Vessel Preparation with Directional Atherectomy to improve Clinical Outcomes

Su Hong Kim MD PhD

Busan Veterans Hospital

Busan, Korea (South)

First of All

I ♥ DCB

DCB showed the superior outcomes at 4 years

OVERVIEW of IN.PACT SFA TRIAL

Objective: Assess the safety and efficacy of IN.PACT Admiral DCB vs. standard PTA for the treatment of superficial femoral and proximal popliteal artery disease due to claudication and rest pain

IN.PACT SFA I
150 subjects enrolled at 13 EU sites
Sep 2010-Apr 2011

+

IN.PACT SFA II
181 subjects enrolled at 44 US sites
Apr 2012-Jan 2013

Robust Level 1 Evidence

- Prospective, multicenter EU and US, randomized (2:1), single-blinded trial
- 331 patients enrolled: IN.PACT DCB (n = 220) *vs.* PTA (n = 111)

Rigorous and Unbiased

- Independent and blinded Duplex Ultrasound Core Lab,[1] Angiographic Core Lab,[2] and Clinical Events Committee[3]
- Independent Safety Monitoring Board
- External monitoring with 100% source data verification

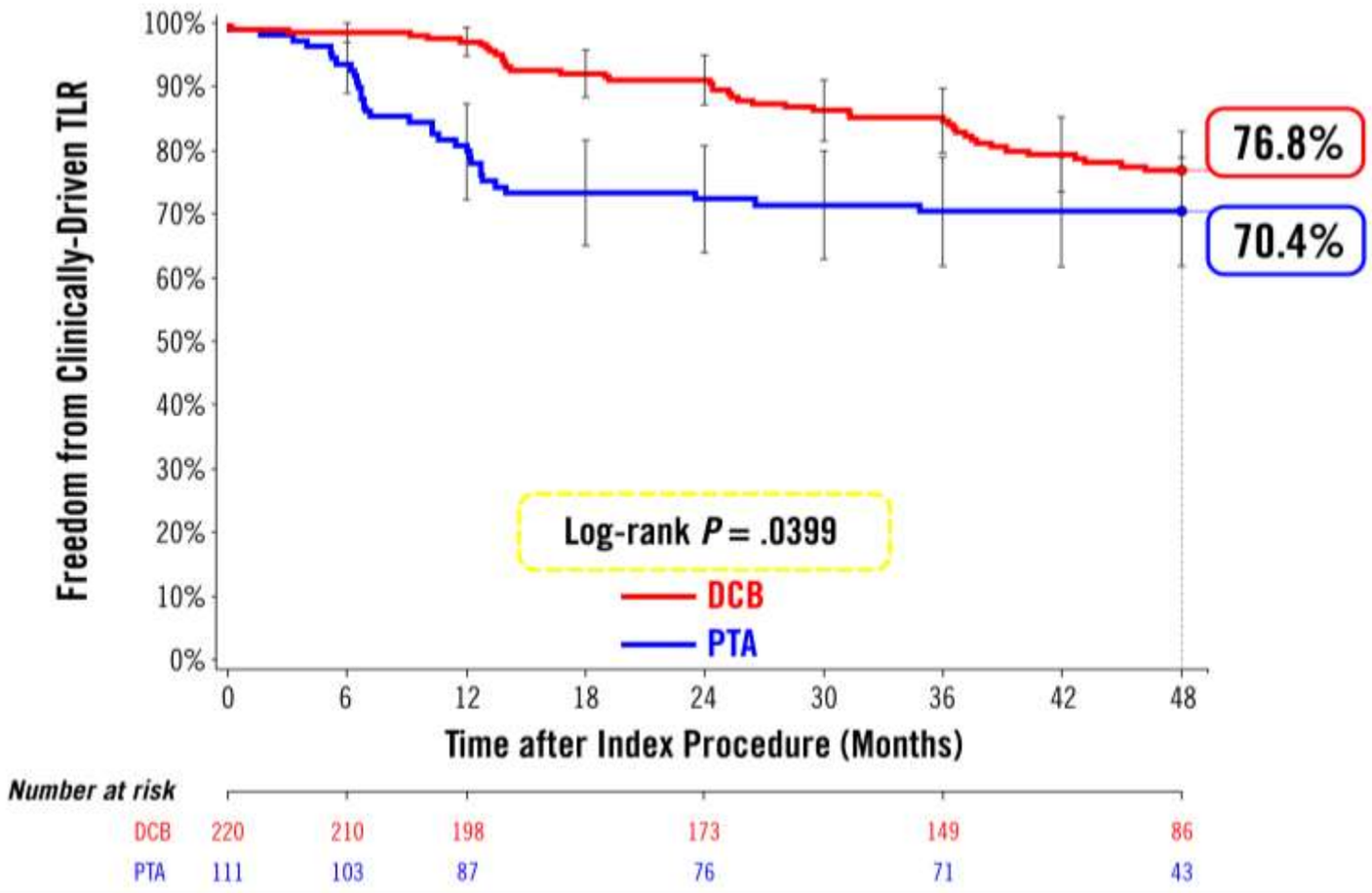
Durability of Outcomes

- Subjects followed up to 5 years

보훈공단 부산보훈병원

1) VasCore DUS Core Laboratory, Boston, MA, US;
2) SynvaCor Angiographic Core Laboratory, Springfield, IL, US;
3) Clinical Events Committee and Data Safety Monitoring services provided by HCRI, Boston, MA, US

DCB showed the superior outcomes at 4 years



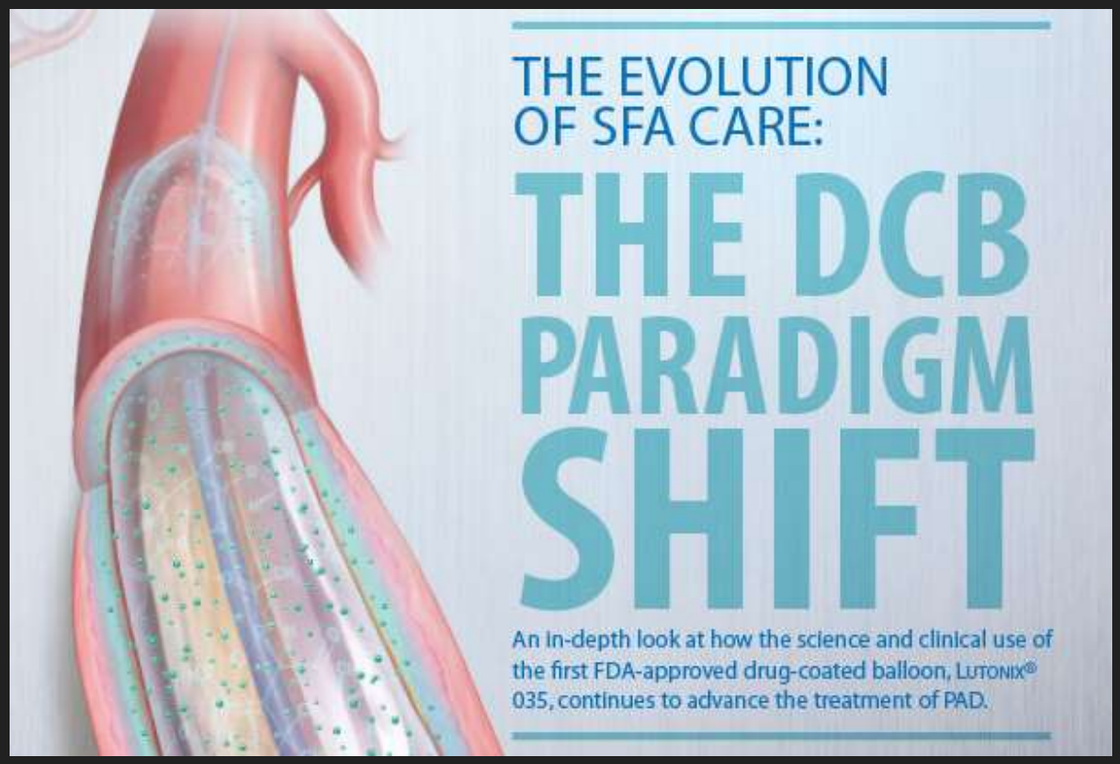
	IN.PACT DCB (N=220)	PTA (N=111)	P-value†
Clinically-driven TLR [1]	23.4% (43/184)	31.1% (32/103)	0.164
Any TLR [2]	24.5% (45/184)	34.0% (35/103)	0.100
Time to First CD-TLR	**739.2 ± 384.0**	**302.9 ± 213.0**	**< 0.001**

1. Clinically-driven TLR adjudicated by an independent Clinical Event Committee, blinded to the assigned treatment based on any re-intervention at the target lesion due to symptoms or drop of ABI of ≥20% or >0.15 when compared to post-procedure baseline ABI
2. Any TLR includes clinically-driven and incidental or duplex driven TLR
3. Freedom from target limb amputation, target vessel revascularization (TVR), and increase in Rutherford class
4. TBI allowed / used in case of incompressible vessels in IN.PACT SFA II phase
5. † Unless otherwise indicated, all tests were for superiority using the Fisher's exact test for binary variables and t-test for continuous variables.

보훈공단 부산보훈병원

Peter A Schneider. VIVA 2017

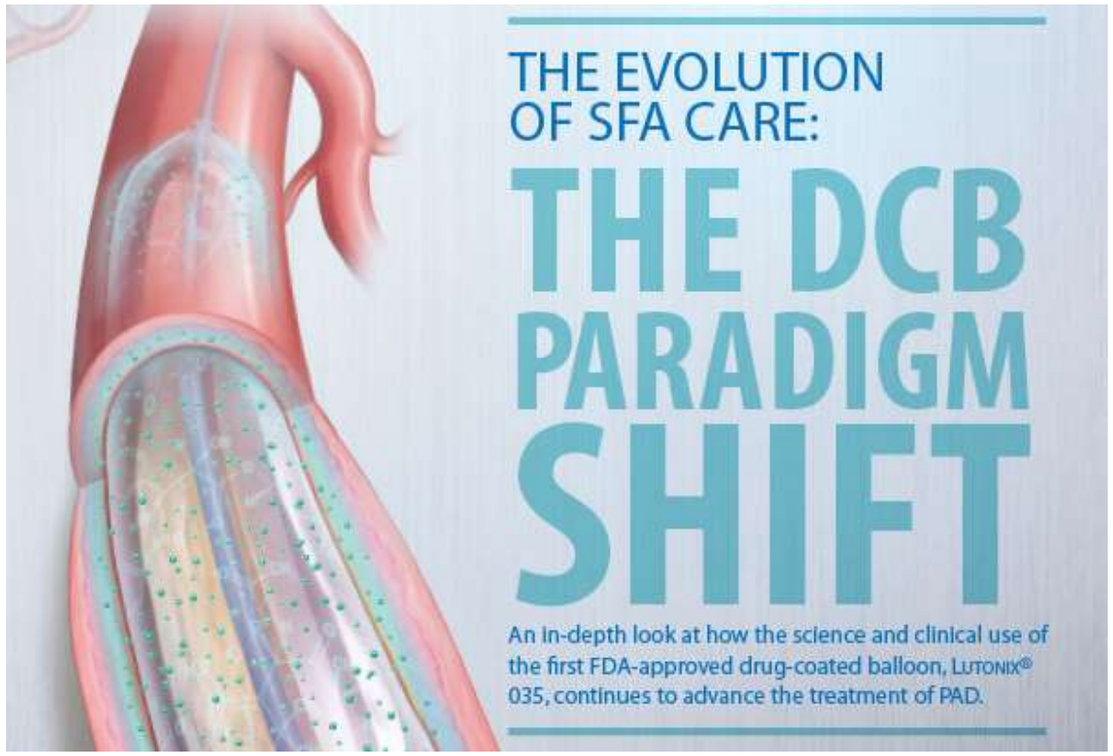
Luminal Gain
Plaque Modification



Vessel Preparation

Goal of Vessel Preparation in PAD

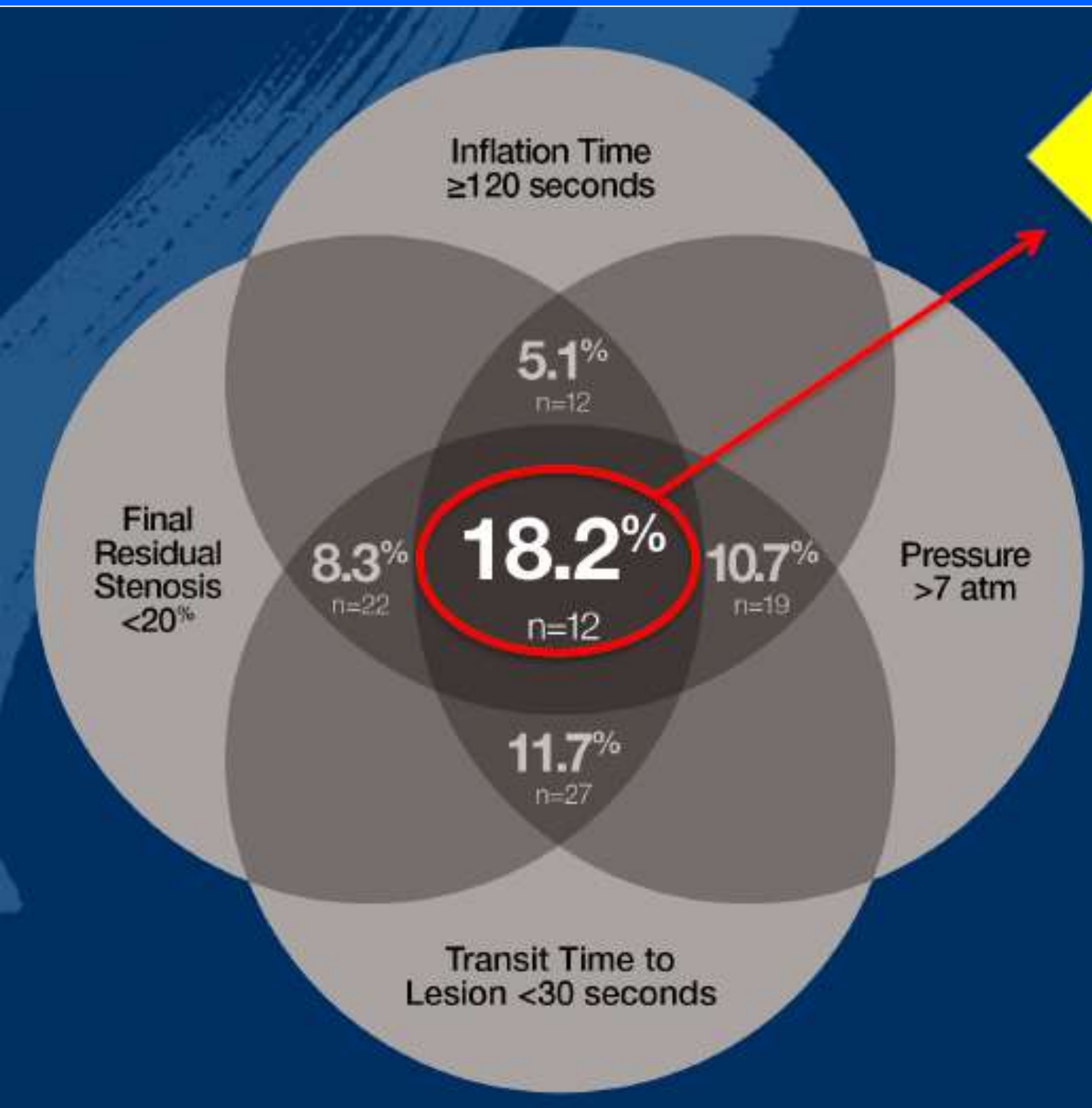
1) Removing Calcification
2) Modifying plaque
3) Gaining lumen



DCBs may be more efficacious
in delivering drug to the vessel wall

보훈공단
부산보훈병원

Procedural Techniques for Optimal Drug Delivery



Percent Increase Over LEVANT 2
12-Month 73.5% PP*

Observational post-hoc, sub-group analysis suggests that LUTONIX® DCB procedural techniques may affect 12 M Primary Patency may be:

- ✓ **Improved with 3 variables***
- ✓ **Optimal with all 4 variables***

* These data are observational only. Further confirmatory clinical evidence is required to support the conclusions that the combination of any of these four procedural techniques will always yield an improved primary patency beyond the published primary patency of 73.5%.

Good Predilation

- Optimal PTA : effect of Short vs. Long Balloon Inflation Times on Morphologic Results

	Inflation Time (sec)		
	30	180	*P*-Value
Major dissection (grades 3 or 4)	16	5	.010
Minor or no dissection (grades 1 and 2)	21	32	.010
Further interventions (Stent, repeat dilatation, dilation with larger diameter)	20	9	.017
Residual stenosis (>30%)	12	5	.097
Complication (embolization, thrombosis)	1	1	-
Mean ankle-brachial index (before, after intervention)	0.66, 0.87	0.65, 0.84	

- 180s Inflation times : improve immediate PTA results, fewer major dissections & modest reduction of residual stenosis
- Significantly Fewer more intervention (eg. provisional stenting)

Zorger N, et al. J Vasc Interv Radiol 2002;13:355-9

보훈공단 부산보훈병원

Vessel Preparation Goals

1) Pretreat with predilation balloon more than 1:1 ratio

2) Remove the barrier to drug delivery

3) Avoid drug loss on the way to lesion

4) Maximize DCB expansion & Vessel Wall contact

5) Minimize dissectioins

Challenges to Optimal Vessel Preparation

1. Flow Limiting Dissection
2. Long Lesion Lengths
3. Chronic Total Occlusions
4. Vessel Calcification

보훈공단
부산보훈병원

Challenges to Optimal Vessel Preparation

1. Flow Limiting Dissection

Product	Study	Dissection Rate	
Lutonix 035	LEVANT 2	Grade C	2.5% (8/316)
	LUTONIX Long Lesion	Grade C	12.2% (10/82)
		Grade D	1.2% (1/82)
Stellarex	ILLUMENATE EU	Flow Limiting	0.4% (1/254)
	ILLUMENATE Global	Grade D	19.7% (81/416)
		Grade E/F	0.2% (1/416)
	ILLUMENATE Pivotal	Grade D	20.0% (40/200)
		Grade E/F	0.2% (1/416)
IN.PACT Admiral DCB	IN.PACT SFA	Grades D-F	0.0% (0/221)
	IN.PACT Global ISR	Grades D-F	4.7% (7/149)
	IN.PACT Global CTO	Grades D-F	23.6% (3/127)
	IN.PACT Global Long Lesion	Grades D-F	14.9% (24/161)

1. Rosenfield, K., et al. (2015). N Engl J Med 373(2): 145-153.
2. Bard Lutonix Instructions for Use, BAW1387400r3.
3. Schroeder, H., et al. (2017). Circulation.
4. Zeller T, LINC Leipzig, Germany 2017.
5. Krishnan, P., et al. (2017). Circulation.
6. Tepe, G., et al. (2015). Circulation 131(5): 495-502.
7. Brodmann, M. VIVA 2015.
8. Tepe, G. Charing Cross 2016.
9. Scheinert, D. EuroPCR 2015.

Challenges to Optimal Vessel Preparation

1. Dissection severity and patency outcomes after POBA

J Endovasc Ther. 2017 Jun;24(3):367-375. doi: 10.1177/1526602817698634. Epub 2017 Mar 20.

Angiographic Dissection Patterns and Patency Outcomes After Balloon Angioplasty for Superficial Femoral Artery Disease.

Fujihara M[1,2], Takahara M[3], Sasaki S[4], Nanto K[5], Utsunomiya M[6], Iida O[5], Yokoi Y[1].

- Japanese Registry Data
- Dissection grades of C (dissection with contrast outside the lumen) or higher were observed in 42% of balloon angioplasty cases
- Presence of a type C or higher dissection was associated with higher rates of bailout stenting, lower primary patency, & high rates of target lesion revascularization (TLR)
- Stepwise relationship between dissection severity and restenosis, suggestive a continuum of risk for dissections grade C through F

DCB and Dissection in outcomes

- Preliminary results : high grade dissections after DCB angioplasty are not associated with restenosis, possible due to vessel remodeling or an altered healing process in the presence of paclitaxel

POBA ≠ DCB

Role of DCBs

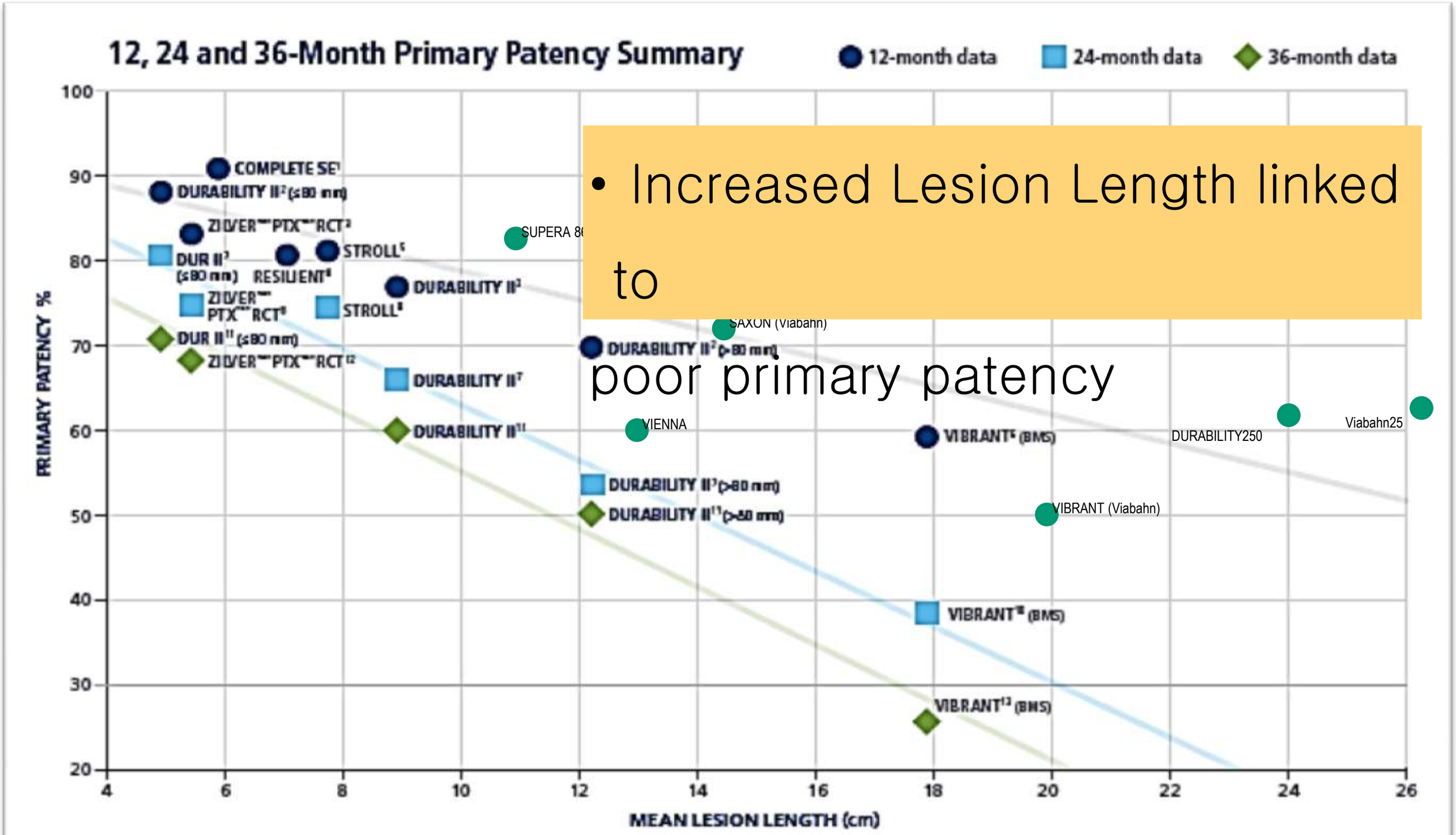
Just Drug Delivery

보훈공단 부산보훈병원

Tepe G, Zeller T, Schnorr B, et al. J Endovasc Ther. 2013;20:792-8

Challenges to Optimal Vessel Preparation

2. Long Lesion Length



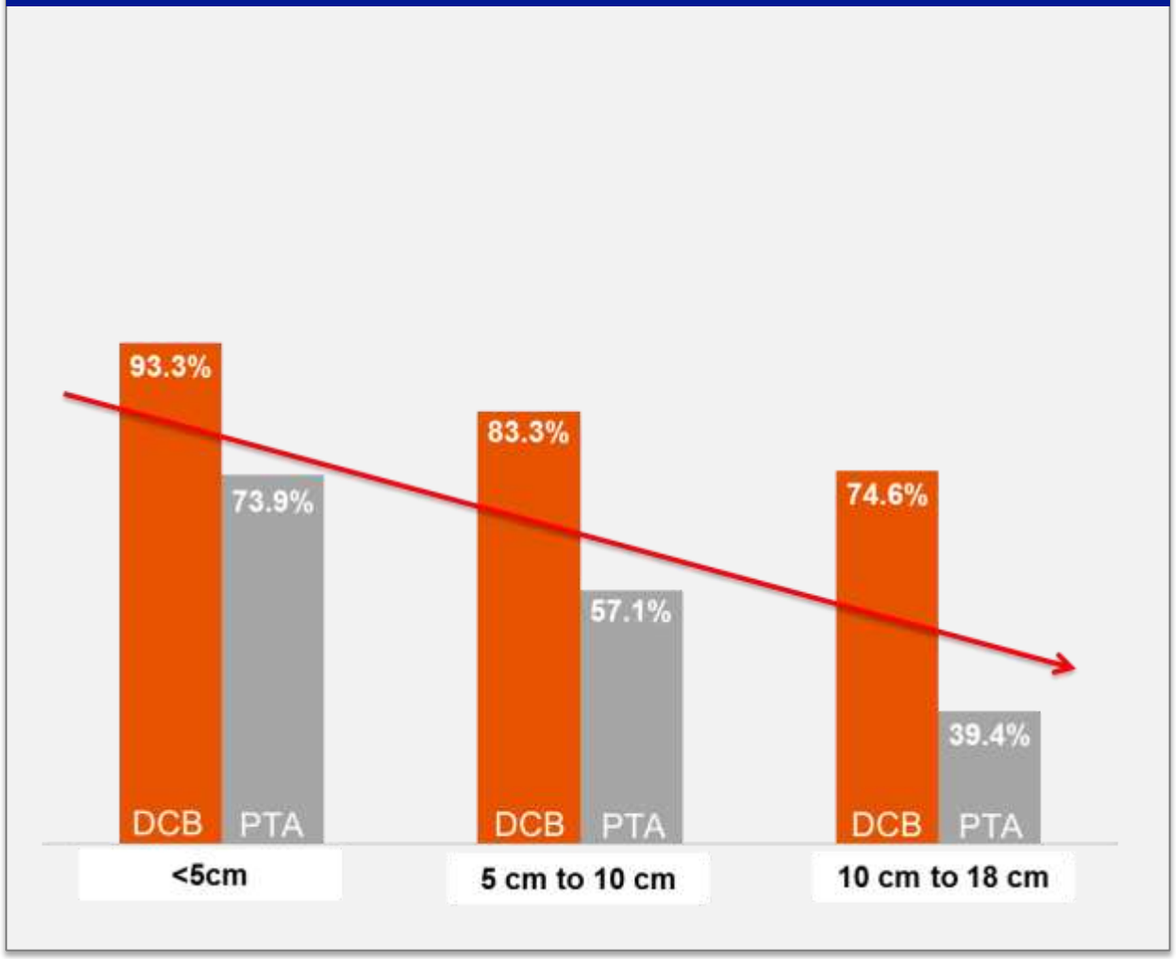
- Increased Lesion Length linked to poor primary patency

[1]Medtronic COMPLETE SE SSED-P110040. [2]Matsumura et al. DURABILITY II 12-month results. JVS 2013. [3]Dake et al. Twelve-month Zilver PTX Randomized study results. CCI 2011. [4]Laird et al. Twelve-month results from RESILIENT Trial. CCI 2010. [5]Jaff M. VIVA 2012. [6]Ansel G. LINC 2010. [7]Schultz G. DURABILITY II 24-month data. NCVH 2013. [8]Dake et al. Twenty-four month Zilver PTX Randomized study results JACC 2013. [9]Tepe, G. Twenty-four month results of the STROLL Trial. ISET 2013 [10]Estimates based on bar chart. Ansel, G. Update on Important SFA Therapies VIBRANT, VIPER, ZILVER PTX. TCT 2012. [11]Rocha-Singh K. DURABILITY II 36-Month Results. VIVA 2013. [12]Dake M. Zilver PTX three-year follow-up. LINC 2013. [13]Geraghty et al. Three-year results of the VIBRANT trial. JVS 2013

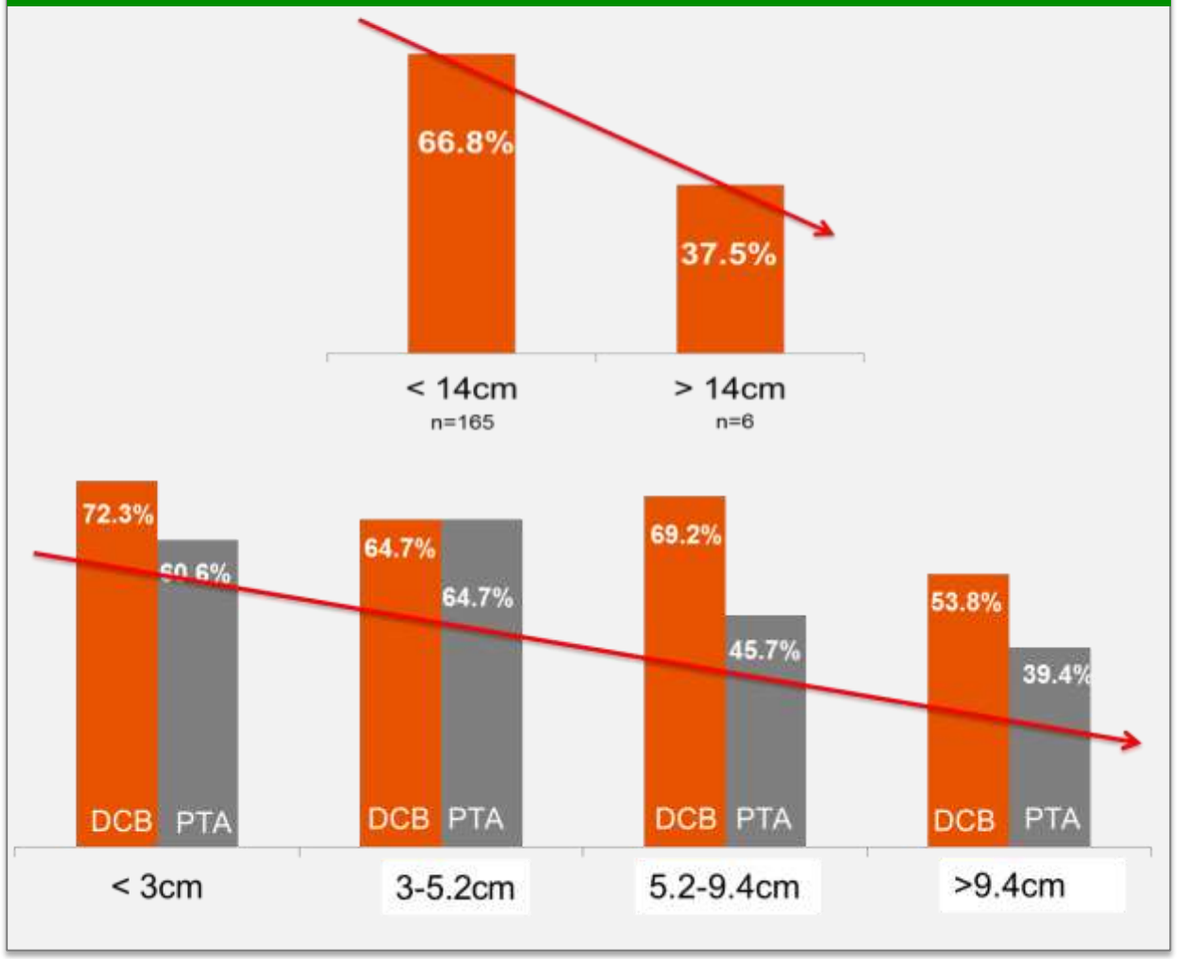
Challenges to Optimal Vessel Preparation
2. Long Lesion Length

Primary Patency decreases as lesion length Increased

IN.PACT SFA
12 Month Primary Patency by Lesion Length



LEVANT II
12 Month Primary Patency by Lesion Length



IN.PACT Admiral Summary of Safety and Effectiveness Data
Lutonix FDA Executive Summary

Challenges to Optimal Vessel Preparation
2. Long Lesion Length

- Long lesion lengths are more likely to dissect after balloon angioplasty because the compliance of the vessel varies depending on the plaque composition.

- Most balloon angioplasty applies the same force across all parts of the vessel and will therefore result in differential expansion along the length of the lesion.

Challenges to Optimal Vessel Preparation

3. Calcium

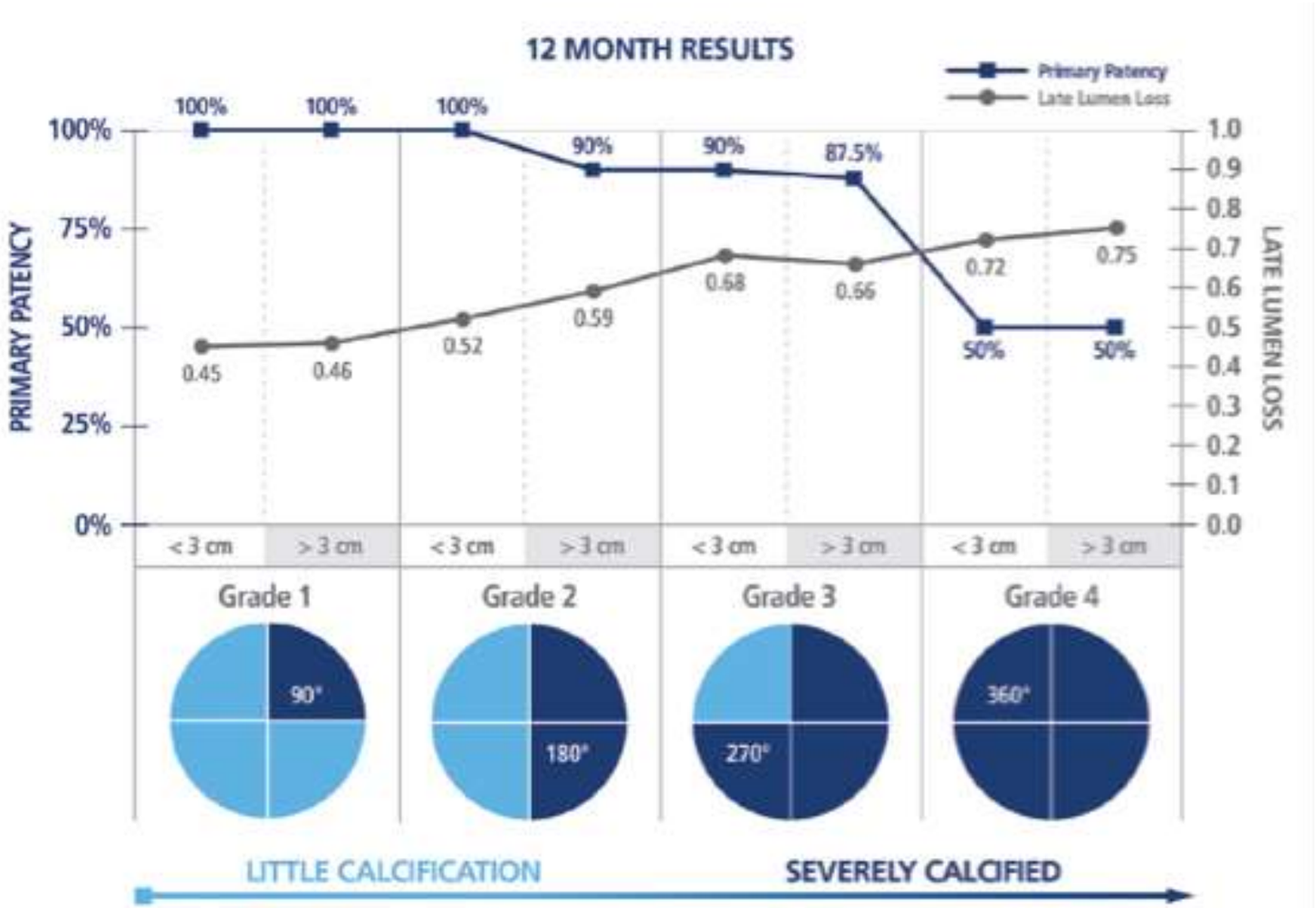


Figure 1. Twelve-month results demonstrating greater late lumen loss and lower patency with increased calcification.

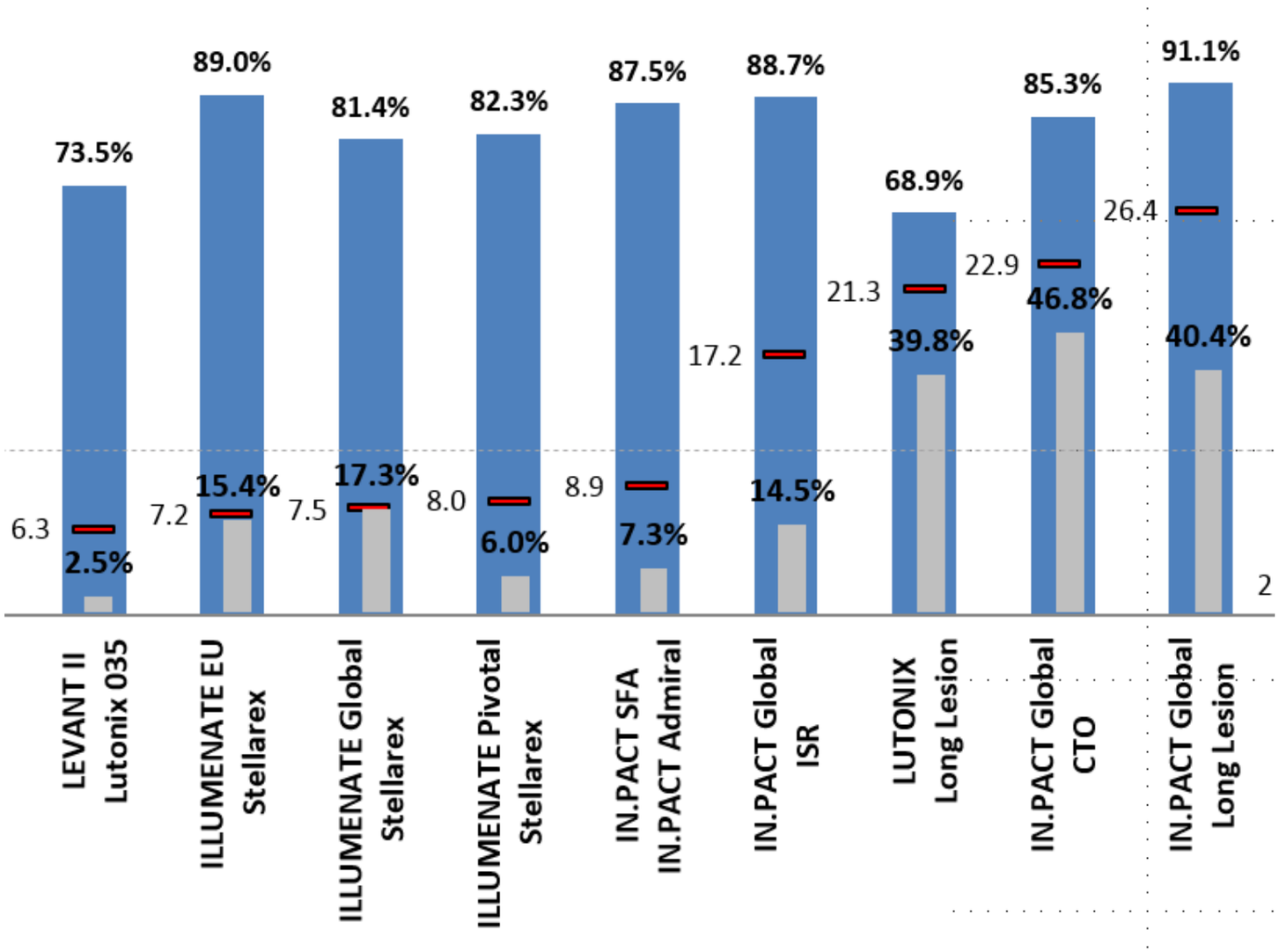
- Calcium is a Barrier to Drug delivery
- Calcium Distribution & Severity linked to the late lumen loss & primary patency

보훈공단 부산보훈병원

- Fanelli F, Cannavale A, Gazzetti M, et al. Cardiovasc Intervent Radiol. 2014;37:898-907.

Challenges to Optimal Vessel Preparation

4. High rates of Provisional Stenting



- In Real World DCB Registries, More complex disease is associated with increased the rate of provisional stenting

- Provisional Stent rates of 40–47%

1. Rosenfield, K., et al. (2015). N Engl J Med 373(2): 145-153.
2. Bard Lutonix Instructions for Use, BAW1387400r3.
3. Schroeder, H., et al. (2017). Circulation.
4. Zeller T, LINC Leipzig, Germany 2017.
5. Krishnan, P., et al. (2017). Circulation.
6. Tepe, G., et al. (2015). Circulation 131(5): 495-502.
7. Brodmann, M. VIVA 2015.
8. Tepe, G. Charing Cross 2016.
9. Scheinert, D. EuroPCR 2015.

2 Ways for Vessel Preparation

Special Balloon

AngioSculpt®

PTA Scoring Balloon Catheter

Atherectomy

Hawk

Jetstream

Atherectomy without DCB Data

study	type	Patients	Lesions	Dissection (≥D)	BO stent	30D MACE	Patency	
							1 year	> 1 years
DEFINITVE LE 1)	DA	598(RCC 1-3)	743	2.2% (13/598)	3.2% (33/1022)	1.0% (6/598)	78%	?
		201 (RCC 4-6)	279	2.5% (5/201)		3.5% (7/201)	71%	?
DEFINITIVE CA 2)	DA	130	168	0.8% (1/131)	4.1% (7/169)	6.9% (9/131)	NR	?
VISION IDE 3)	DA	130	130	NR	4.0%	17.6% (6Mo)	NR	?
OASIS 4)	OA	124	201	NR	2.5% (2/201)	3.2(4/124)	NR	?
COMPLIANCE 360 5)	OA	25	38	NR	5.3% (2/38)	NR	81.2%	?
CALCIUM 360 6)	OA	25	29	3.5% (1/29)	6.9% (2/29)	0%	NR	?
PATHWAY PVD 7)	RA	172	210	9% (15/172)	7% (14(210)	1.0% (2/172)	61.8%	?
CELLO 8)	Laser	65	65	NR	23.2%	0%	54.3%	?
EXCITE-ISR 9)	Laser	169	169	2.4% (≥C)	4.1% (7/169)	5.8% (9/155)	71.1% (6MO)	?

1. McKinsey J, et al. JACC Cardiovasc Interv 7(8):923-33:2014.
2. Roberts D, et al. Catheter Cardiovasc Interv 84(2):236-44:2014.
3. Schwindt A – Presented at VIVA, Las Vegas 2015.
4. Safian RD, et al. Catheter Cardiovasc Interv 73(3):406-12:2009.
5. Dattilo R, et al. J Invasive Cardiol 26(8):355-60:2014.
6. Shammas NW, et al. J Endovasc Ther 19(4):480-8:2012.
7. Zeller T, et al. J Endovasc Ther 16(6):653-62:2009.
8. Dave R, et al. J Endovasc Ther 16(6):665-75:2009.
9. Dippel EJ, et al. JACC Cardiovasc Interv 8(1 Pt. A):92-101:2015.

Directional Atherectomy

SilverHawk
TurboHawk
HawkOne

DEFINITIVE LE

DEFINITIVE AR

보훈공단
부산보훈병원

DEFINITIVE LE trial

- Prospective Multinational, Single Arm Study
- Core-Lab Adjudicated
- Objective : evaluate the effectiveness of standalone SilverHawk/TurboHawk plaque excision systems for EVT of PAD in the FP & tibioperoneal arteries

- Primary Outcomes
- Claudicant : primary patency by Duplex US @ 12 Mos (PSVR ≤2.4 with no clinically driven reintervention)
- CLI : Freedom from major unplanned amputation @ 12

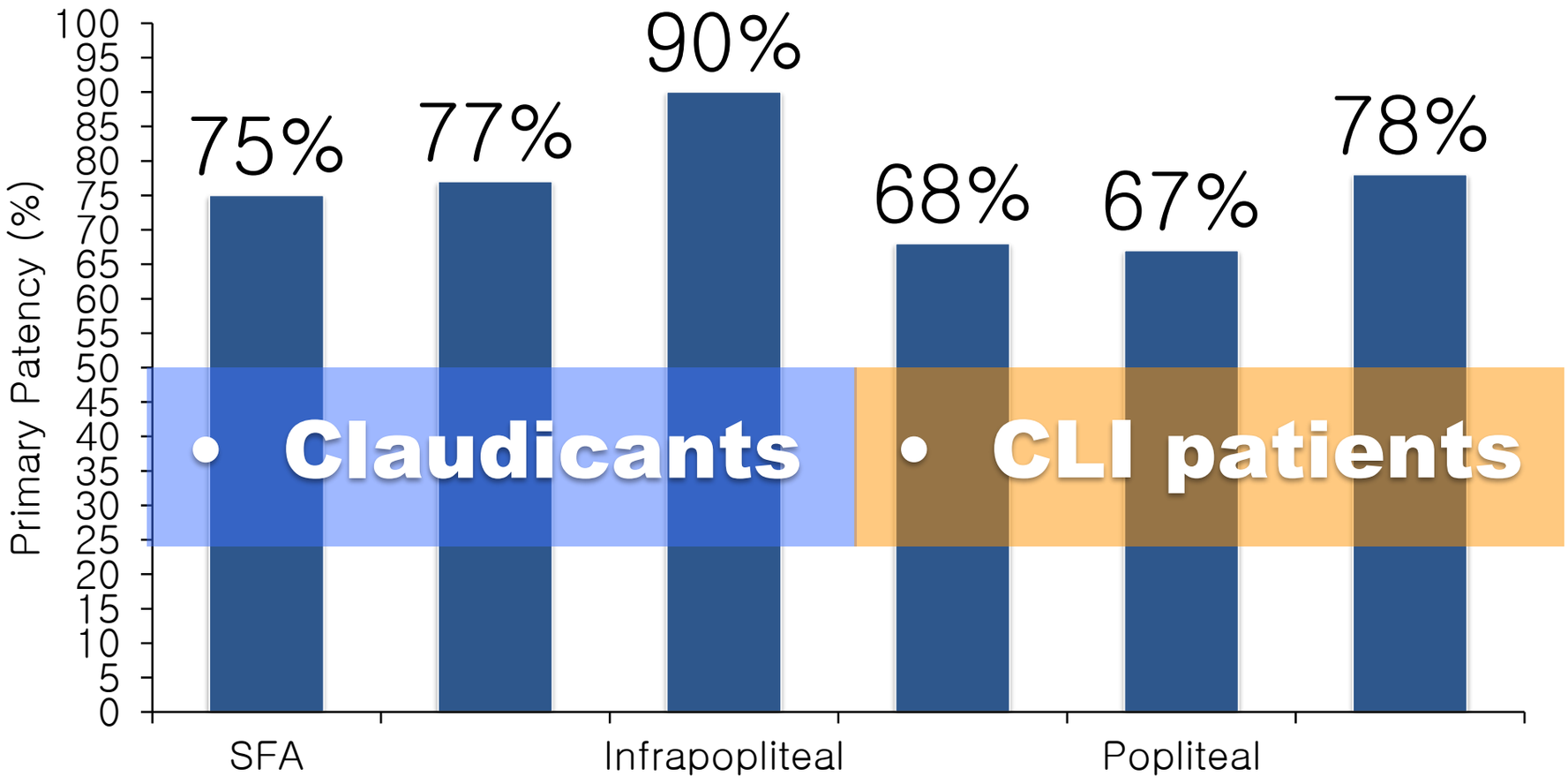
- **800 patients**
- **47 sites (US/EU)**
- **FU : 1 Year**

McKinsey ae al. JACC 2014;7(8):923

보훈공단 부산보훈병원

DEFINITIVE LE trial : Results

Primary Patency at 12 Mos (KM)



Mean Length	8.1cm	6.0cm	5.5cm	8.6cm	5.4cm	6.0cm
No. of Lesions	536	114	93	135	48	96

McKinsey ae al. JACC 2014;7(8):923

보훈공단 부산보훈병원

Atherectomy followed by DCB Data

study	type	Patients	Lesions	Dissection *	BO stent	30D MACE	Patency	
							1 year	> 1 years
DEFINITVE AR1)	DCB	54	54	19% (10/54)	3.7% (2/54)	NR	89.6%	?
	DAART	48	48	2% (1/48)	0%		93.4%	
	DAART-Ca	19	19	0%	5.3% (1/19)		–	
Cioppa2)	DAART	3-	30	6.7% (2/30)	6.7% (2/30)	13% (4/30) (1YR)	90%	?
Stavroulakis (popliteal) 3)	DAART	21	26	NR	NR	14% (3/21)	95%	90% (18 Mo)
Foley 4)	DCB	61	99	14% (14/99)	39% (39/99)	NR	81%	?
	OA+DAART	28	40	13% (5/40)	18% (7/40)		77%	
Stavroulakis (CFA)5)	DCB	26	26	31% (8/26)	4% (1/26)	NR	68%	?
	DAART	21	21	5% (1/21)	5% (2/21)		90%	

1)Presented by Zeller T. VIVA 2014, Las Vegas

2) Cioppa A, et al. Cardiovasc Revasc Med 2012;13:219-23

3) Stavroulakis K, et al. J Endovasc Ther 2015;22:847-52

4) Foley TR, et al. Cath Cardiovasc Interv 2017;89:20178-85

5) Stavroulakis K, et al. J Endovasc Ther. 2017, Doi:10.1177/1526602817748319

* Zeller, et al., Defined dissection as more than grade C

* Chioppa, et al., Defined dissection via chroma flow involving more than 60% of cross-sectional diameter with blood flow in the false lumen

DEFINITIVE AR trial

- Pilot study to assess the effect of treating a lesion with DI followed b DCB vs. DCB alone
- Primary Outcomes
- Target Lesion Percent Lesion Stenosis at 1 year (Angiographic Core Lab)

- **121 patients**
- **10 sites (Europe)**
- **FU : 1 Year**

Zeller T. VIVA 2014

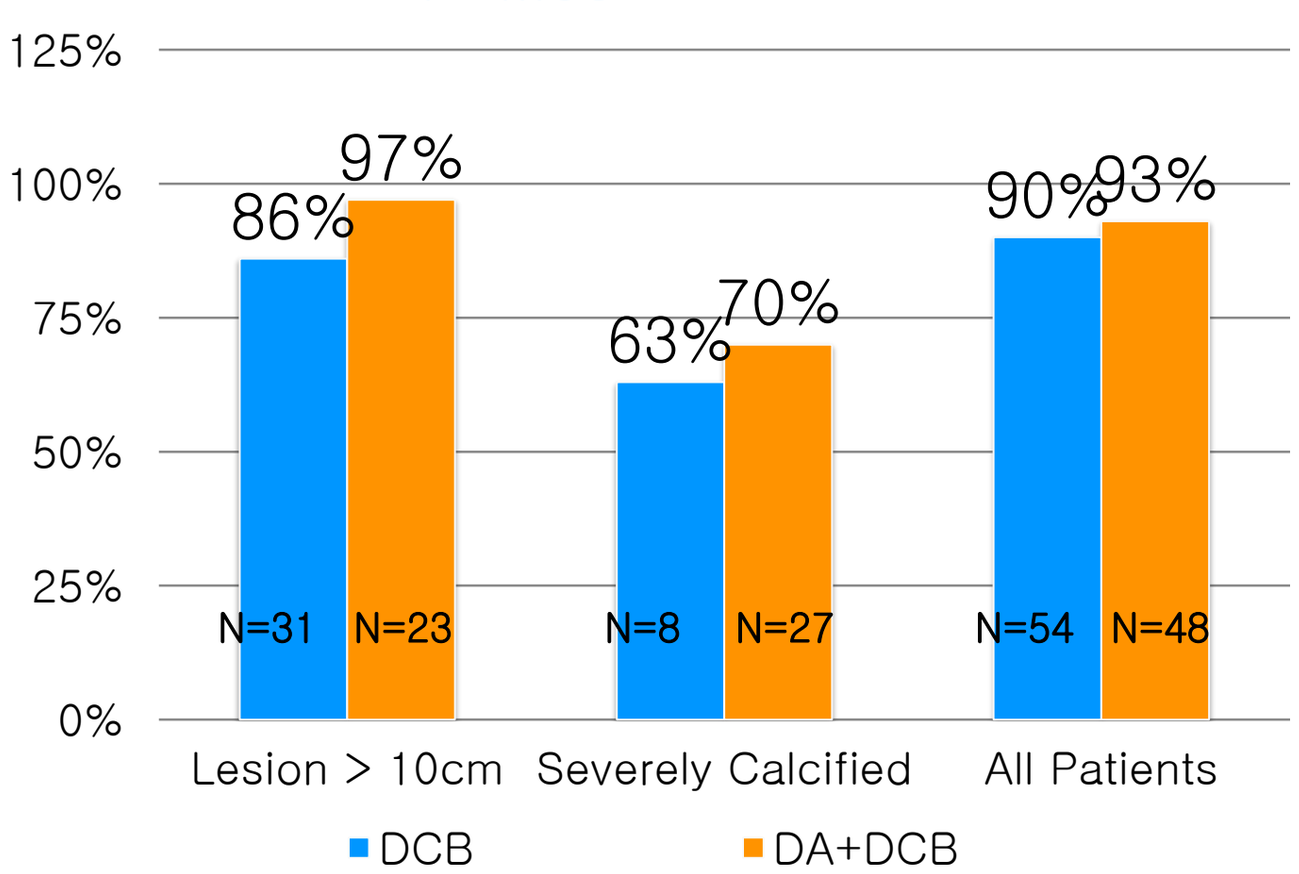
보훈공단 부산보훈병원

Atherectomy & DCB Efficacy

- DEFINITIVE AR : DA+DCB (DAART) vs. DCB alone
- Adjunctive atherectomy may improve procedural and clinical outcomes following DCB treatment of the SFA and/or popliteal artery, particularly for longer or severely calcified lesions

Procedural Results		
	DCB alone	DA+DCB
Technical Success	64.2%	89.6%
Bail-out Stent	3.7%	0%
Flow limiting Dissection	19%	2%

DUPLEX ULTRASOUND PATENCY at 12 Mos



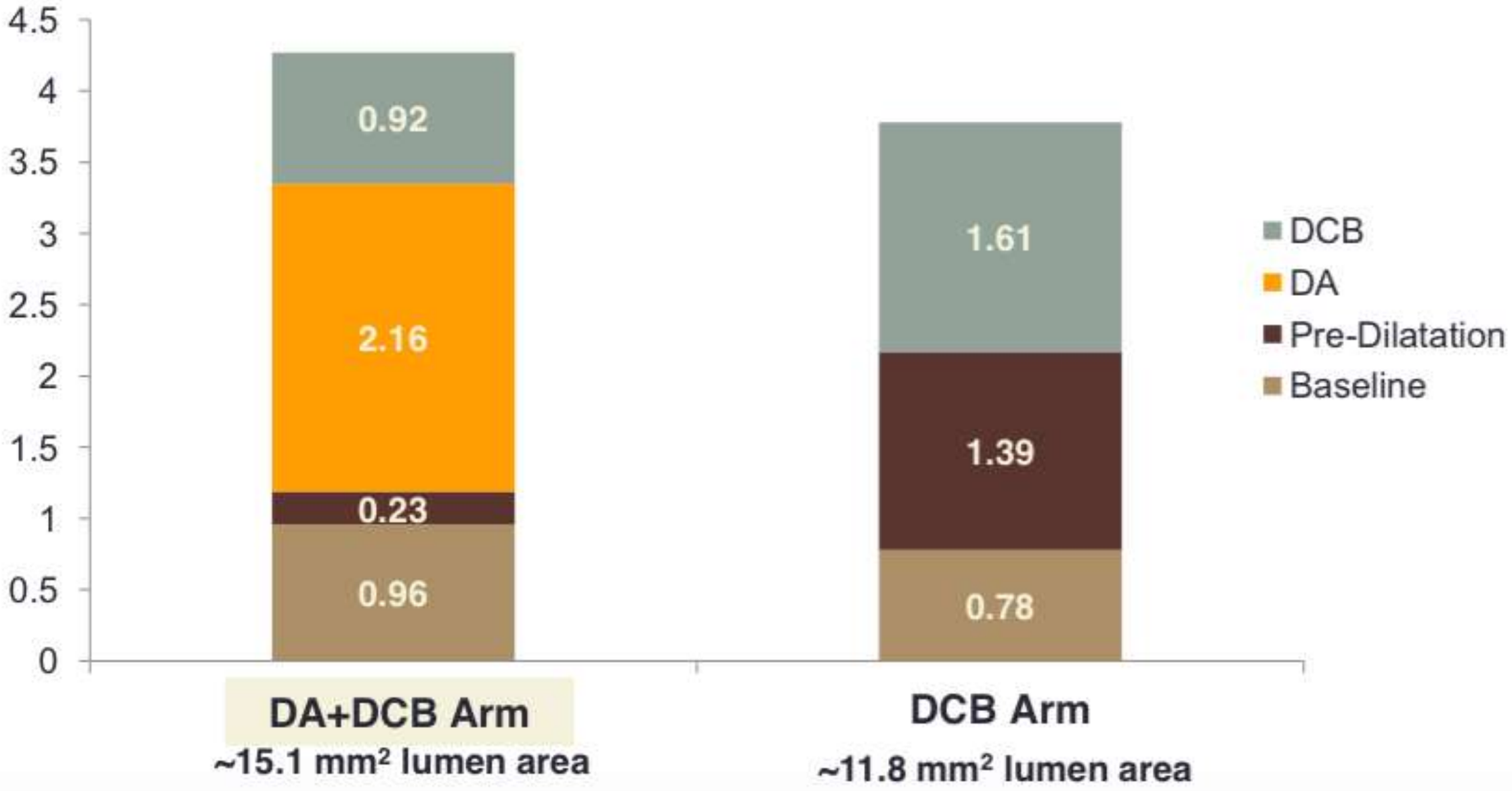
Zeller T. VIVA 2014

보훈공단 부산보훈병원

What is the Impact of Lumen Gain with DAART?

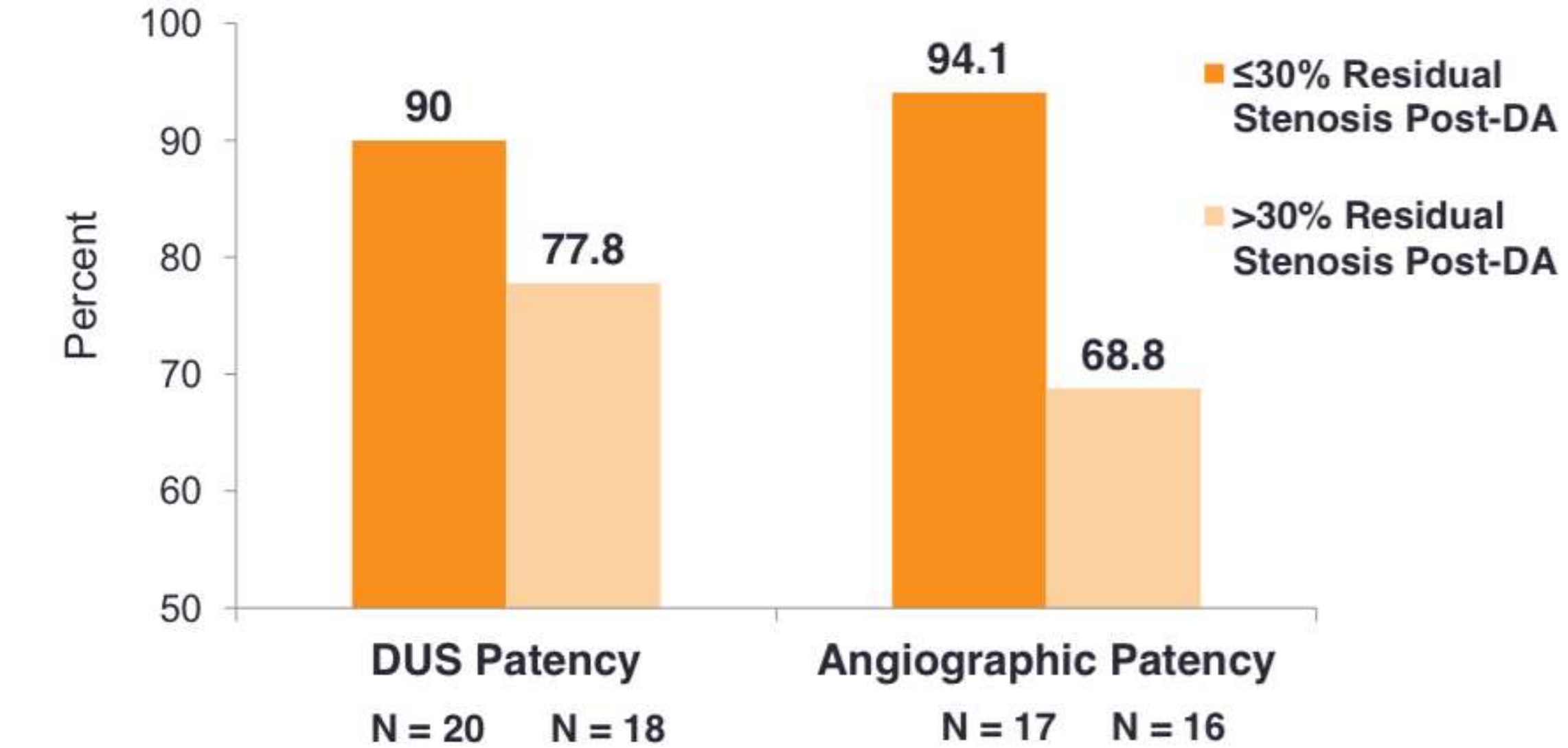
Post Procedure MLD (DAART vs DCB alone)

DA+DCB resulted in a significantly larger minimum lumen diameter (MLD) following the protocol-defined treatment in DEFINITIVE AR



12 Mos Patency : DAART RCT

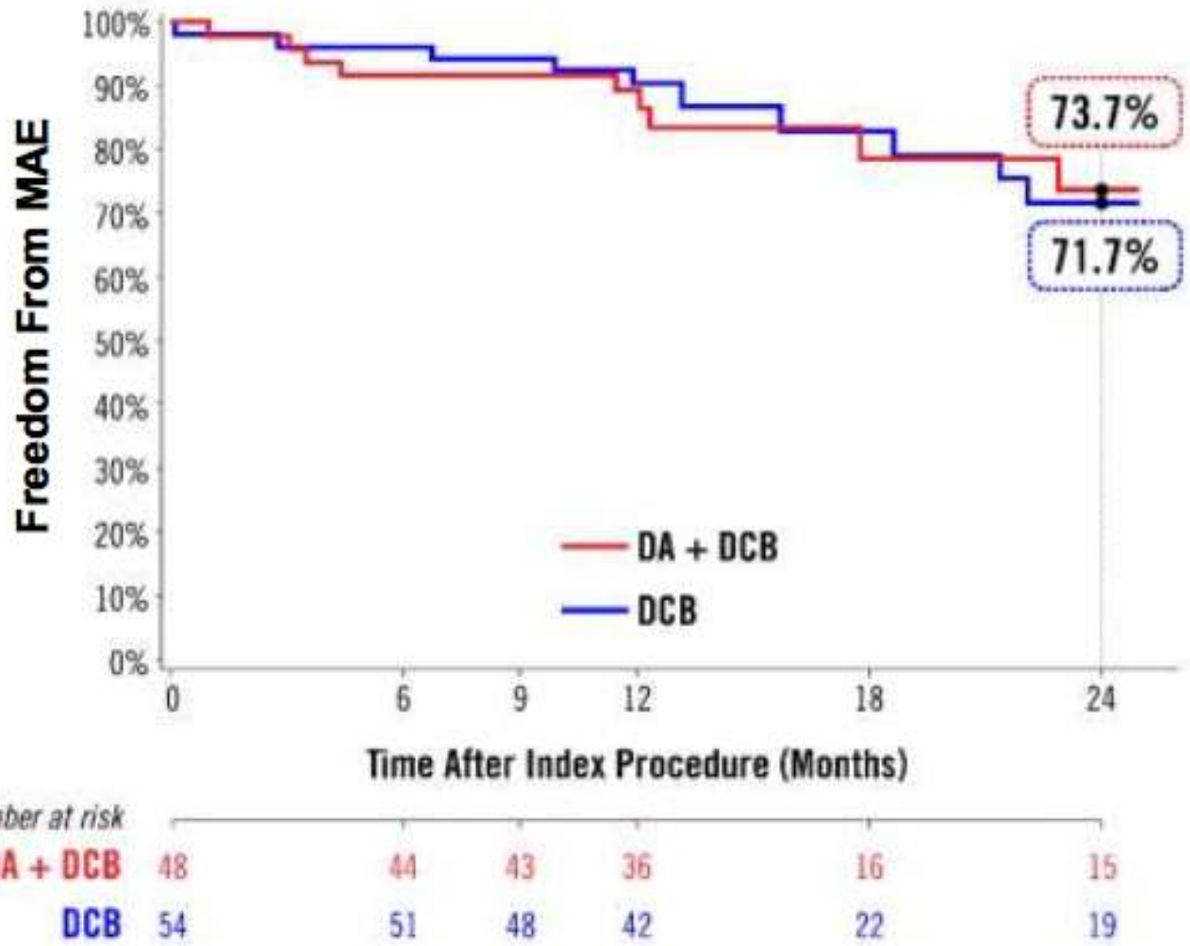
Increased lumen gain with DA before DCB may result in improved 12 Mos patency



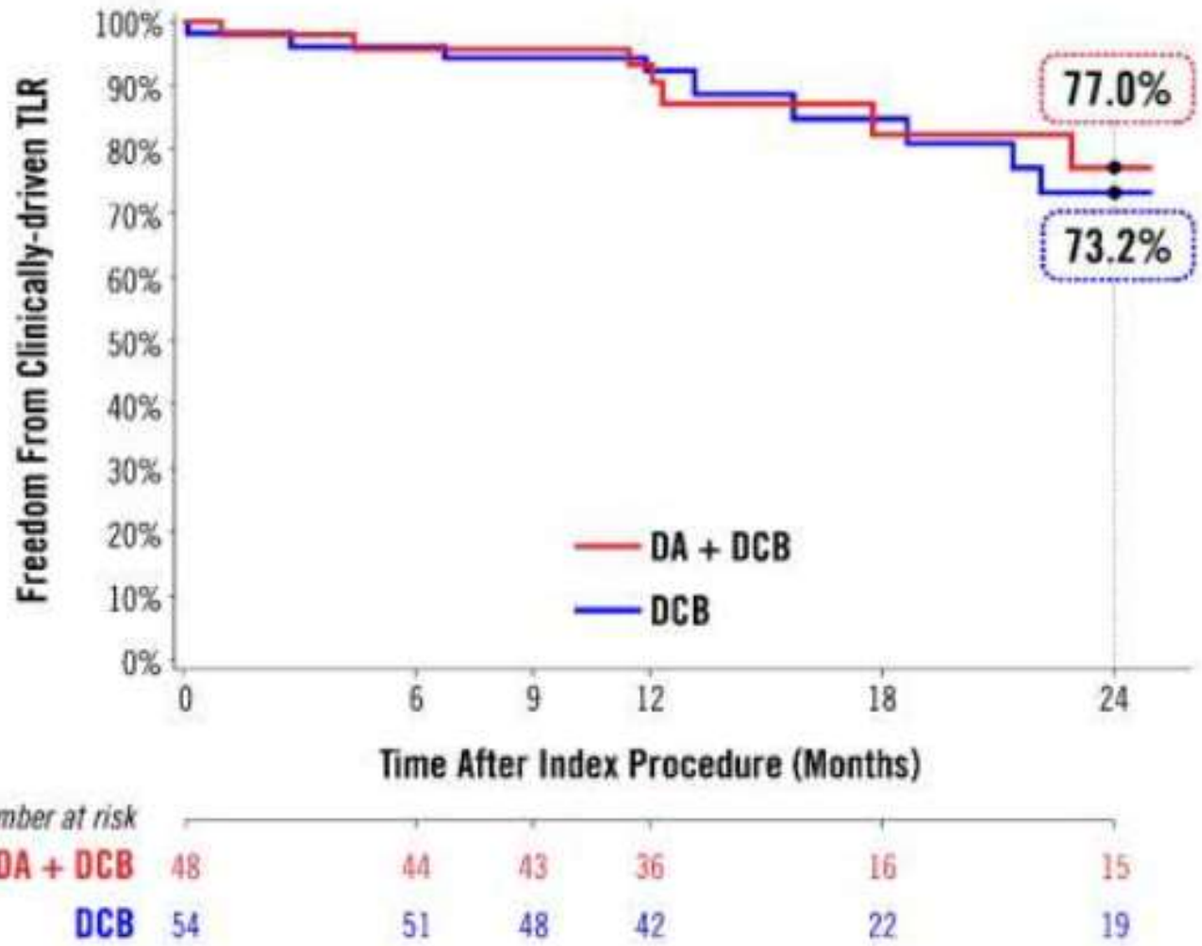
- directional atherectomy to measurably remove atheroma is important. It directly translated to improved patency.
- DCBs cannot make up the difference when atherectomy does a poor job of debulking a lesion.

DEFINITIVE AR: 2 year extension

Freedom from MAE[2]



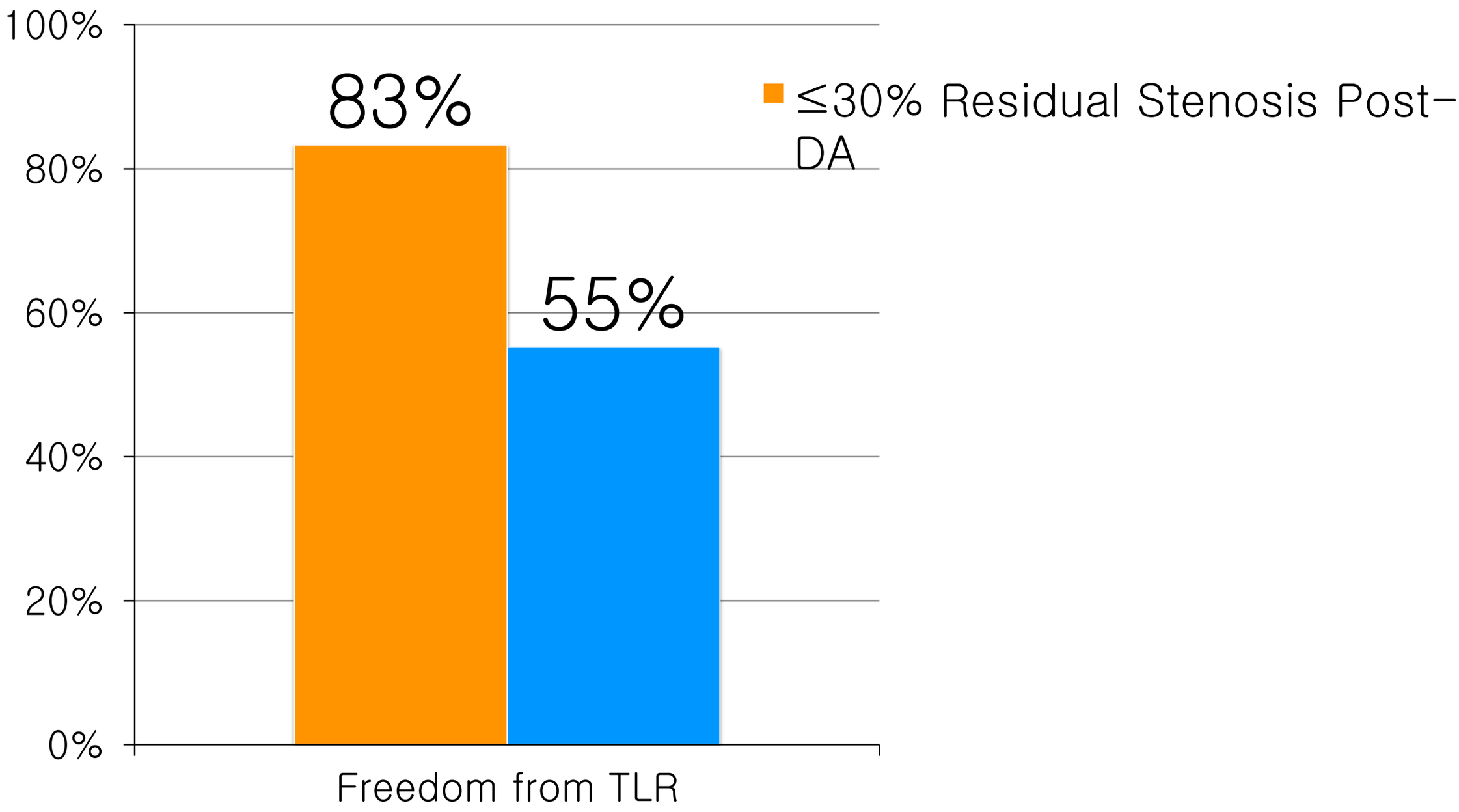
Freedom from Clinically-Driven TLR[3]



1. Presented by Tepe G at LINC, Leipzig, Germany 2017.
2. MAE (Major Adverse Event) defined as major unplanned amputation of the treated limb, all-cause mortality or clinically-driven target lesion revascularization.
3. Clinically-driven TLR (target lesion revascularization) defined as any reintervention or artery bypass graft surgery involving the target lesion in which the subject has a ≥ 70% diameter stenosis (Peak Systolic Velocity Ratio (PSVR) > 3.5 may substitute if a pre-intervention angiogram is not available) and at least two of the following: worsening RCC, worsening WIQ score, or an ABI drop > 0.15 from baseline.

DEFINITIVE AR: 2 year extension

Freedom from TLR : less than 30% residual stenosis



Tepe, Charing Cross 2017

보훈공단 부산보훈병원

Reimbursement Guideline for DAART in KOREA

Lesion with Calcium	Atherectomy	Filter	DCB	**DAART/RAART OK**
	Hawk / Jetstream	Spider FX / Nav-6	IN.PACT / Lutonix	
Lesion without Calcium (length ≥ 10cm)	Atherectomy	Filter	DCB	**DAART/RAART OK**
	Hawk / Jetstream	Spider FX / Nav-6	IN.PACT / Lutonix	
Lesion without Calcium (length < 10cm)	Atherectomy	OR	DCB	**DAART/RAART NO**
	Hawk / Jetstream		IN.PACT / Lutonix	

- In ISR lesions Atherectomy with Hawk system is not reimbursed

WRAP UP

- Vessel preparation is important clue in enhancing DCB efficacy.
- Atherectomy with DCB is a useful tools for FP disease.

보훈공단
부산보훈병원
VHS Busan Hospital