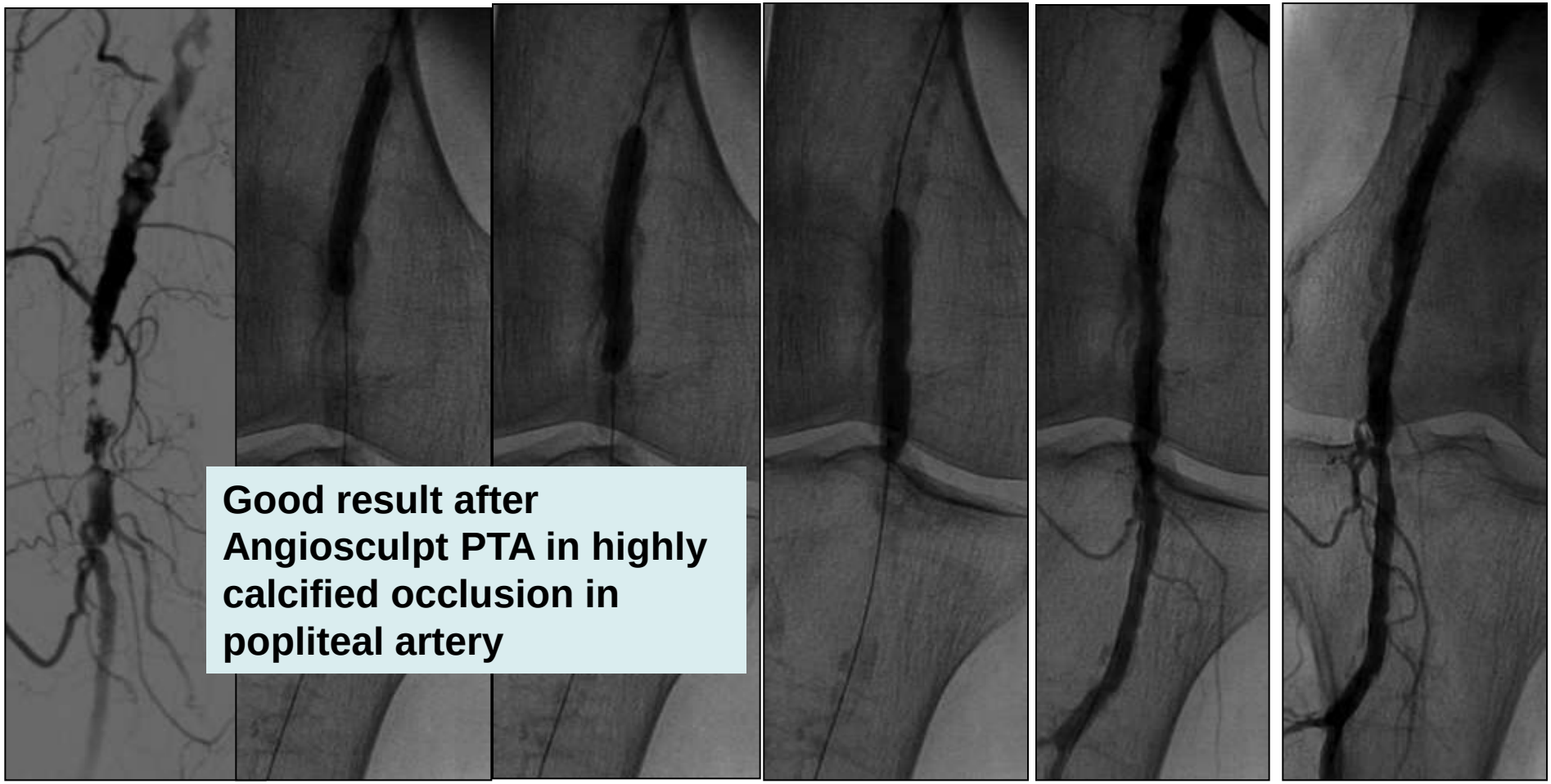
Good stent expension after prior lesion preparation in highly calcified SFA

2. Angiosculpt for stent avoidance

90 year old female

Claudicatio right calf (50 m)

Art. HTN, HLP



Good result after Angiosculpt PTA in highly calcified occlusion in popliteal artery

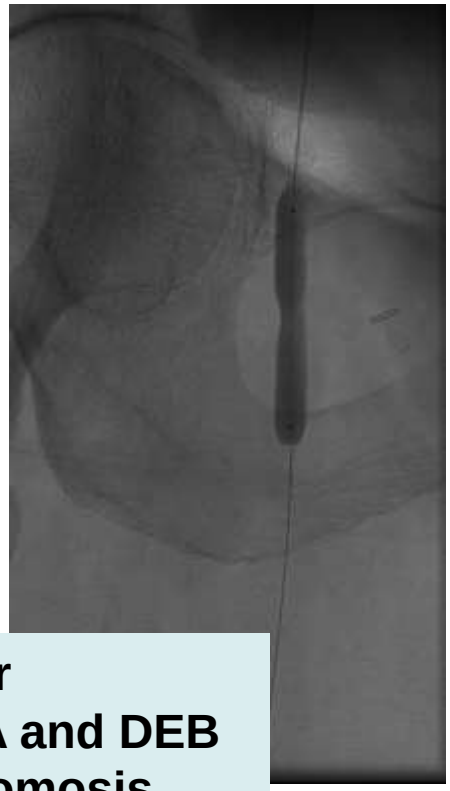
3. Angiosculpt in saphenous vein bypass anastomosis stenosis

60 year old male

Claudicatio right calf

Fem-pop saphenous vein bypass 2009

Art. HTN, HLP



Good result after Angiosculpt PTA and DEB in bypass anastomosis stenosis

4. Angiosculpt in prosthetic bypass anastomosis stenosis

77 year old male
Critical limb ischemia (rest pain) right
Fem-pop prosthetic bypass right 2008
Art. HTN, HLP, Diabetes

Good result after Angiosculpt PTA and DEB in prosthetic bypass anastomosis stenosis

5. Combination therapy

77 year old female
Claudiatio right calf (100 m)
Art. HTN, HLP, Diabetes

No restenosis at 12 months follow up after atherectomy plus Angiosculpt PTA and DCB

pre

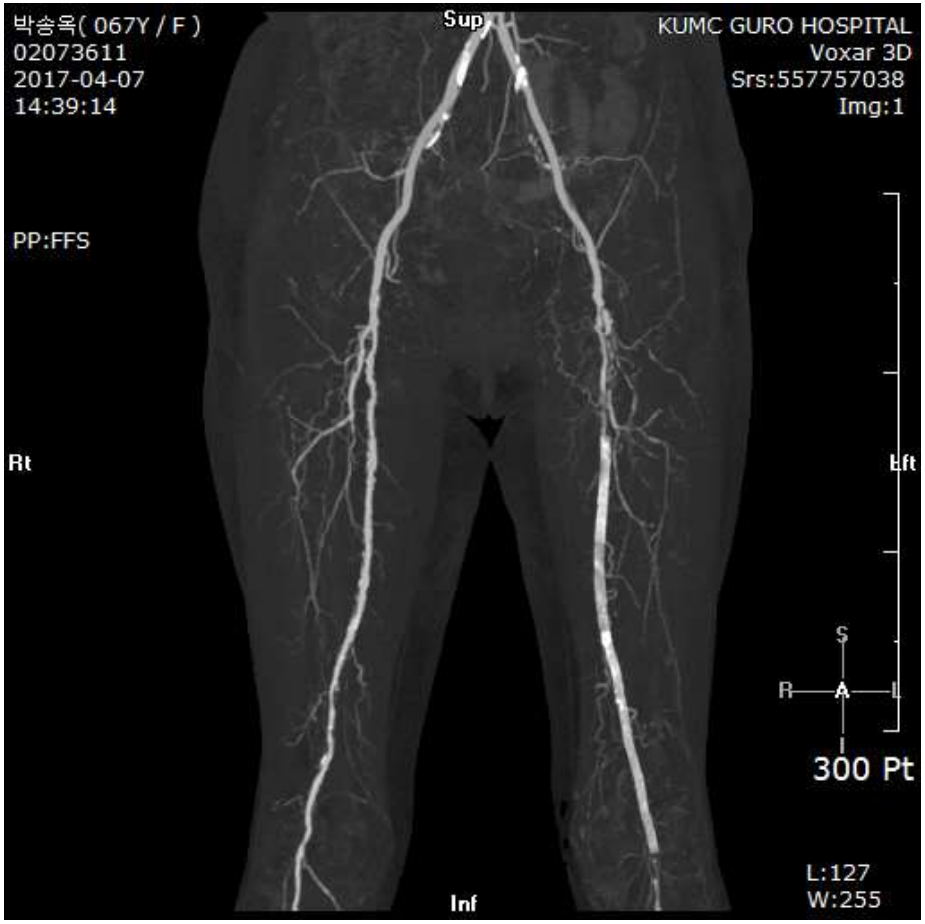
Post Silverhawk

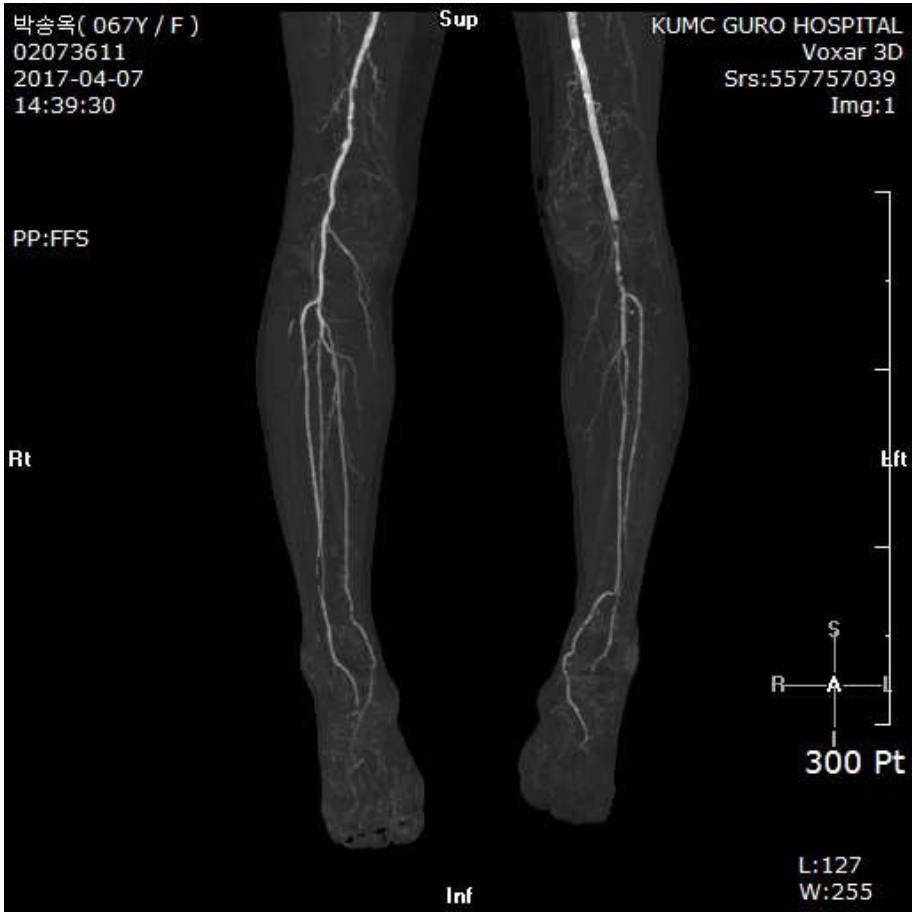
Post Angiosculpt

Post DEB

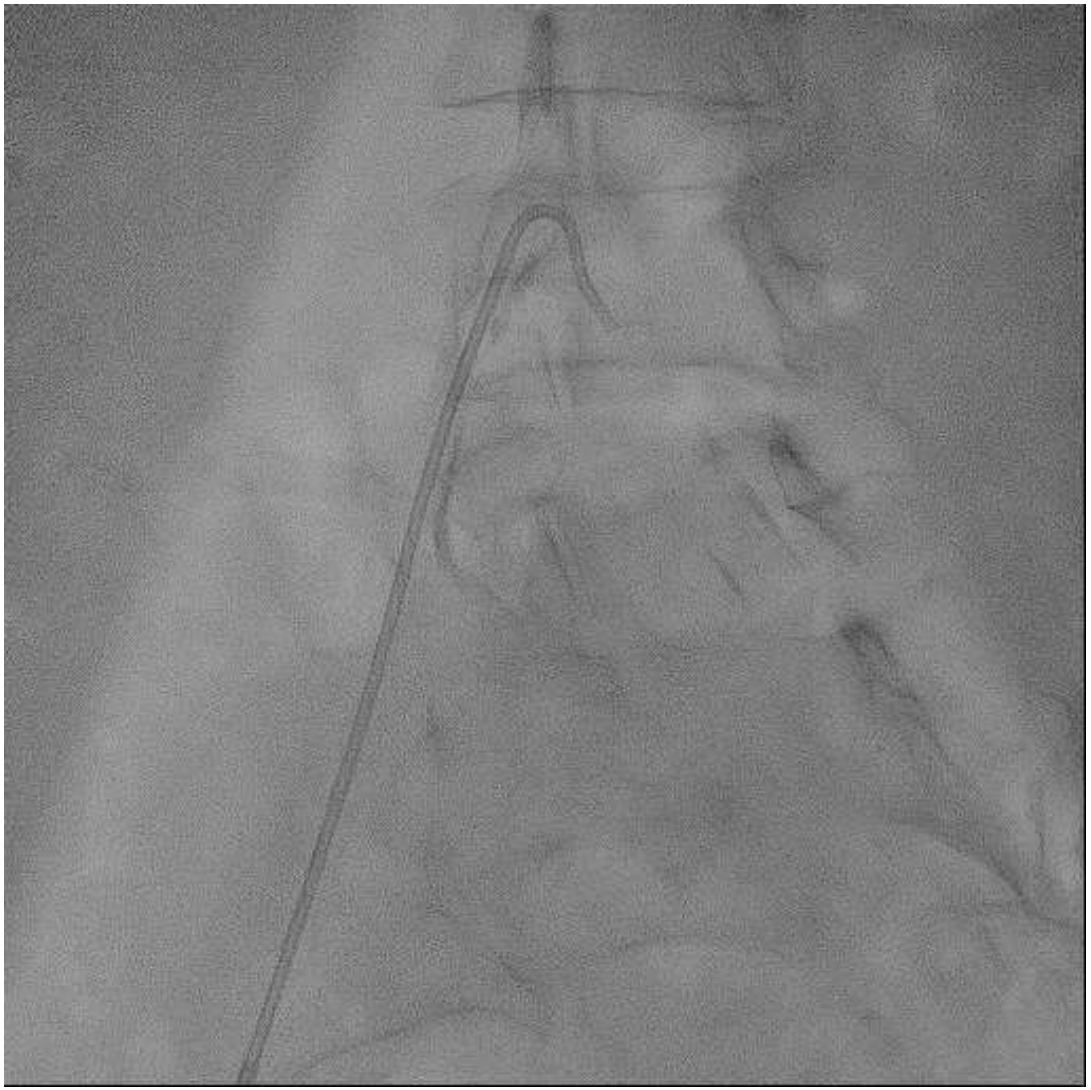
12 m Follow up

Severe ISR Case
; Jetstream, Scoring Balloon, NC Balloon, DCB

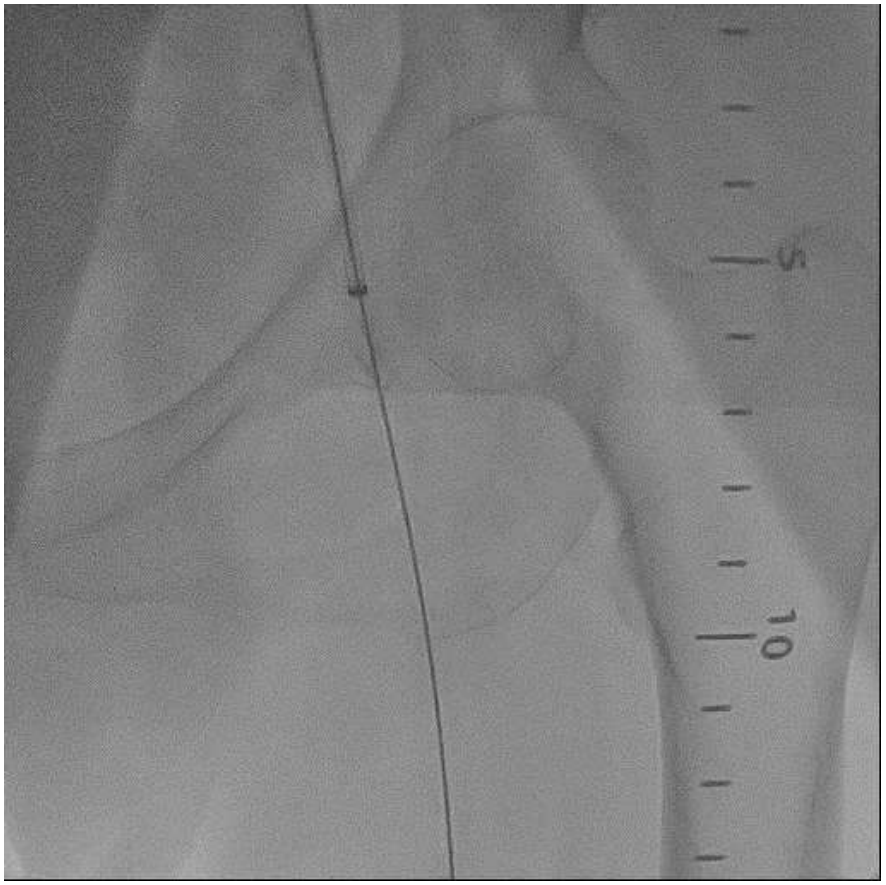




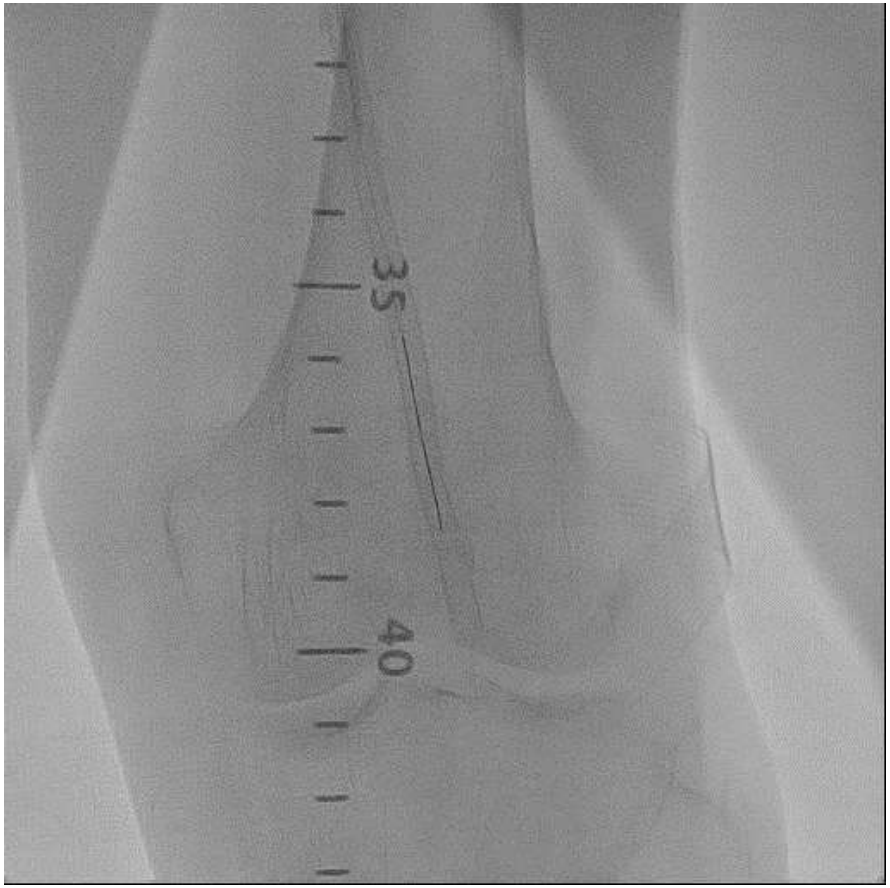
Baseline Angiography



Combined 035 and 018 wiring

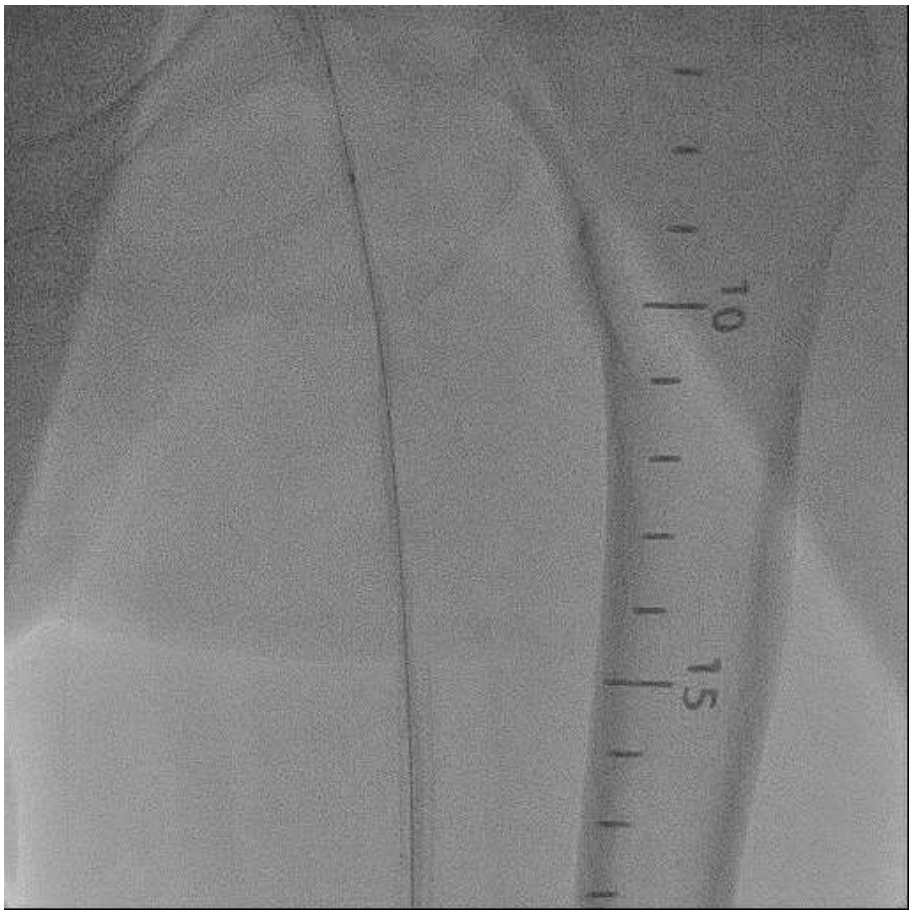


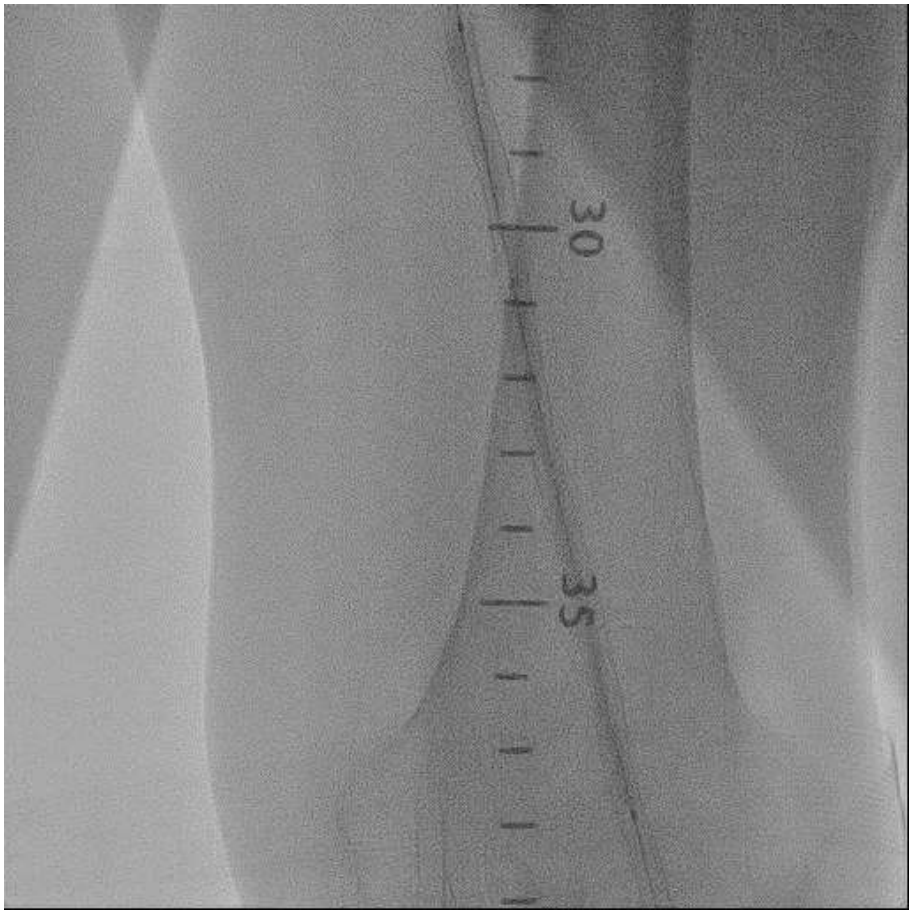
035 Angled Terumo



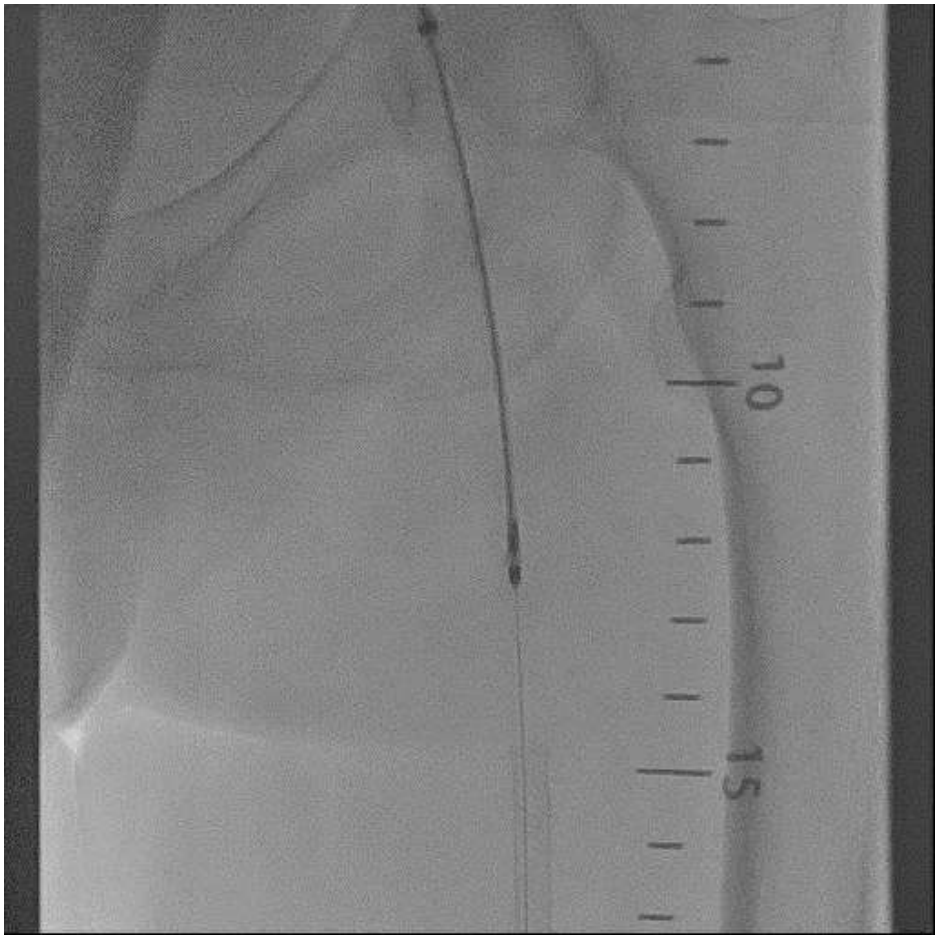
018 Connect Flex

Predilation with 2.5mm Balloon

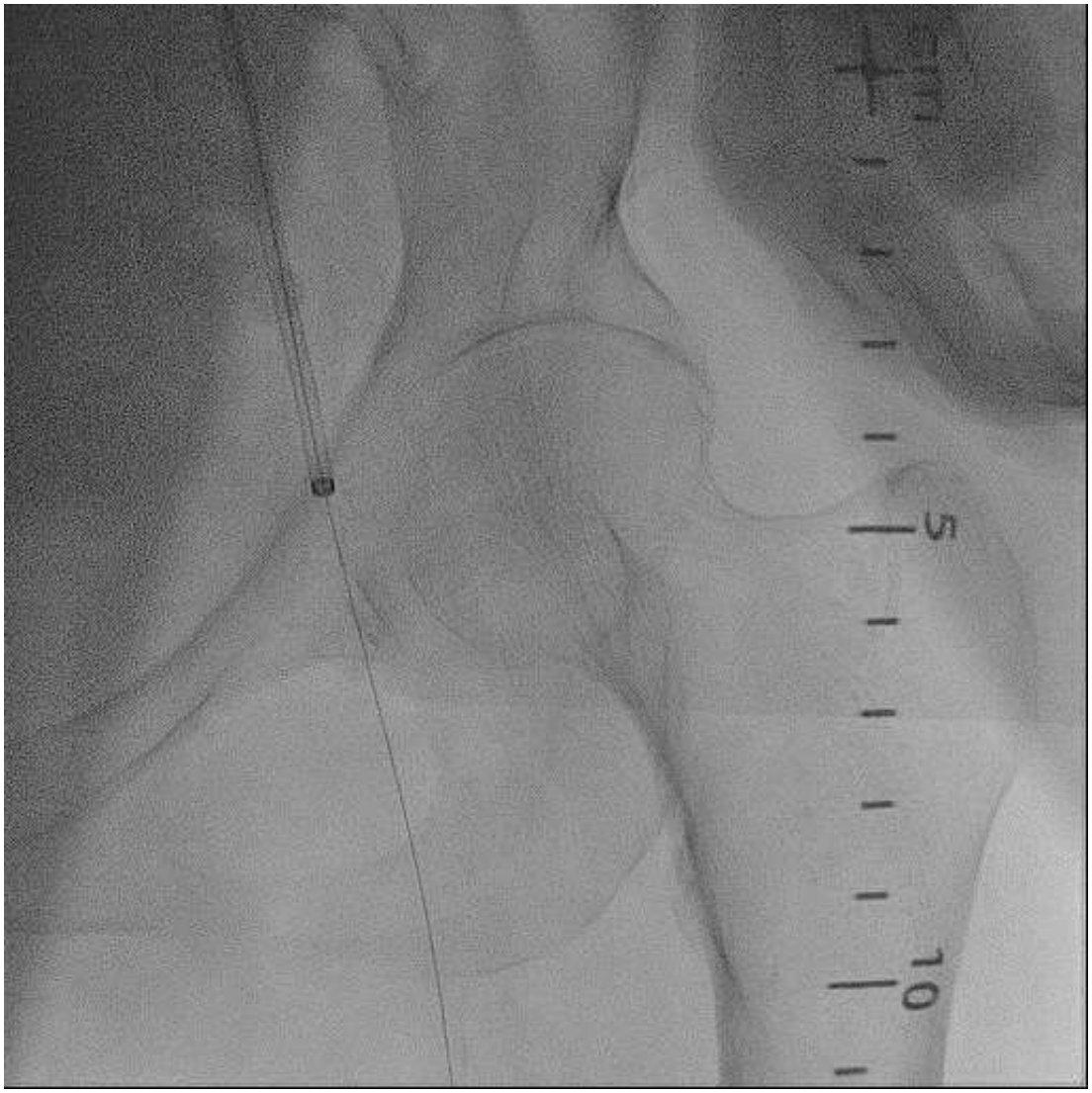




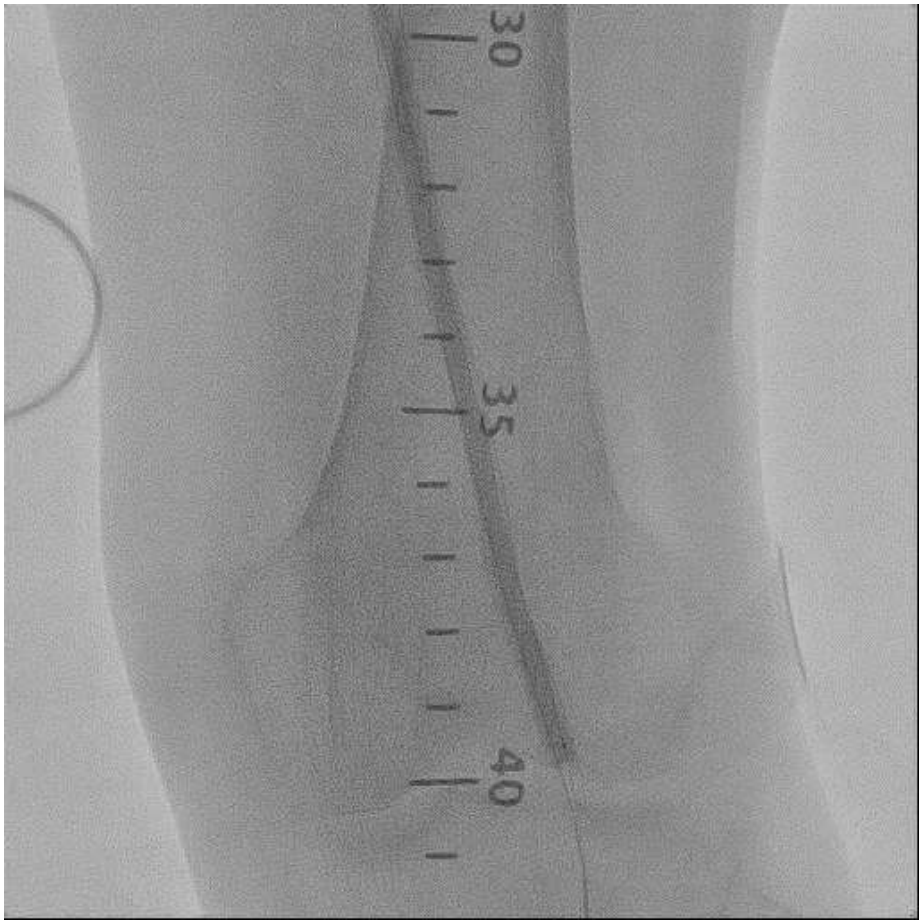
Jetstream

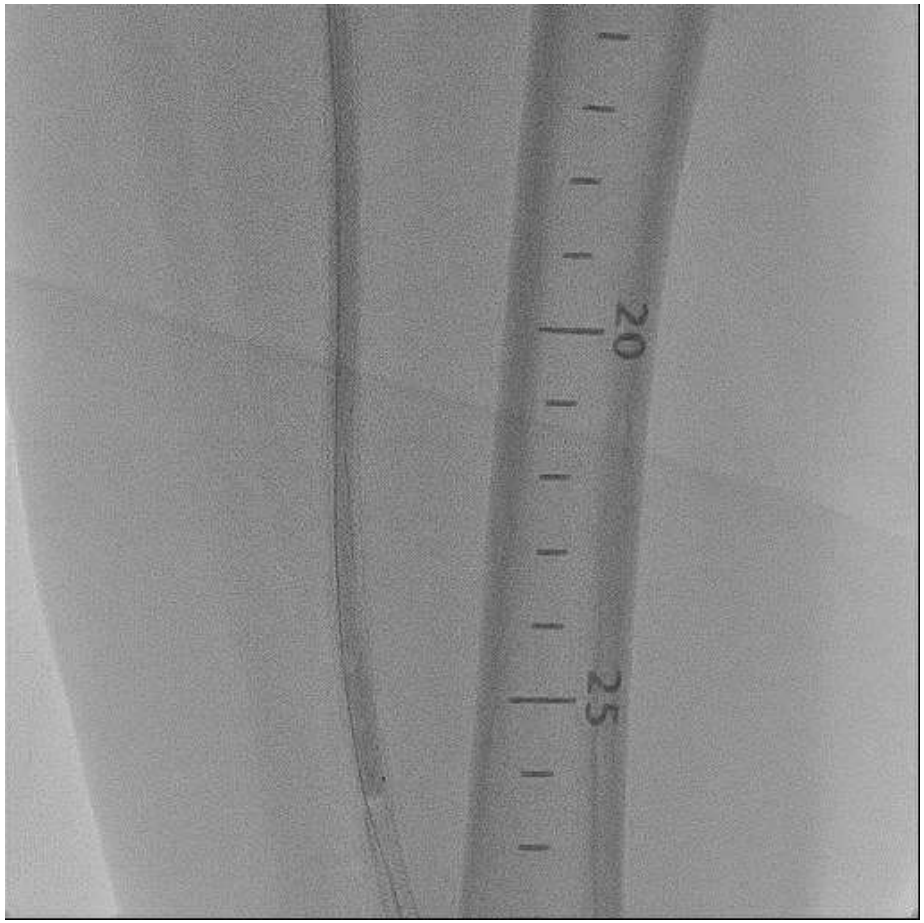


Immediate After Jetstream

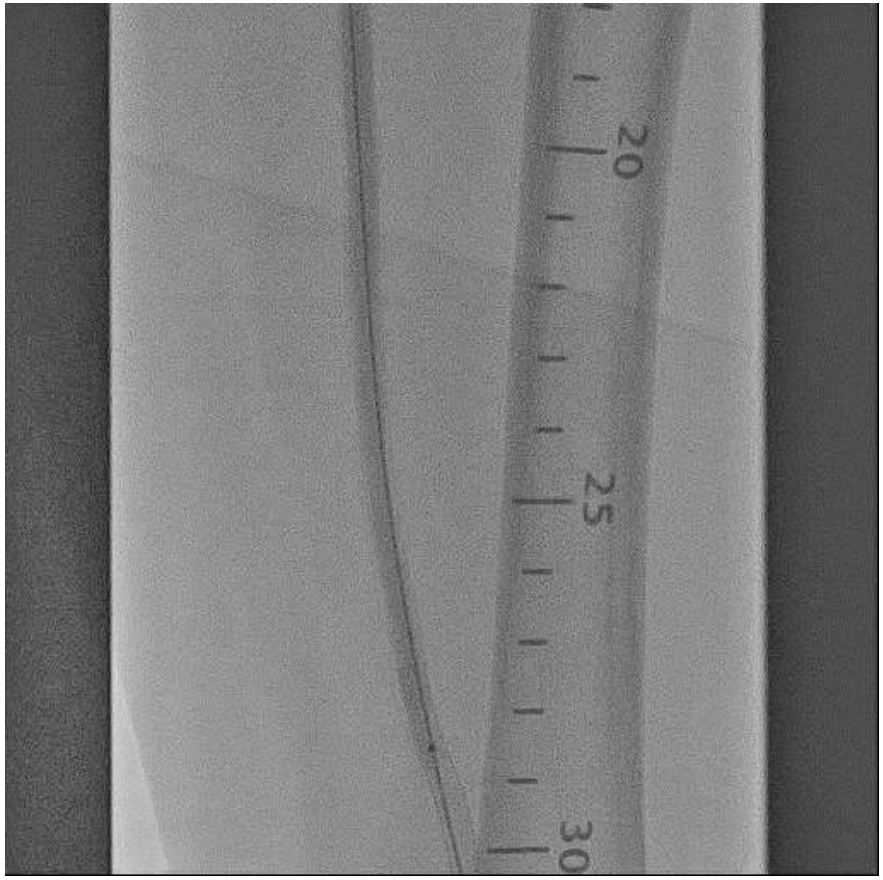


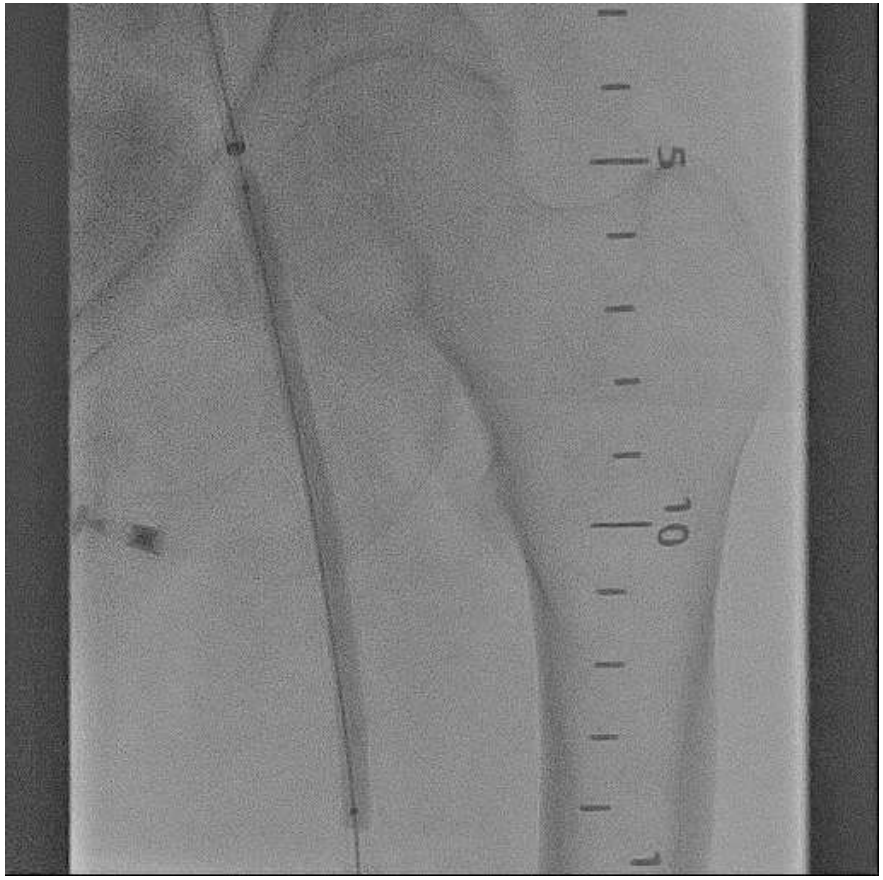
VascuTrak Scoring Balloon



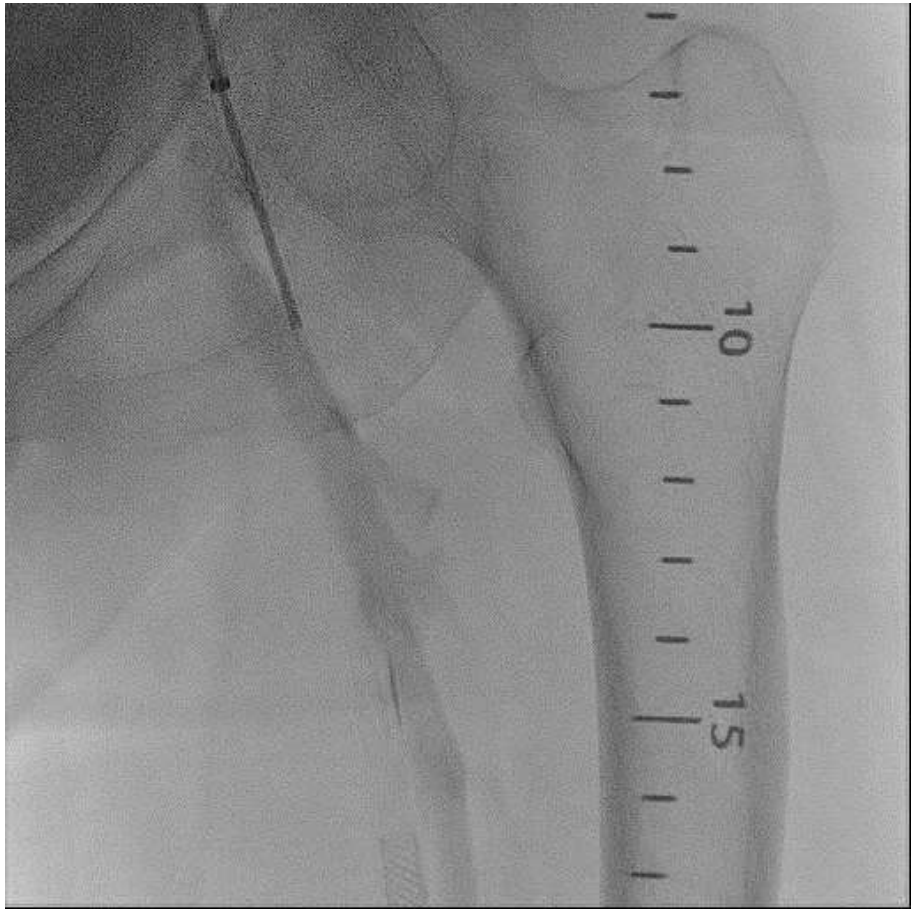


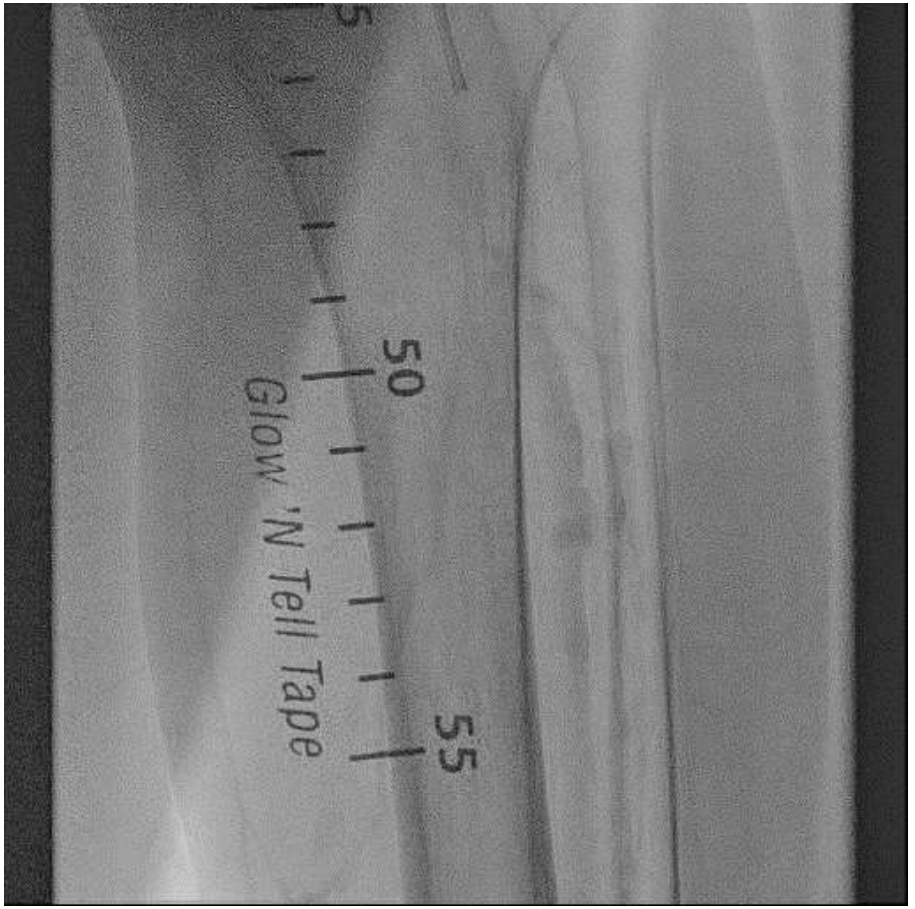
NC Ballooning





Post NC and Lutonix DCB





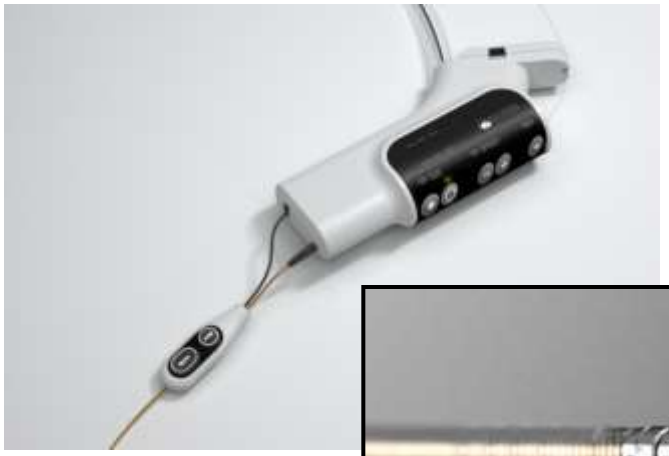
Suggested Benefits of Scoring Balloons

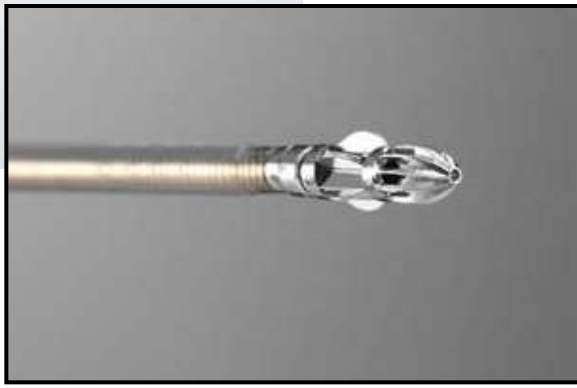
- Calcified & Fibrotic Lesions
- Bifurcation Lesions
- In-Stent Restenosis
- Preparing Vessel for Stenting

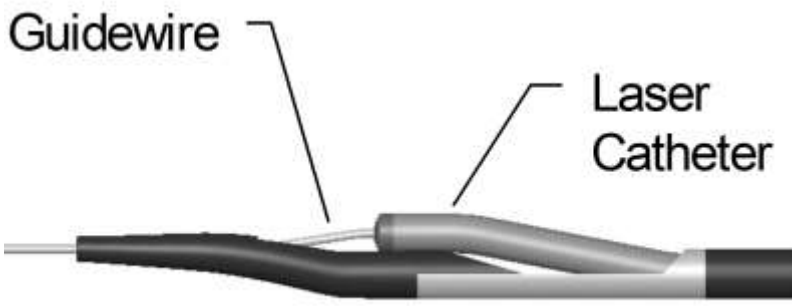
Atherectomy before DCB ????

Debulking

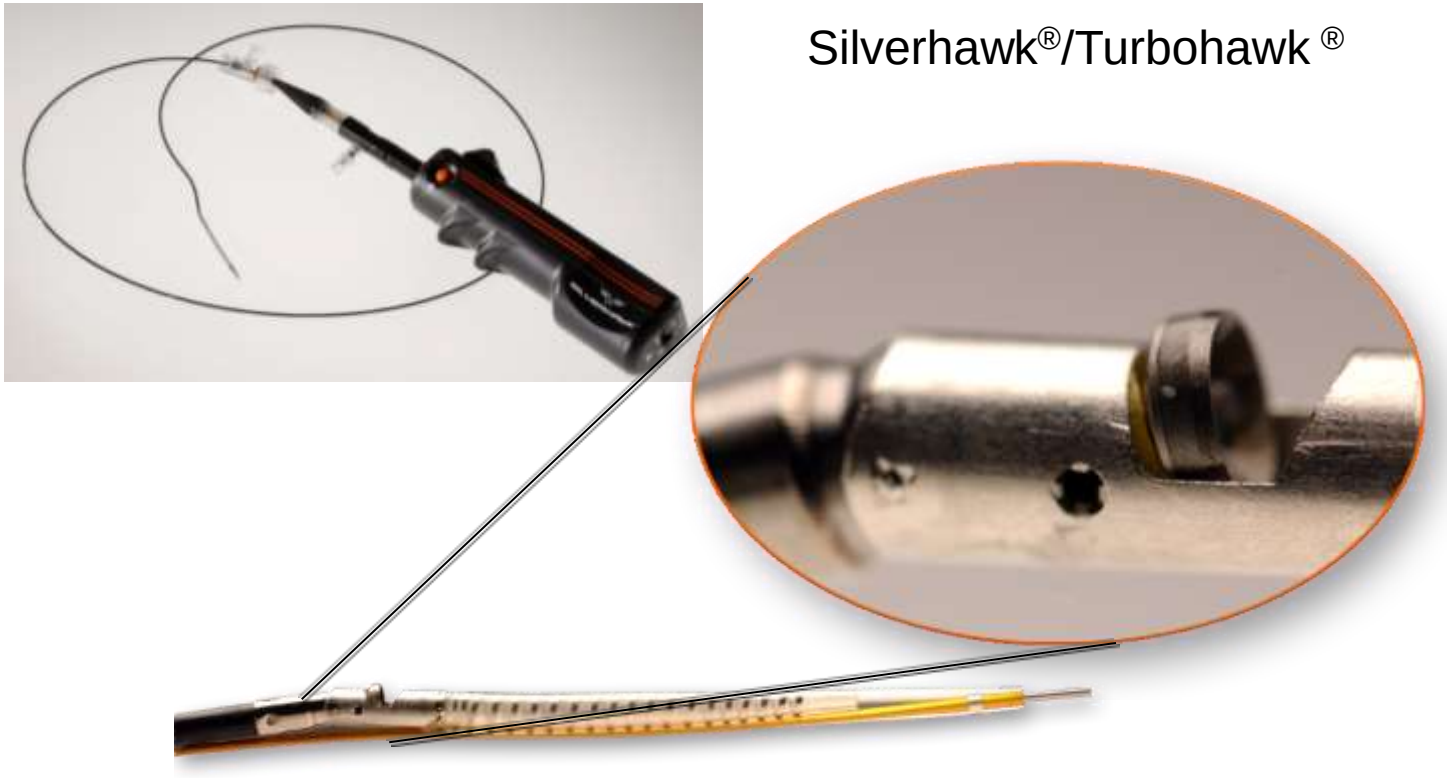
Atherectomy Devices





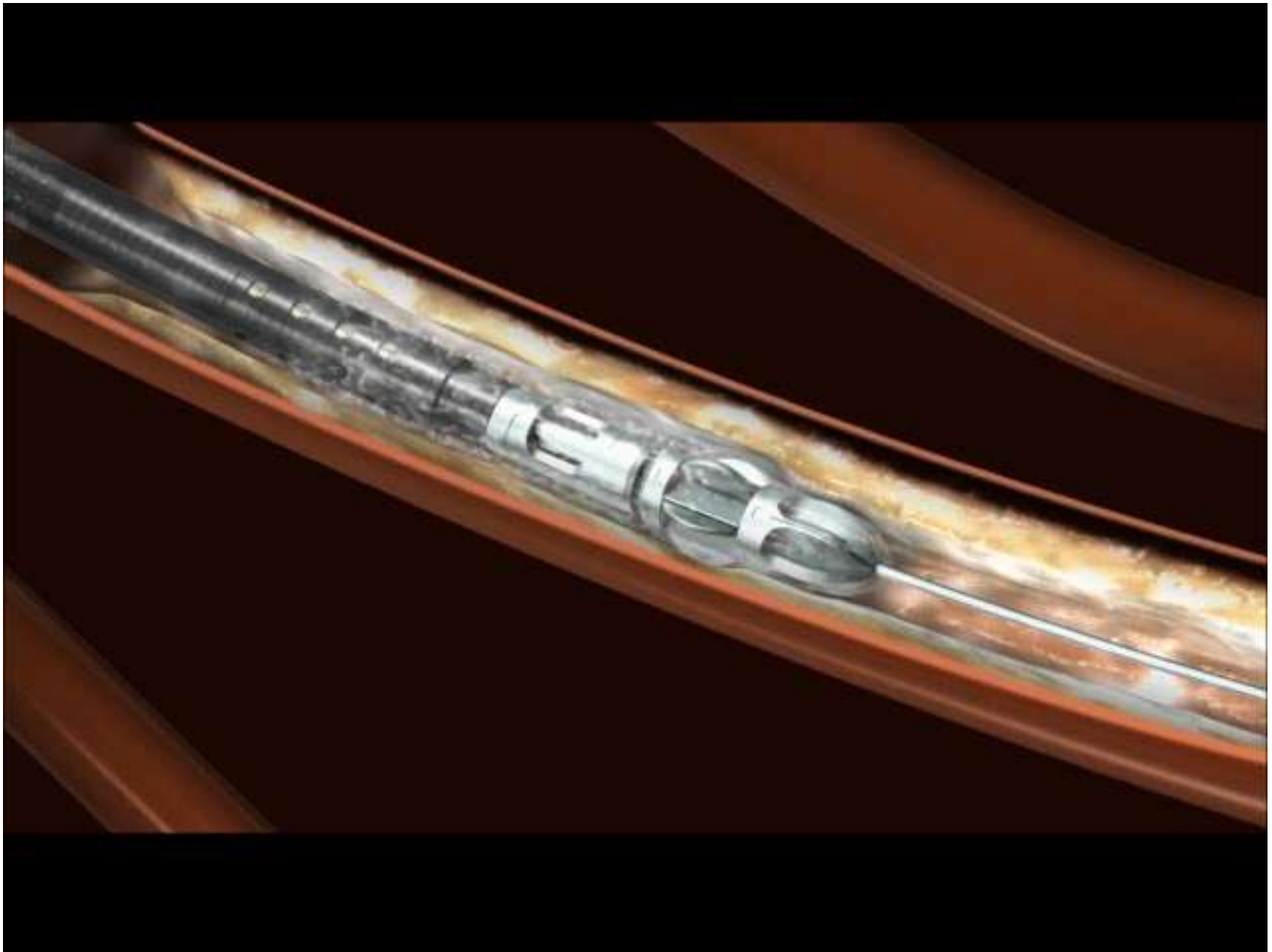


Debulking Techniques



Silverhawk®/Turbohawk ®

Jetstream



Debulking Techniques

Rotablator®

Background of Atherectomy

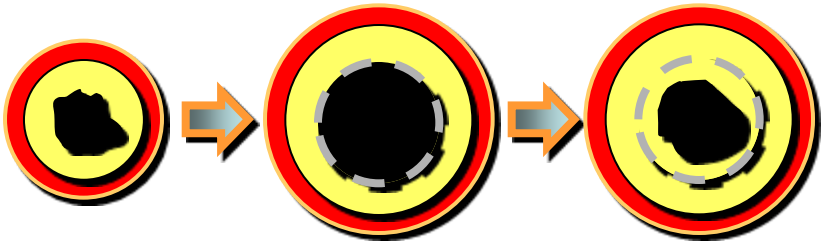
Angioplasty contemporarily shifts the plaque…

…Problem = recoil/ restenosis

…Problem = dissection

…Problem = vessel stretch causes injury

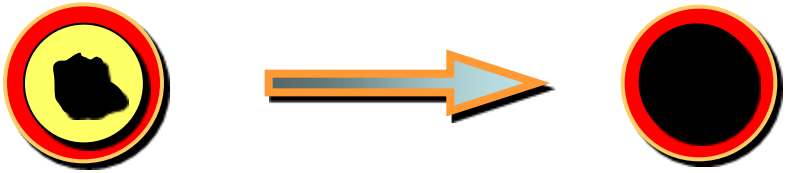
Stenting permanently shifts the plaque…



…Problem = Intima Hyperplasia usually after 3 - 9 months in the SFA

DCA removes the plaque…

…Problem = relative contraindication in vessel segments with high ~~external forces (knee)~~

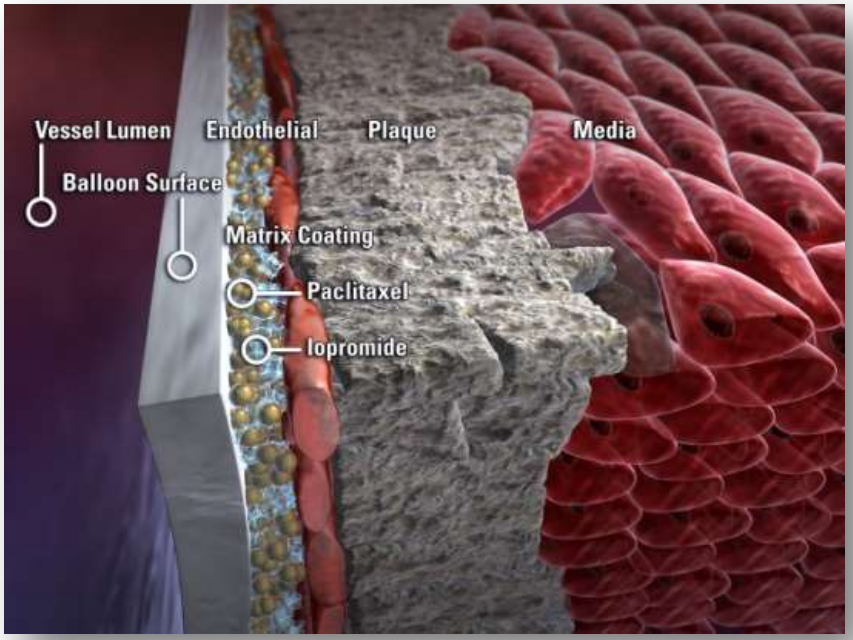


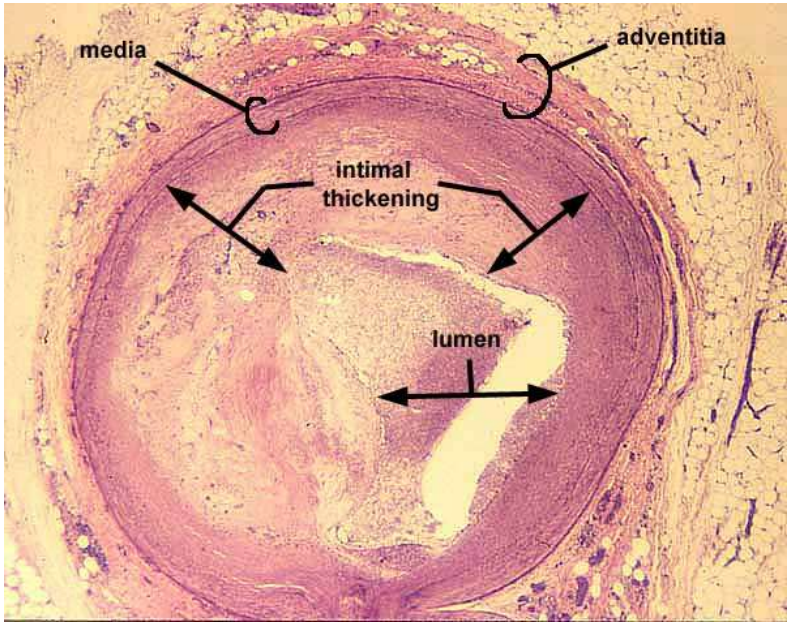
…no dilatation - avoids barotrauma and recoil

…smoothens the lumen

…reduces the need of stents

Rationale for Plaque Excision and Drug-Delivery as an Essential Combination





- **Mechanically recanalize the vessel without overstretch**
- **Remove the perfusion barrier – better and more homogenous drug uptake?**
- **Reduce the likelihood of bail-out stenting and preserve the native vessel**

Is upfront atherectomy prior to DCB effective?

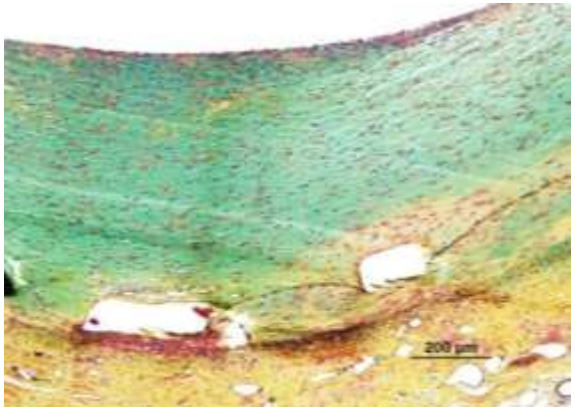
Animal data

ISR model

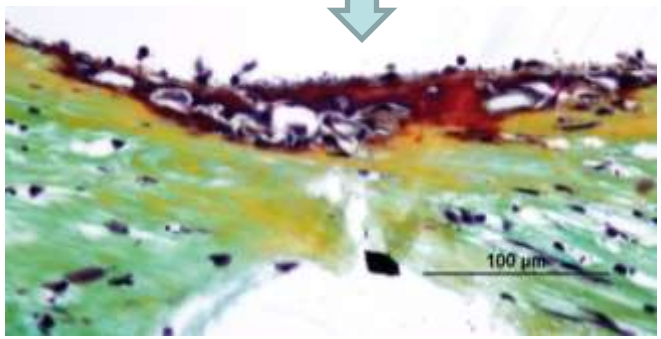
Preclinical Study

Histology Example

Control: PTX-coated balloon

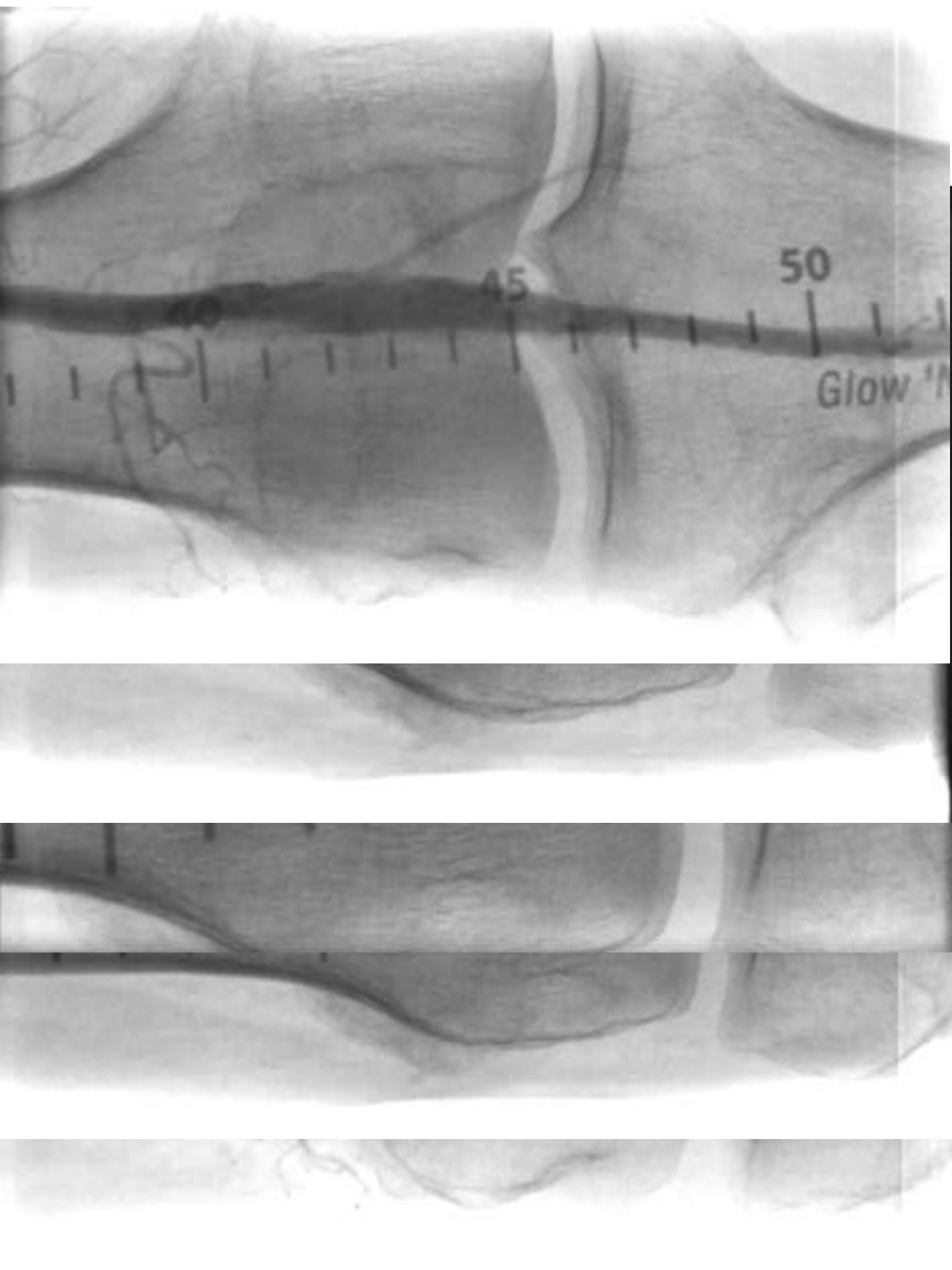


Test: plaque excision + PTX- coated ballo

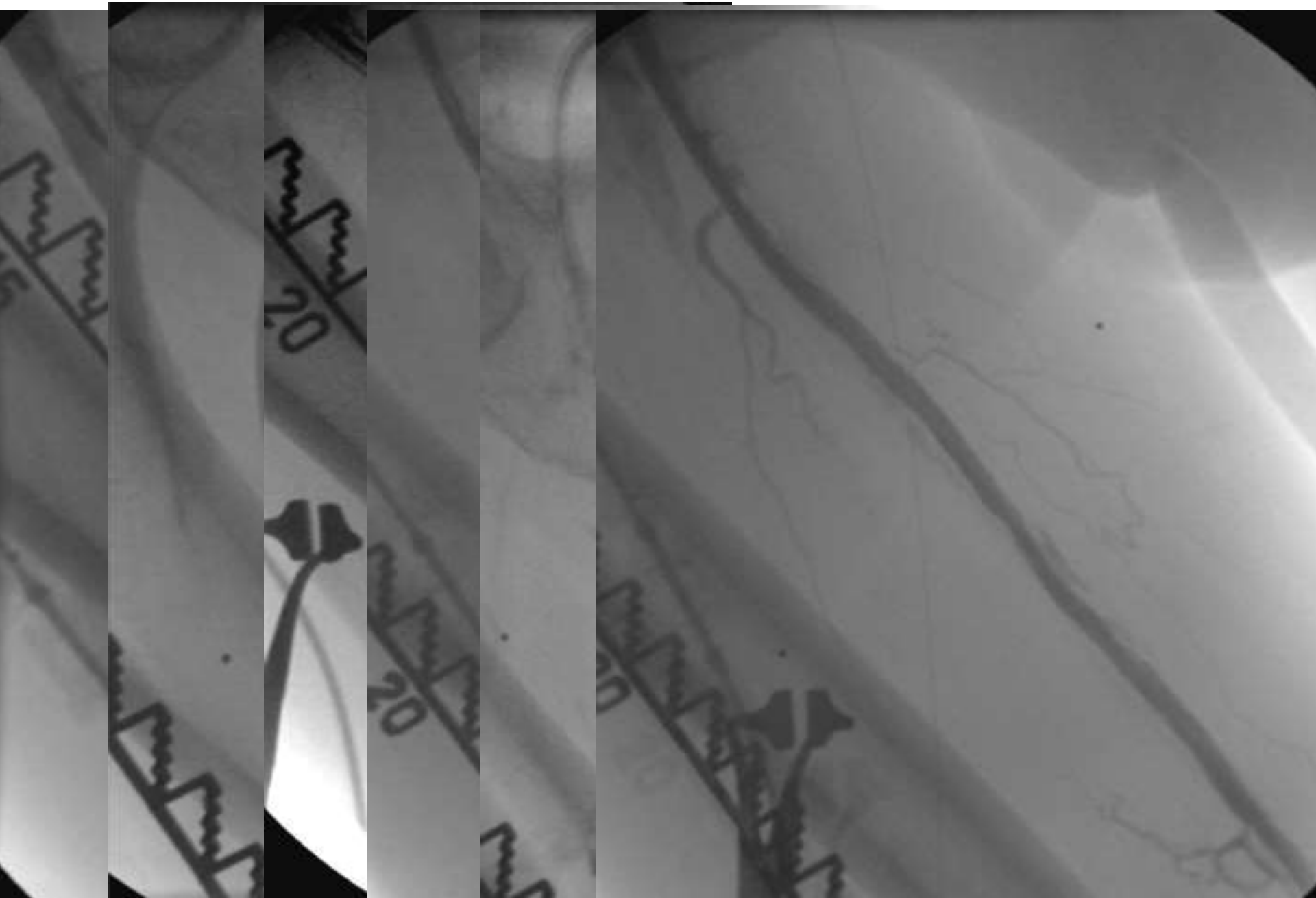


In areas of directional atherectomy, minimal neointimal hyperplasia was noted. The healing response was similar to what has been observed in sirolimus and paclitaxel coated stents pre-clinical work

Histology performed by CVPath

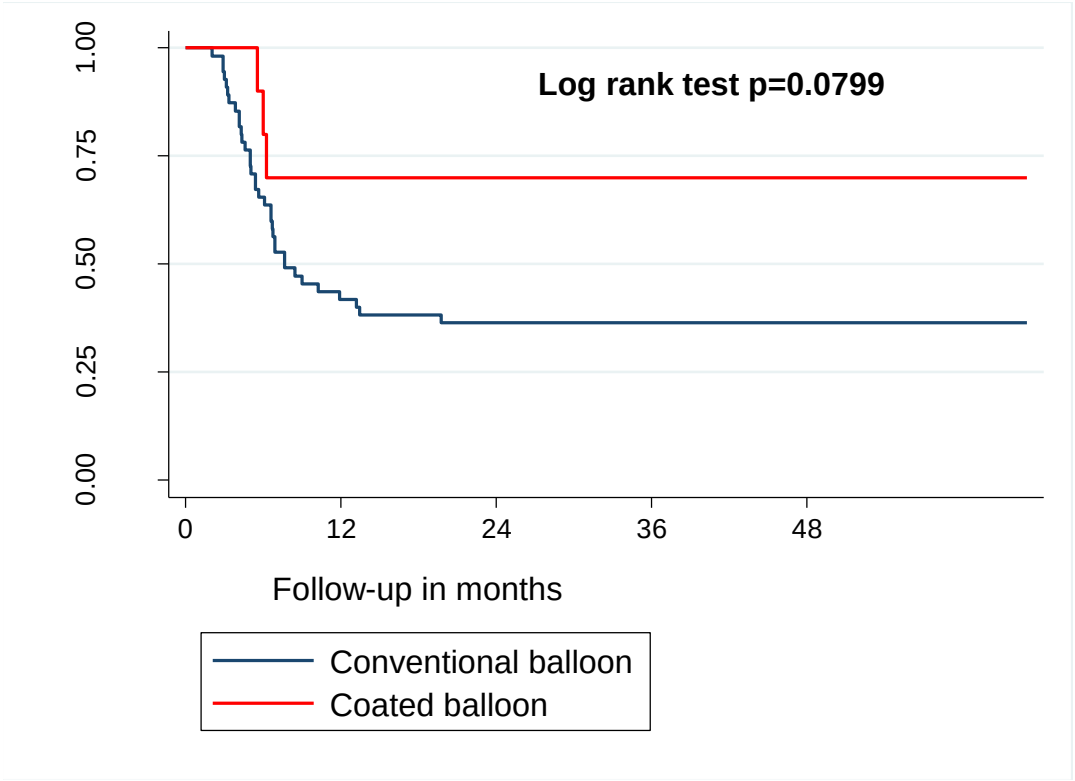

45
50
Glow

Jetstream – *Calcified Lesion*



Directional SilverHawk Plaque Excision

Event free survival without TLR



	OR	SE	P	Lower 95% CI	Upper 95% CI
Dyslipidemia	**5.25**	**4.787**	**0.070**	**0.873**	**31.4**
Nicotin	**0.280**	**0.157**	**0.024**	**0.929**	**0.844**
Lesion length	**1.00**	**0.002**	**0.003**	**1.002**	**1.010**
Balloon type*	**0.186**	**0.115**	**0.007**	**0.055**	**0.629**

SFA - *Severely Calcified lesions*

high promising signal of safety and efficacy in combination with Atherectomy to treat severly calcified SFA lesions

A.Cioppa (Cardiovasc. Revasc. Medicine 2012)

Contents lists available at SciVerse ScienceDirect

Cardiovascular Revascularization Medicine

Combined treatment of heavy calcified femoro-popliteal lesions using directional atherectomy and a paclitaxel coated balloon: One-year single centre clinical results☆

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ABSTRACT

Background: The use of Directional Atherectomy (DA) for the treatment of calcified femoro-popliteal lesions seems to improve the acute procedural success, however without reducing the long term restenosis rate. Drug coated balloons (DCB) reduced restenosis rate in non heavy calcified lesions. Aim of this study was to demonstrate safety and efficacy of a combined endovascular approach using DA and DCB for the treatment of heavy calcified lesions of the femoro-popliteal tract.

Methods: From January 2010 to November 2010, 240 patients underwent PTA of the femoro-popliteal tract in our institution. Within this cohort a total of 30 patients had Life Limiting Claudication (LLC) (n = 18) and 12 a Critical Limb Ischemia (CLI) with baseline Rutherford class 4.2 ± 1.2 underwent PTA of heavy calcified lesions with intravascular ultrasound guided DA and DCB. All procedures have been performed using a distal protection device. Stent implantation was allowed only in case of flow limiting dissections or suboptimal result (residual stenosis > 50%) by visual estimation. After the intervention patients were followed up to 12 months.

Results: Procedural and clinical success, was achieved in all cases. Bail-out stenting was necessary in only two (6.5%). At twelve month follow up median Rutherford class was 2.2 ± 1.2, ABI was 0.8 ± 0.1 and Limb salvage rate was 100%. Two minor, foot finger or forefoot amputations, were performed to reach complete wound healing and/or preserve deambulation. Duplex control was performed in all the cases (n = 30). In three cases duplex scan showed a significant target lesion restenosis requiring a reintervention (TLR = 10%) leading a total one-year secondary patency rate of 100%. All the three restenosed patients were insulin dependent diabetics and none of them were stented during the procedure.

Conclusion: The data suggest that combined use of DA and DCB may represent a potential alternative strategy for the treatment of femoro-popliteal severely calcified lesions. These very promising data and the considered hypothesis have to be confirmed in a multicentre randomised trial.

30-patient single-center Registry

- LLC / CLI = 6% / 94%
- Diabetics = 60%
- Mean lesion length = 115±35 mm
- Tot Occlusions = 13%
- Calcium Score* 3 = 100%

•dist. Filter + TurboHawk + IN.PACT

- bail-out Stenting = 7%

•12-month results:

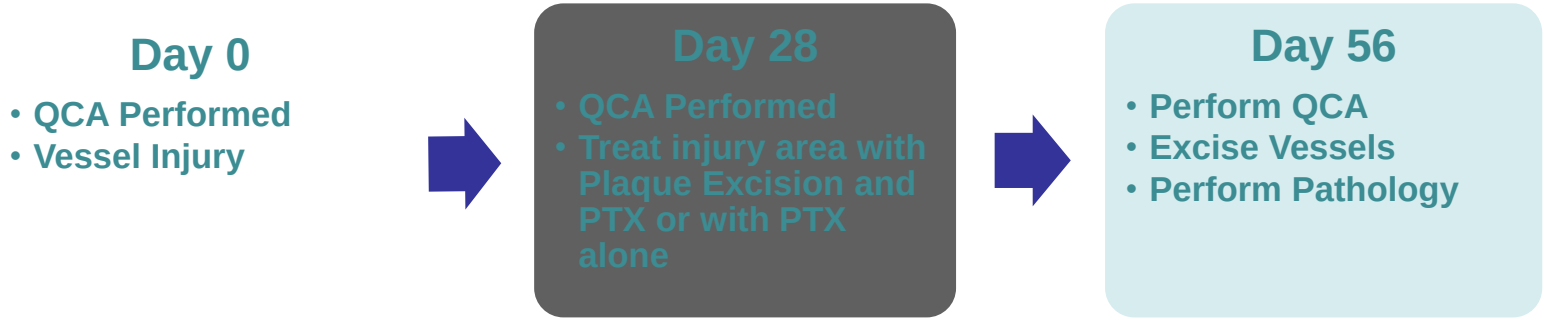
- Primary Patency = 90%
- TLR = 10%
- Second. Patency = 100%

* 0= absence of calcium; 1= calcium on one side of lumen <1cm length; 2= calcium on both side <1cm length; 3=calcium on both side >1 cm length

Pre-clinical work evaluated safety of Plaque Excision prior to drug delivery

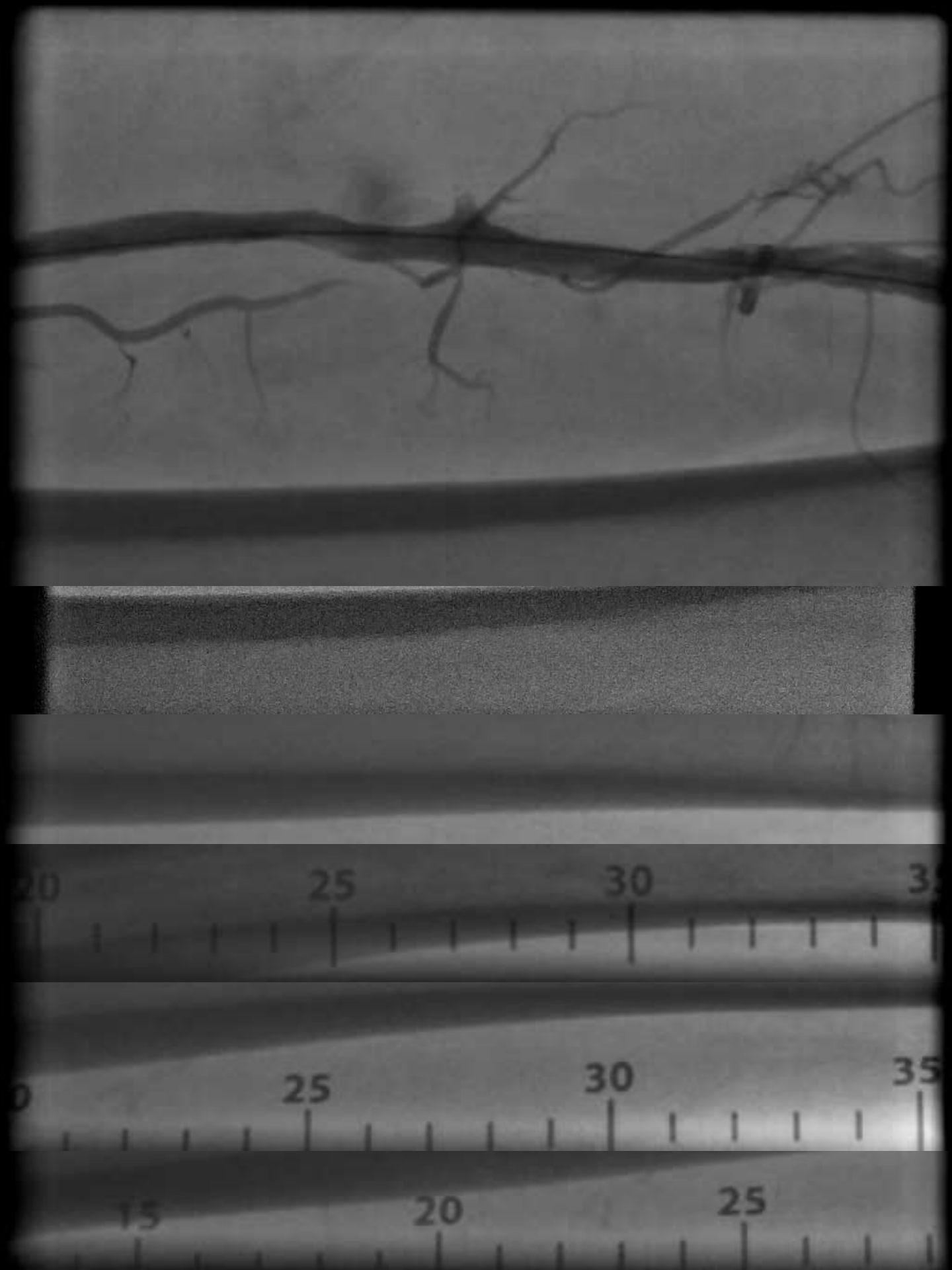
Data from pre-clinical studies indicate the safety profile of the SilverHawk™ device used in combination with a Paclitaxel-coated balloon is acceptable; use of this combination in a human clinical study is appropriate.

Pre-clinical Study Methodology:



Pre-clinical Conclusions:

- **Lack of aneurysms found in either the test or control group**
- **Similar luminal area between the control and treatment groups at Day 56**
- **Lack of medial thinning**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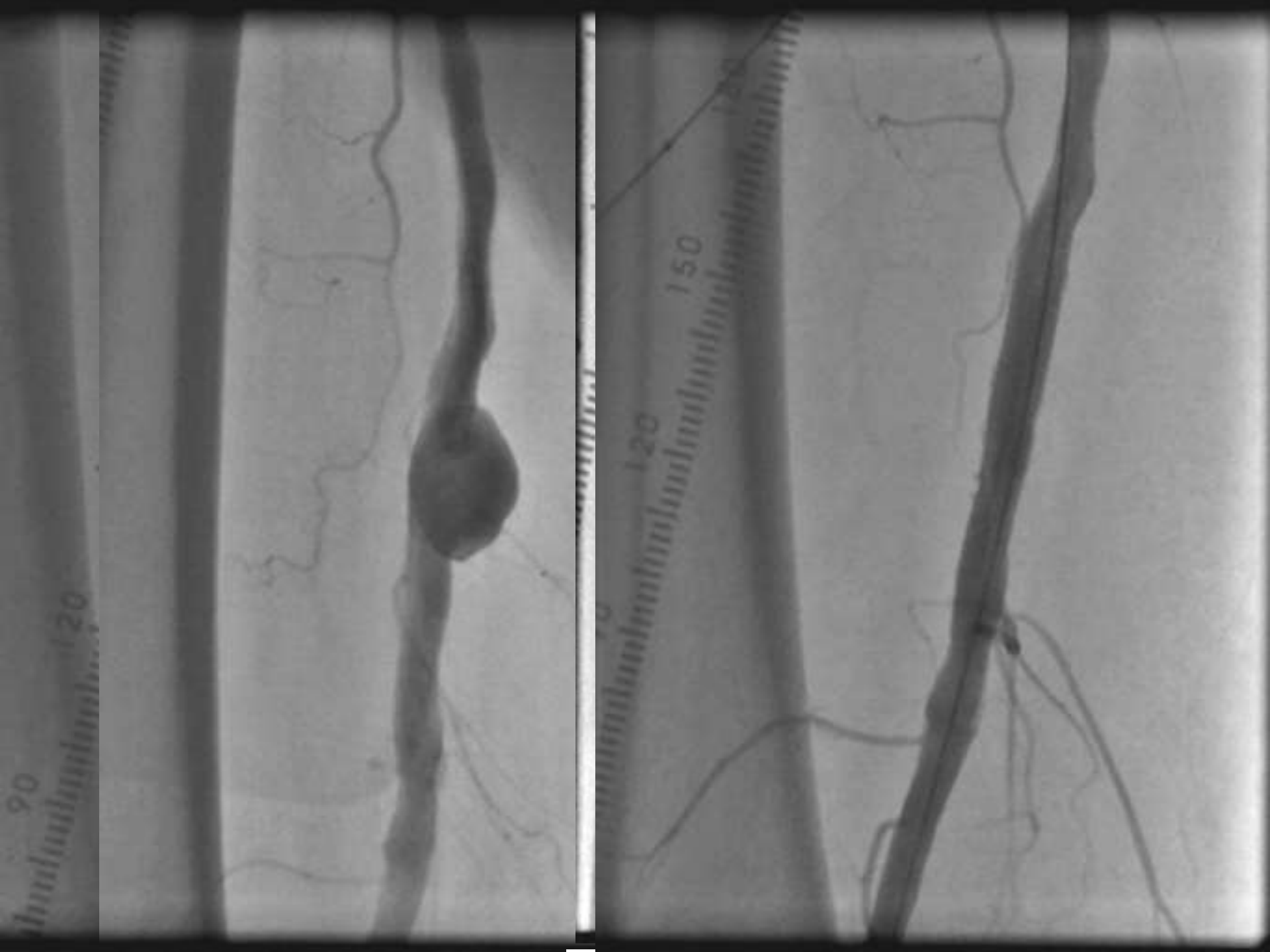
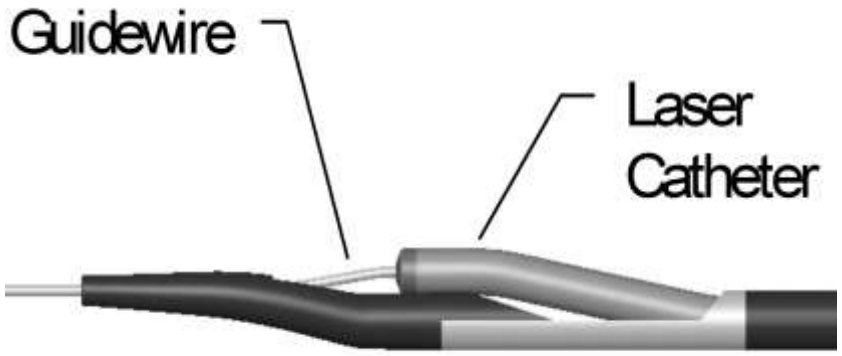

90
120
150
120

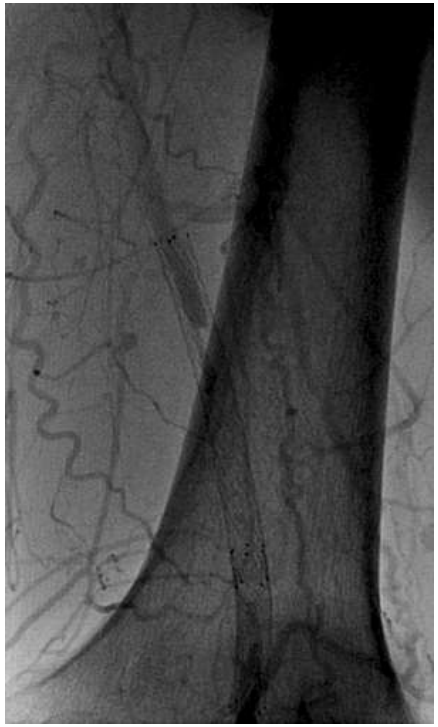
Atherectomy & DCB?

- **PHOTOPAC: Laseratherectomy & DCB vs. DCB in instent-restenosis**
  - PIs: Scheinert / Zeller



- **DEFINITIVE AR: DCA & DCB vs. DCB in native vessels**
  - PIs: Tepe / Zeller

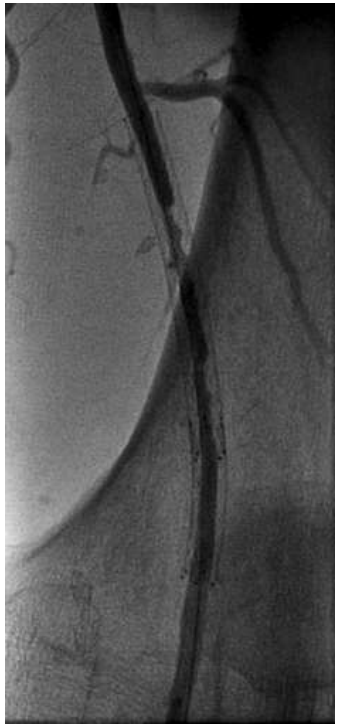
Case 1: Atherectomy



Pre-

Rotarex

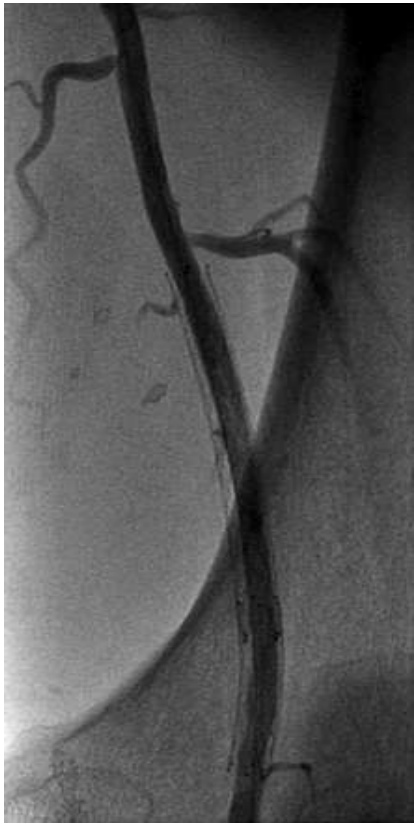
Case 1: Atherectomy



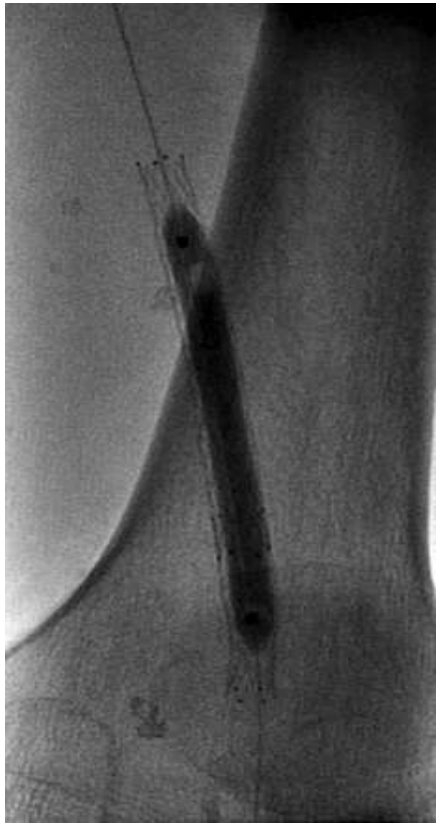
Post Rotarex

Silverhawk

Case 1: Atherectomy



Post Silverhawk



DEB

Post DEB

Case 2: Atherectomy

Silverhawk

Case 2: Atherectomy

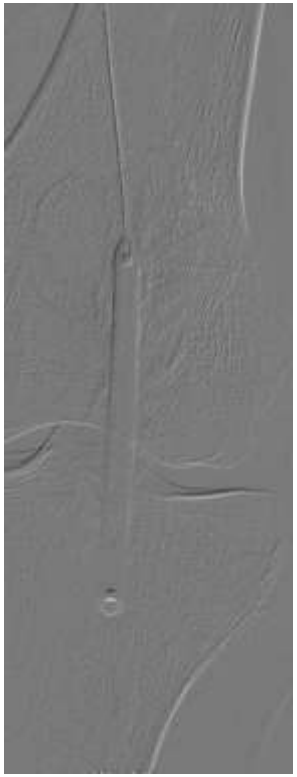
Post Silverhawk plus DEB

4 W F/U

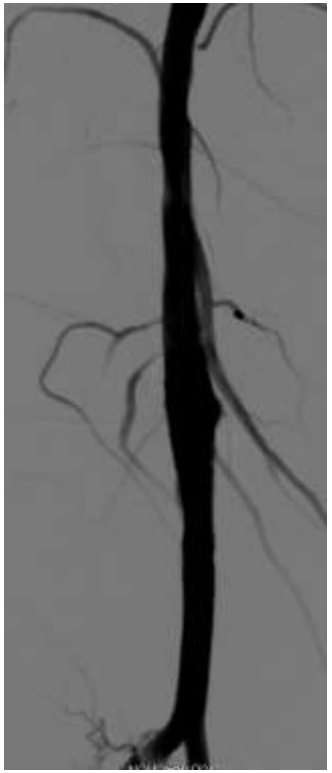
Case 3: Atherectomy

Pre

Post Silverhawk

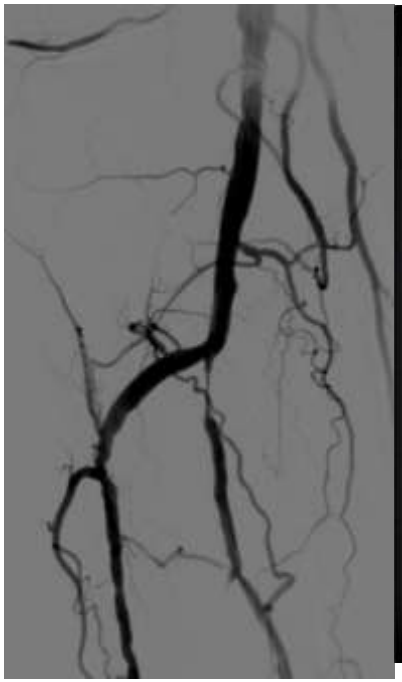


DEB



final

Case 4: Atherectomy



Pre

Silverhawk

final

Balloon for PTA

	014	018	035
Abbott	Armada14	Fox cross	Armada35
Boston	Coyote (M)		*Mustang (NC)*
Cook	Advance 14 (M)	Advance 18	Advance 35
Cordis	Sleek (M)	Savvy	PowerFlex
Medtronic	Amphirion (M)		***InPact (DCB)***
Covidien	Nanocross		Evercross
Biotronik	Passeo 14	Passeo 18 ***Passeo-18 Lux (DCB)***	Passeo 35, *Passeo 35-HP (NC)*
Bard			Rival, *Conquest (NC)* ***Lutonix (DCB)***

*M; monorail type available
NC; Non-compliant balloon
DEB; Drug-eluting balloon

Stents for PTA

	014/018	035	
Abbott	Xpert (SES), **Supera**	Absolute Pro	Omnilink (BES)
Bard		LifeStent	
Cordis	Precise (SES)-Carotid Palmaz Blue/Genesis (BES)-Renal	*Smart*	
Gore		**Viabahn** (Stentgraft)	
Cook		Zilver, Zilver PTX (DES)	
Medtronic	Maris deep (SES);014 & 018 Chromis Deep (BES)	Complete SE	Scuba (BES)
Boston		Wall Stent, Epic, Inova, Eluvia (DES)	
Covidien		Protege	
Biotronic	Pulsar (018)	Pulsar (035)	
Terumo		Misago	

***SES; Self-expanding stent, BES; Balloon-expandable stent,**
DES; Drug-eluting stent **BTK stents; disappeared in the market

Plaque Modification/Debulking Devices in Korea

1. **Cutting balloon (Boston)**
2. **Scoring Balloon; *Vascutrak (Bard),* AngioSculpt (Spectranetics) or NSE balloon (Goodman)--pending**
3. **Directional Atherectomy Device**

   ; Silverhawk, Turbohawk, HawkOne (Covidien)
4. **Jetstream (Boston)**
5. **Rotablator (Boston)**

My SFA Strategy in 2017

1. More elaboration on balloon angioplasty with adequate size (at least 2-3 min).
2. Mostly finalize with DCBs (popliteal-1, SFA-2)
3. Calcified, hard ISR lesion; plaque modification with debulking, scoring ballooning and NC ballooning
4. Stented CTO; Jetstream, NC and DCB
5. No stent zone; DAART, bailout stenting-Supera
6. Heavily calcified lesion in mid to distal SFA and popliteal; Supera
7. Poor balloon response; Primary DESs (Zilver PTX or Eluvia)

Initial Look at the Global Lutonix DCB BTK Registry Study 6 Month Outcomes

A Prospective, Multicenter, Single-Arm Real-World Registry Investigating the Clinical Use and Safety of the Lutonix Drug Coated Balloon PTA Catheter for Treatment of Below-the-Knee (BTK) Arteries

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Vascular Centre Arnsberg Clinic

Dierk Scheinert, M.D.
Universitätsklinikum Leipzig

Study Design

Study Design	Prospective, Multicenter, Single Arm Registry
Objective	To demonstrate safety and assess the clinical use and outcomes of the Lutonix DCB for treatment of stenosis or occlusion of native below-the- knee arteries in a heterogeneous patient population in real world clinical practice
Number of patients/sites	Up to 500 subjects to be enrolled at up to 35 international sites
Inclusion Criteria	Rutherford Class: 3-5, ≥ 70% stenosis lesion, target vessel(s) reconstitute(s) at or above the ankle with inline flow to at least one patent
Exclusion Criteria	Neurotrophic ulcer or heel pressure ulcer or ulcer potentially involving calcaneus (index limb)
Primary Endpoints	Safety: Freedom from BTK MALE+POD at 30-days Efficacy: Freedom from TLR at 6 months
Follow-up	1, 6, 12 and 24 Months

Patient Follow-Up

EVENT	Pre-Procedure	Procedure	Post-Procedure	30 Day	6 Month	12 Month	24 Month
Visit Window				±2 Weeks	±1 Month	±1 Month	±2 Months
Inclusion/Exclusion Criteria	√	√					
Informed Consent	√						
Medical History	√						
Routine Physical Exam	√		√	√[1]	√	√	√[1]
Current Medication	√			√	√	√	√
Rutherford Classification	√			√[1]	√	√	√[1]
Adverse Event Monitoring		√	√	√	√	√	√
Wound Healing Assessment	√			√[1]	√	√	√[1]

[1]Required only if clinical visit occurs

Demographics / Baseline Characteristics

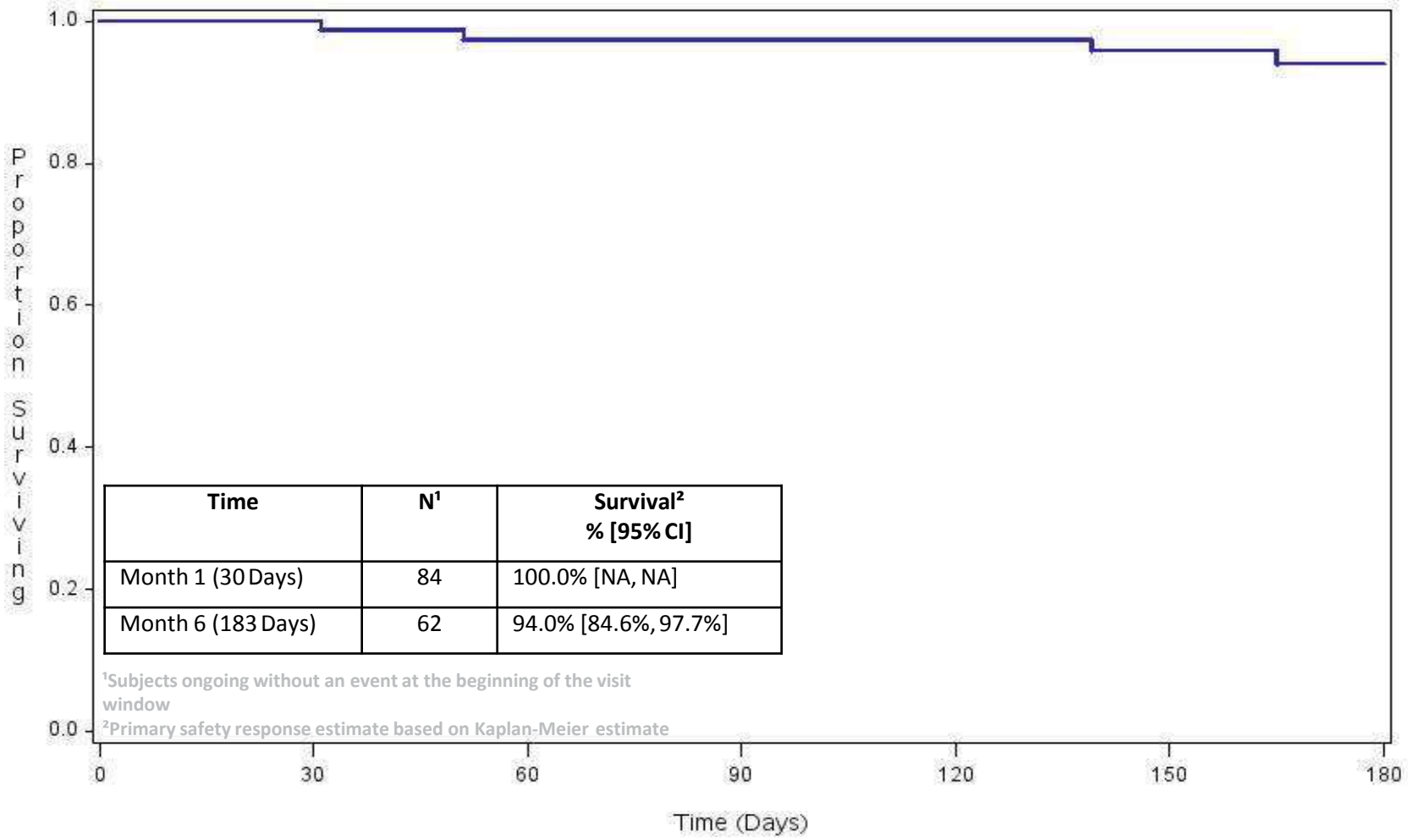
Description	BTK Study Registry (N=85)
Age (Years), Mean ± SD (n)	73.9 ± 10.2 (85)
Gender, % (n/N)	
Female	29.4% (25/85)
Male	70.6% (60/85)
BMI ≥30 kg/m², % (n/N)	25.0% (21/84)
Hypertension, % (n/N)	87.1% (74/85)
Dyslipidemia, % (n/N)	60.0% (51/85)
Current/Previous Smoker, % (n/N)	47.1% (40/85)
Diabetes	57.6% (49/85)
Rutherford Category	
3	19.0% (16/84)
4	16.7% (14/84)
5	64.3% (54/84)

Lesion Characteristics

Description	BTK Study Registry (N=85)
Lesion Location[1]	
Popliteal	9.4% (8/85)
Tibioperoneal Trunk	27.1% (23/85)
Anterior Tibial	34.1% (29/85)
Posterior Tibial	24.7% (21/85)
Peroneal	25.9% (22/85)
Total Target Length (mm), Mean ± SD (n)	102 ± 79.5 (85)
Average RVD (mm), Mean ± SD (n)	2.7 ± 0.57 (85)
(min, max)	(2.0, 4.0)
Calcification, % (n/N)	63.8% (51/80)
Severe Calcification, % (n/N)	10.5% (8/76)

[1]Subjects may be in more than one category.

Freedom from Primary Safety Events



Time	N[1]	Survival[2] % [95% CI]
Month 1 (30 Days)	84	100.0% [NA, NA]
Month 6 (183 Days)	62	94.0% [84.6%, 97.7%]

[1]Subjects ongoing without an event at the beginning of the visit window

[2]Primary safety response estimate based on Kaplan-Meier estimate

Freedom at 30-Days from the composite of all-cause death, above-ankle amputation or major re-intervention, i.e., new bypass graft, jump/interposition graft revision, or thrombectomy/thrombolysis of the index limb involving a below-the-knee artery.

Additional Safety Profile

Freedom From	N[1]	Survival[2] % [95% CI]
All Cause Death Survival	63	89.2% [79.5%, 94.4%]
Major Amputation	63	95.2% [85.8%, 98.5%]
Re-intervention for Thrombosis/Thrombolysis	62	96.1% [84.9%, 99.0%]
Re-intervention For Distal Embolization	63	100.0% [NA, NA]
TVR	59	89.8% [79.8%, 95.0%]
Unexpected Device or Drug Related Event	63	100.0% [NA, NA]

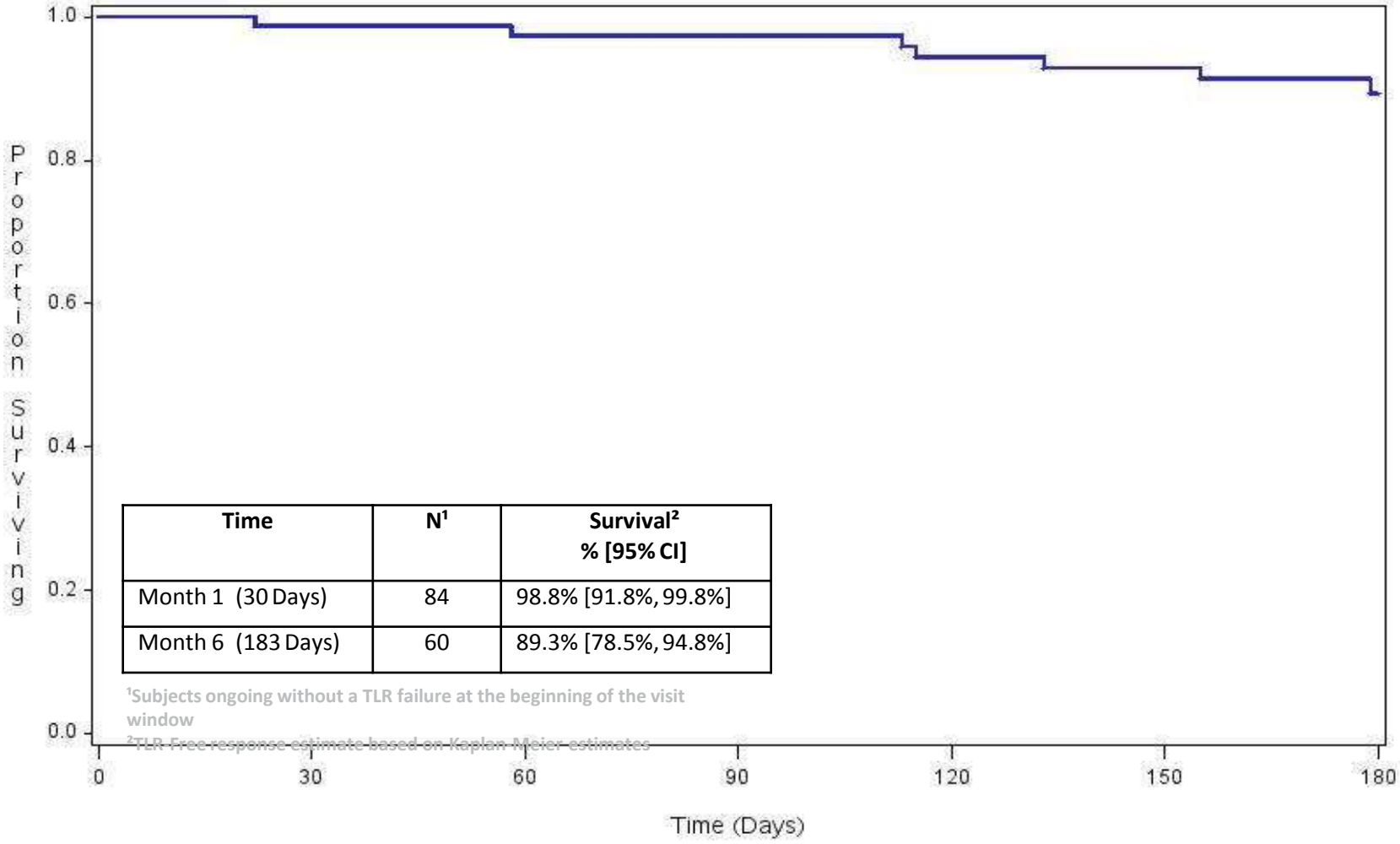
[1]Subjects ongoing without a failure at the beginning of the visit window

[2]Survivor rate based on Kaplan-Meier Estimate

Freedom from TLR

Lutonix Inc.
Protocol: CL0024 BTK Registry
Interim Data 20170110

Figure 14.3-2, Freedom from TLR Failure with Kaplan-Meier Method, ITT Subjects



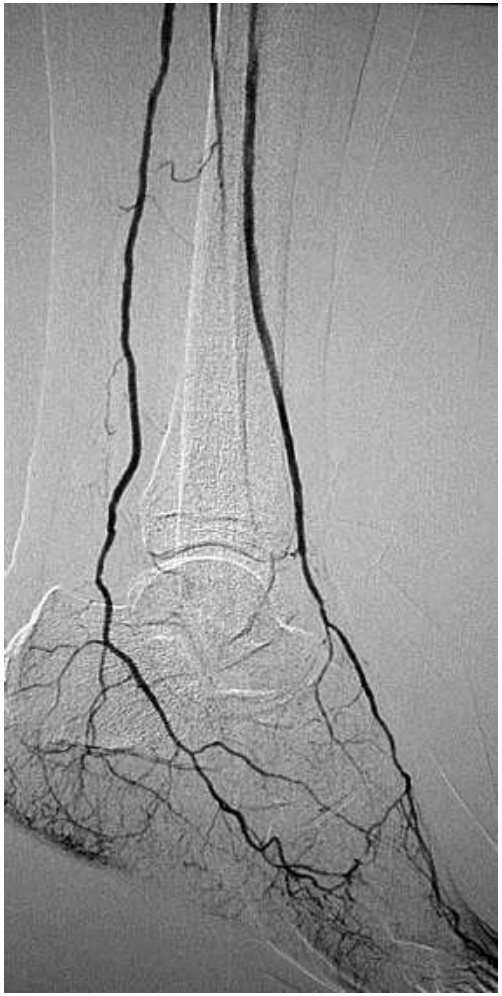
Time	N[1]	Survival[2] % [95% CI]
Month 1 (30 Days)	84	98.8% [91.8%, 99.8%]
Month 6 (183 Days)	60	89.3% [78.5%, 94.8%]

[1]Subjects ongoing without a TLR failure at the beginning of the visit window
[2]TLR Free response estimate based on Kaplan Meier estimates

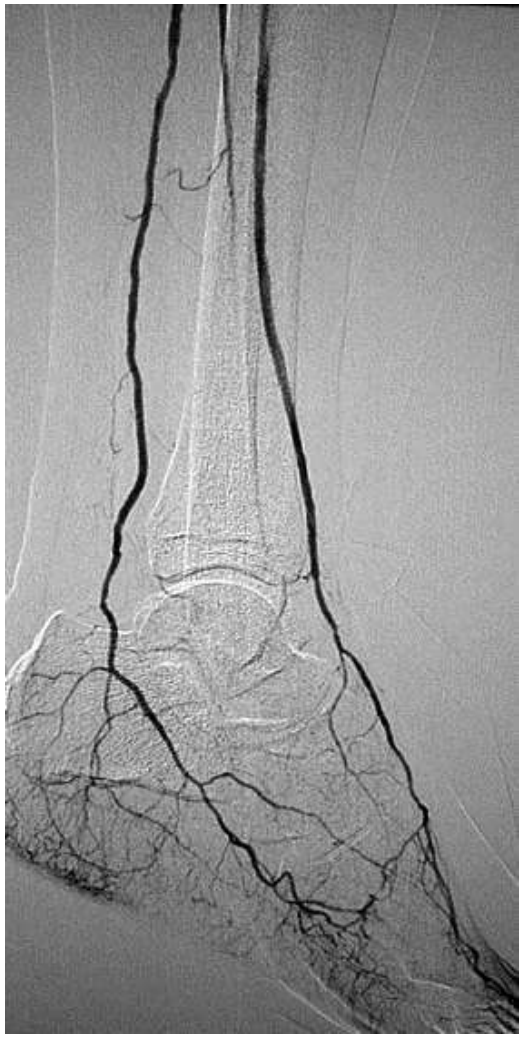
Male, 70 J, Diabetes, Endstage Renal Insufficency

Klinikum Arnsberg

Recanalisation with DCB Lutonix 2.5mm



Follow-up



Klinikum Arnsberg

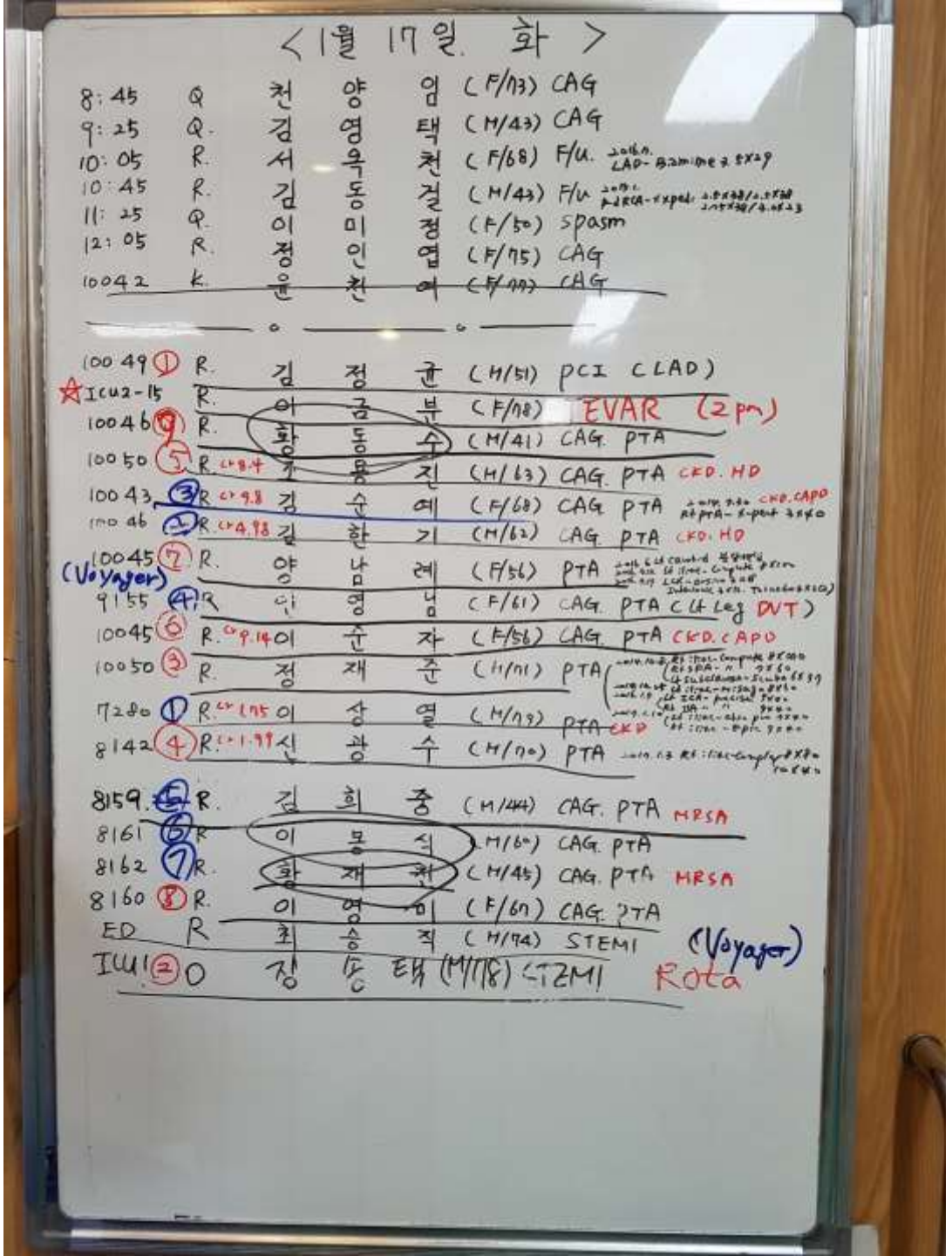
Lutonix BTK Registry ; Conclusions

- **Only BTK Registry Multi Center On-going Study**
- **Promising Treatment Effect in Below-the–Knee Arteries**
- **Safety Consistent with the Strong Safety Profile of the Lutonix DCB in PAD**
- **Freedom from TLR 89.3%**
- **Less than 5% Amputation Rate**
- **ZERO Re-interventions for Distal Embolizations**

Jan 17 (Tue), 2017
My Procedures in one day
(8am to 2am)-15 EVTs

1. Routine angiography; 7
2. Complex coronary PCI 3
3. TEVAR for AD; 1
4. IVC filter, thrombectomy and Stenting for May Thurner Synd
5. Complex PTA (Iliac, SFA, BTK) --13

Postponed 3 complex PTAs..



Save the Date !!

CCI Guro Live 2017

October 19~21, 2017

Oct 19 Evening symposium
Oct 20 Coronary
Oct 21 Peripheral

Korea University Guro Hospital, Seoul, Korea

Thank You for Your Attention!

Korea University Guro Hospital, Seoul, Korea