Tibial Interventions
Atherectomy is a necessity?!

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

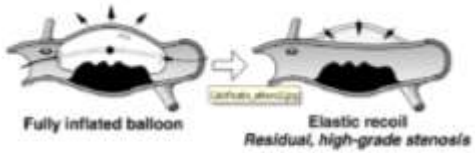
Affiliation/Financial Relationship	Company
• Grant/Research Support	• iDev, Covidien, TriReme
• Consulting Fees/Honoraria	• Covidien, Boston Scientific, Angiosculpt, Pathway(MedRad)
• Major Stock Shareholder/Equity	• Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular
• Royalty Income	• None
• Ownership/Founder	• None
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

Clinical Limitations & Unmet Needs

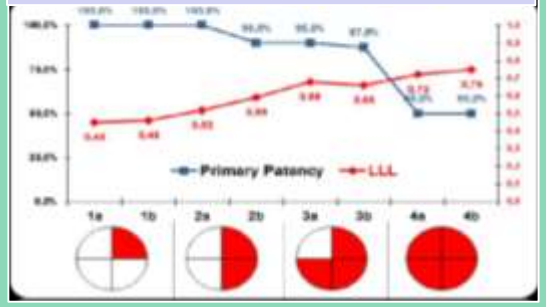
Calcium as a Barrier

Calcium Limits Vessel Expansion[1]

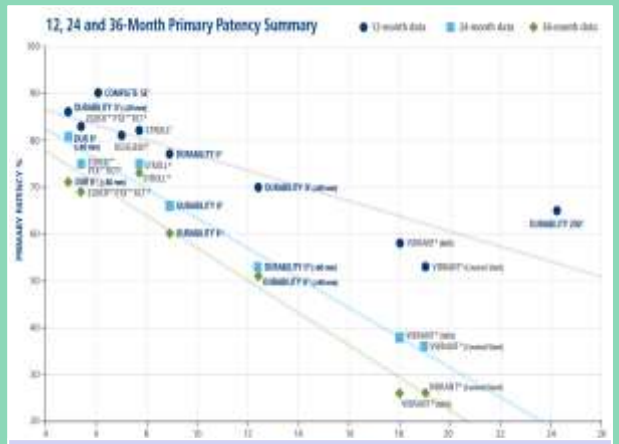
Significant difference in vessel compliance leads to overstretch in non-diseased tissue causing dissections, recoil, excessive injury, and poor outcomes



Calcium May Limit Drug Effect[2]



Longer Lesion Length



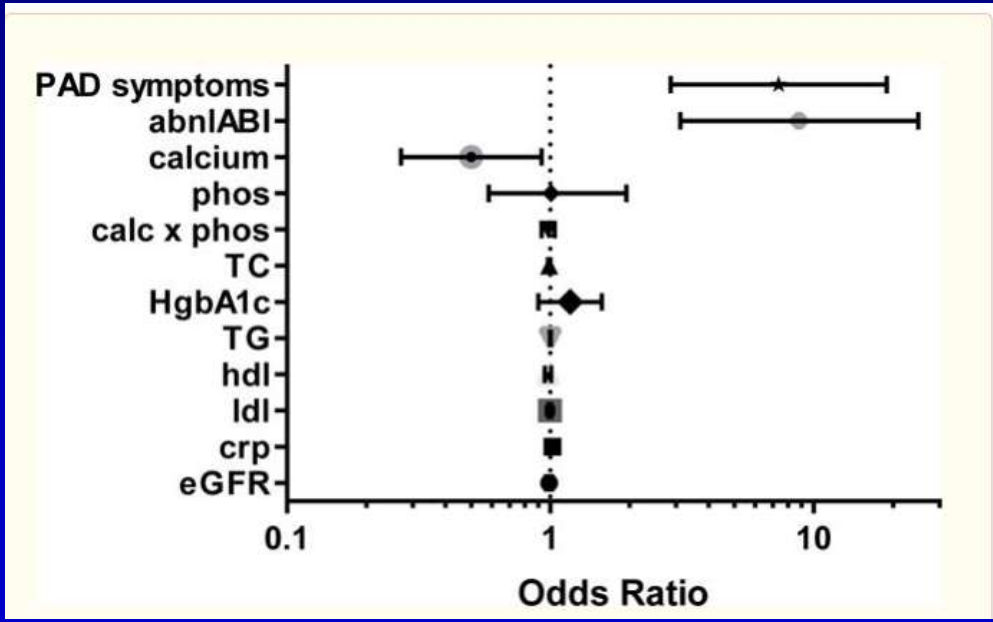
Increased lesion length is an independent predictor of decreased patency[5].

[1]Freed MS, Manual of Interventional Cardiology, [2]Fanelli DEBELLUM, [3]Laird, CCI, June 2010, [4]SMART Control IFU, [5]Matusumura, DURABILITY IIJVS, July 2013, [6]Davaine, European Journal of Vascular and Endovascular Surgery 44 (2012)

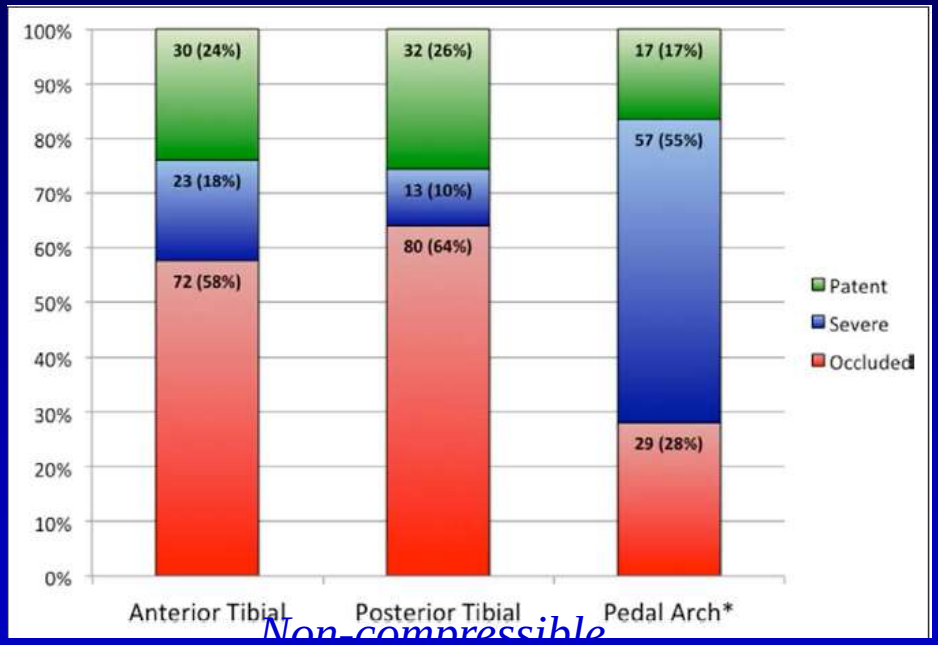
Tibial calcification

- Association with PAD and abnormal ABI independent of serum calcium, other biochemical levels (CRP etc)
- Association with renal failure and independent to age, gender, diabetes and tobacco

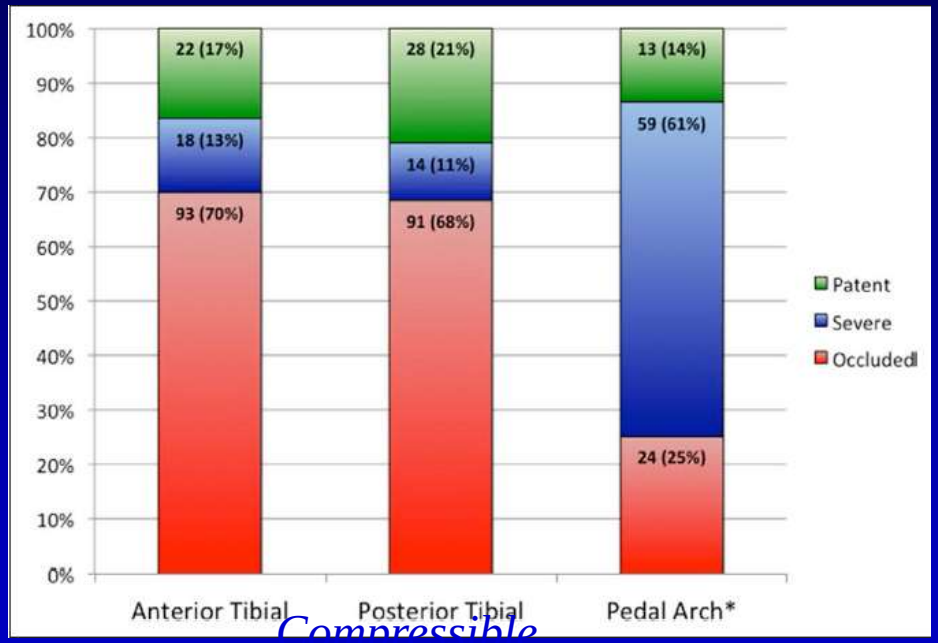
- *Calcification is a marker for amputation and poor wound healing*



Deas DS et al Vas Med 2015 Aug 20(4); 326-331.
Guzman et al JACC 2008



Non-compressible



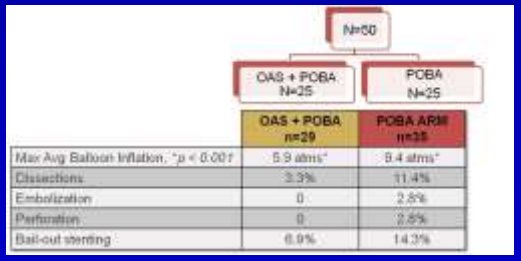
Compressible

Randwawa et al Circ Cardio Interv, 2017 May

Arterial compliance

- Several studies (registries, non-CL adjudicated) have suggested a debulk first strategy assists with arterial compliance and lower balloon pressures for dilation (Compliance 360, Calcium 360)

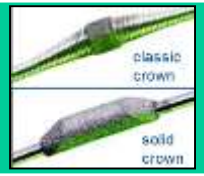
Per Lesion	CONFIRM I n = 1146	CONFIRM II n = 1734	CONFIRM III n = 1886
Mean Inflation	5.7 atms	5.3 atms	5.9 atms
Bail-Out Stent (due to dissections)	3.8%	5.8%	5.2%
Perforation	0.9%	0.6%	0.7%
Distal embolization	n/a	2.2%	2.2%
Vessel closure	2.1%	1.2%	1.4%



	OAS + POBA n=29	POBA ARM n=25
Max Avg Balloon Inflation, *p < 0.001	5.9 atms*	9.4 atms*
Dissections	3.3%	11.4%
Embolization	0	2.8%
Perforation	0	2.8%
Bail-out stenting	6.9%	14.3%

- *Vessel preparation through compliance change with Orbital Atherectomy enables lower-pressure adjunctive balloon angioplasty leading to low procedural events*
- *Less medial damage → Better long term durability*
- *Orbital Atherectomy procedural efficacy with lower bail-out stents PRESERVES TREATMENT OPTIONS in future*

Atherectomy Devices

	Jetstream™ Atherectomy System (Boston Scientific)	Peripheral Rotablator™ Rotational Atherectomy System (Boston Scientific)	Diamondback 360™, Stealth 360™ Atherectomy System (Cardiovascular Systems, Inc)	SilverHawk™, TurboHawk™ Plaque Excision System (Covidien)	Turbo-Elite™ Laser Atherectomy Catheter (Spectranetics)
					
Front-Cutting	✓	✓			N/A
Differential Cutting	✓	✓	✓		N/A
Active Aspiration	✓				
Concentric Lumens	✓	✓			
Lesion Morphology:					
Calcium	✓	✓	✓	✓	✓
Soft/Fibrotic Plaque	✓			✓	✓
Thrombus	✓ (indicated for thrombectomy and atherectomy)				✓

Sources: Endovascular Today Buyer's Guide 2014. JETSTREAM System Brochure, Boston Scientific Website, 2014. Peripheral Rotablator product website, Boston Scientific, 2014. Diamondback 360 product website, CSI, 2014. Covidien website, Directional Atherectomy products, 2014. Turbo-Elite Laser Atherectomy Catheter Instructions for Use, May 2014.

DEFINITIVE LE

Subgroup	Claudicants (n=743)		CLI (n=279)	
	Patency (PSVR ≤ 2.4)	Lesion Length (cm)	Patency (PSVR ≤ 2.4)	Lesion Length (cm)
All (n=1022)	78%	7.5	71%	7.2
Lesion type				
Stenoses (n=806)	81%	6.7	73%	5.8
Occlusions (n=211)	64%	11.1	66%	10.3
Lesion Location				
SFA (n=671)	75%	8.1	68%	8.6
Popliteal (n=162)	77%	6.0	68%	5.4
Infrapopliteal (n=189)	90%	5.5	78%	6.0

DEFINITIVE LE

WOUND HEALING IN CLI

(RCC 5 & 6 at Baseline)

3Months *52%*

6 Months *61%*

12 Months ***72%***

Images Courtesy of Eric Scott, MD

DEFINITIVE LE

LIMB SALVAGE IN CLI

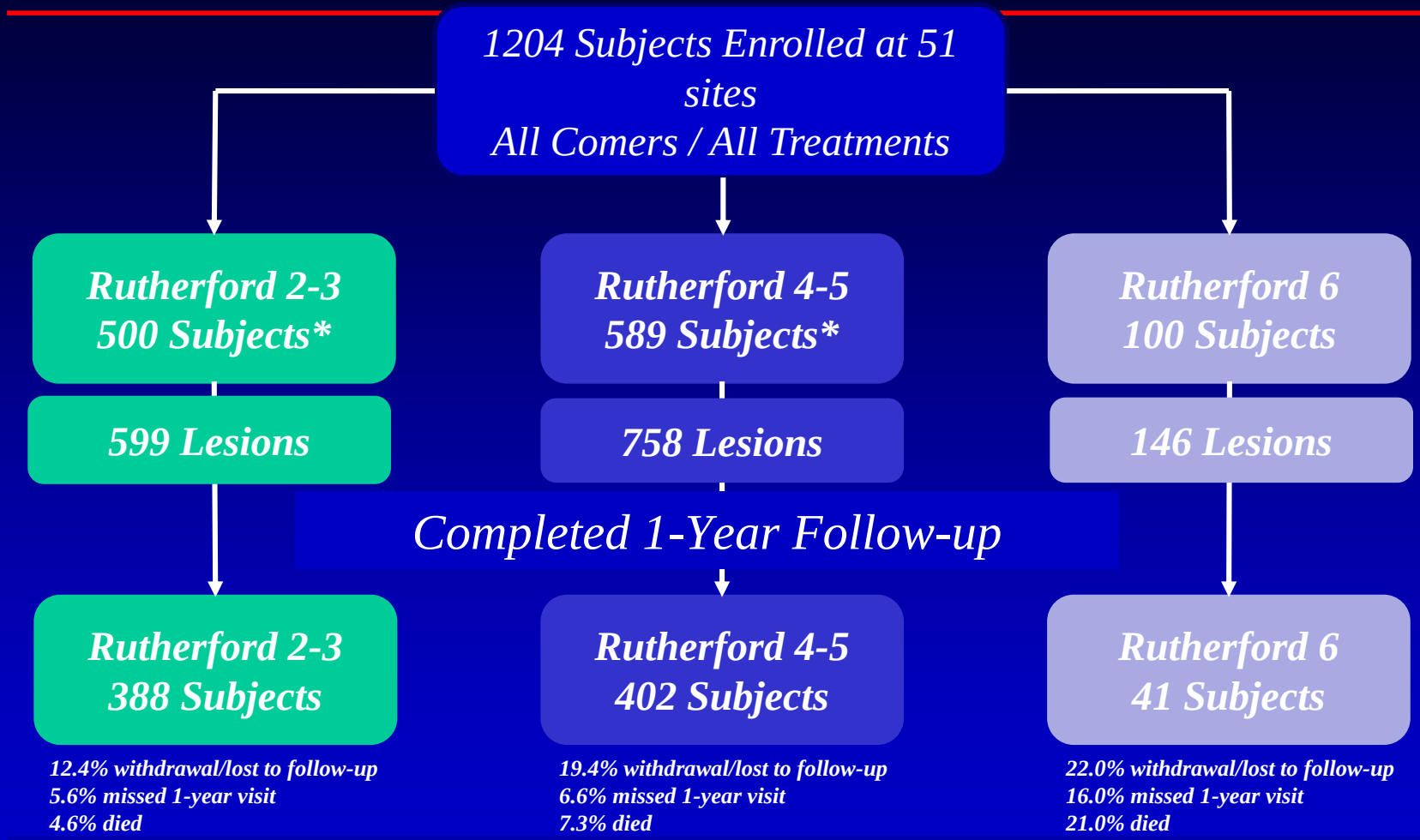
(RCC 5 & 6 at Baseline)

201 Limbs

12 Months

Limb Salvage ***95%***

LIBERTY Enrollment and 1-Year Follow-up

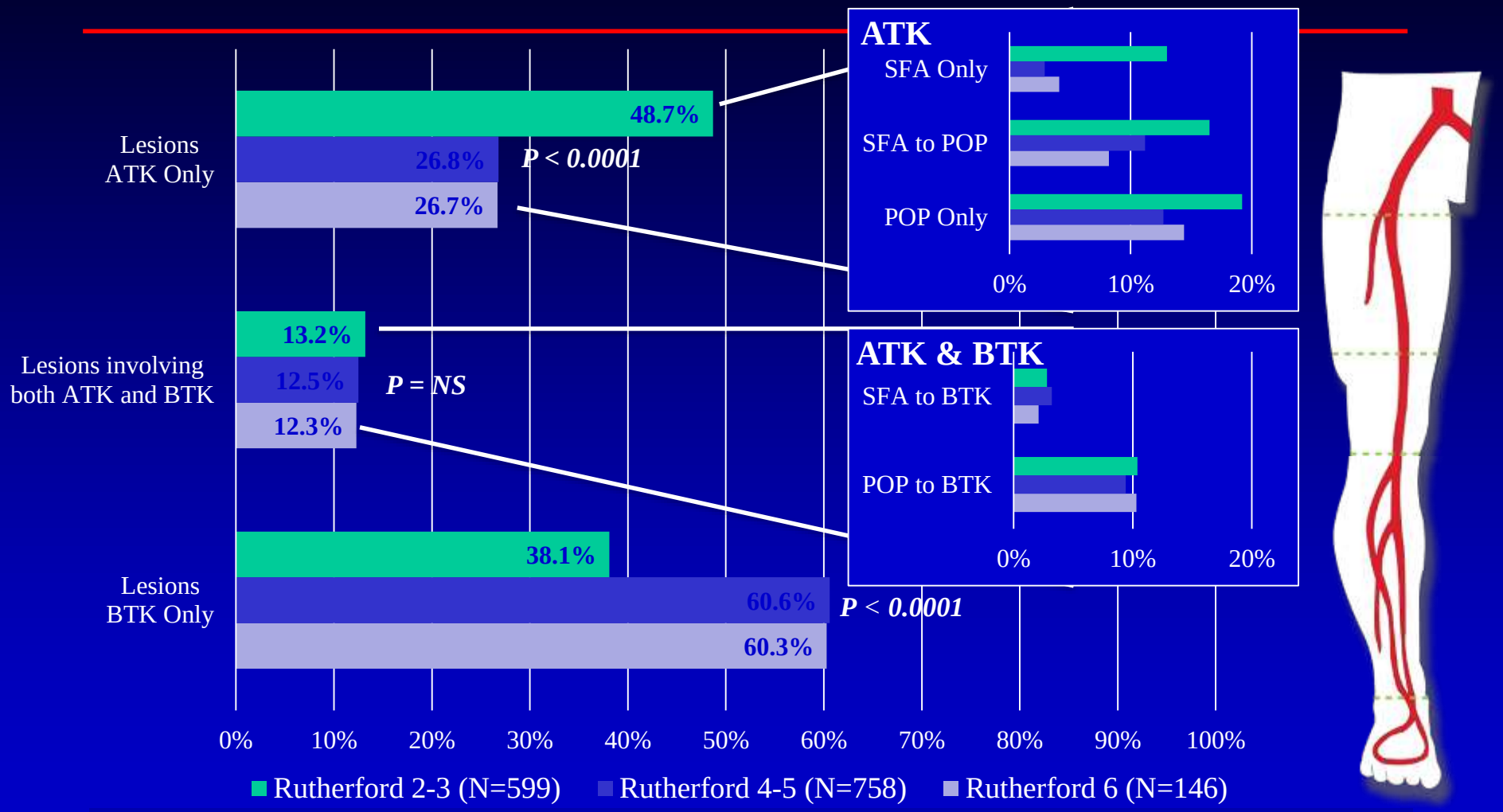


LIBERTY 360: Prospective, observational, multi-center study to evaluate procedural and long-term clinical and economic outcomes of endovascular device interventions in patients with symptomatic lower extremity PAD (N=1,204 Subjects)

**Due to site closure and lack of PI signature, baseline & procedure data from 15 subjects were excluded.*
Rutherford 2, N=97; Rutherford 3, N=403; Rutherford 4, N=285; Rutherford 5, N=304.
Core Lab reported lesions.
23-May-2017 Data

LIBERTY Target Lesion Locations

Proximal lesion location is lower in the leg (BTK) as severity of Rutherford Classification increases.



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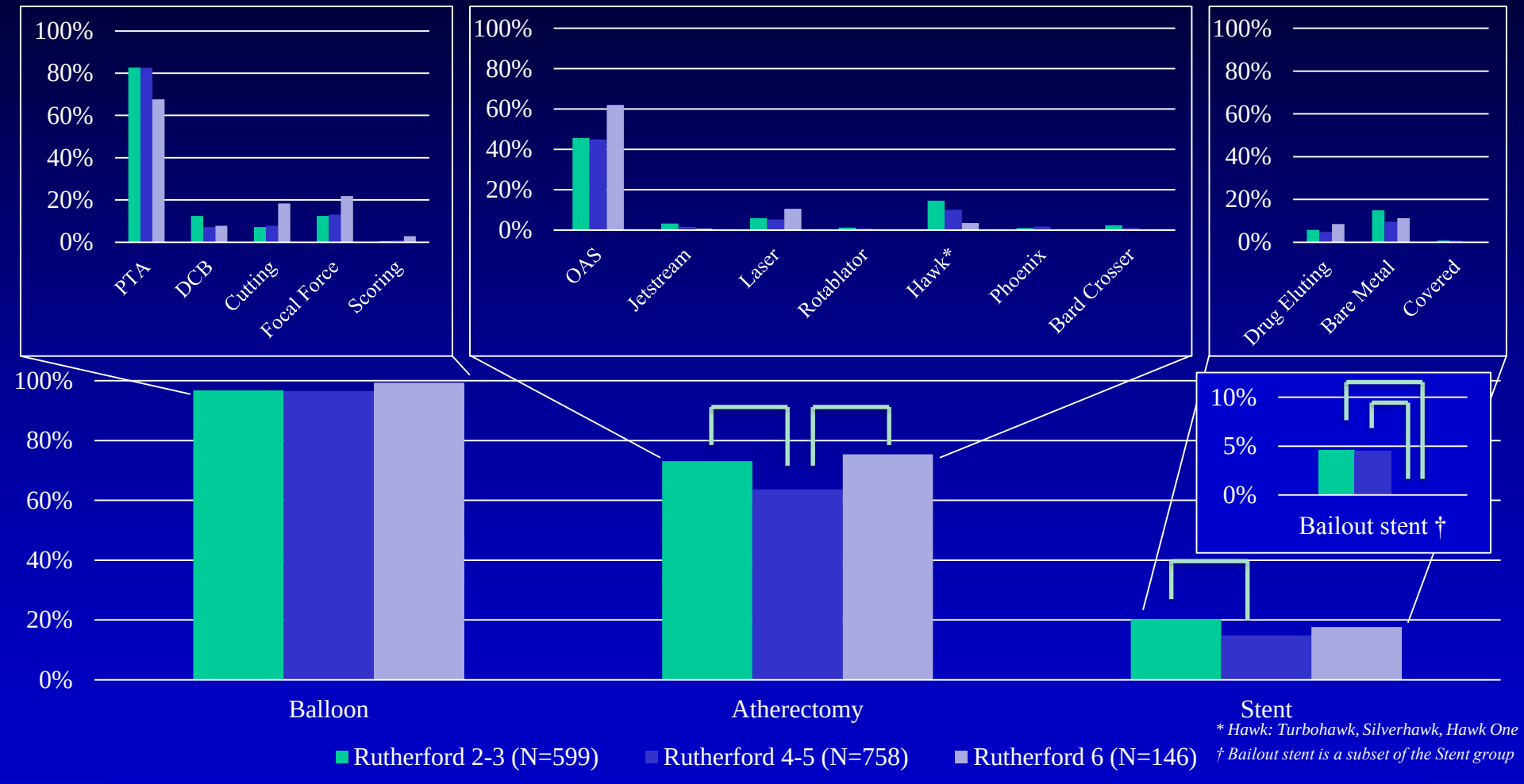
p-values: Monte Carlo approximation of a Fisher's Exact Test
Core Lab reported lesions (Lesions with reported values may be less than total number of lesions treated in each arm).
23-May-2017 Data

LIBERTY Device Usage by Lesion

Balloon and/or atherectomy were preferred devices with orbital atherectomy (OAS) the most frequently used atherectomy device. RC6 subjects saw significantly higher use of focal force/cutting balloons, OAS, and laser atherectomy. Bailout stenting was significantly less frequent in RC6 compared to either RC2-3 or RC4-5.



** Hawk: Turbohawk, Silverhawk, Hawk One*

† Bailout stent is a subset of the Stent group

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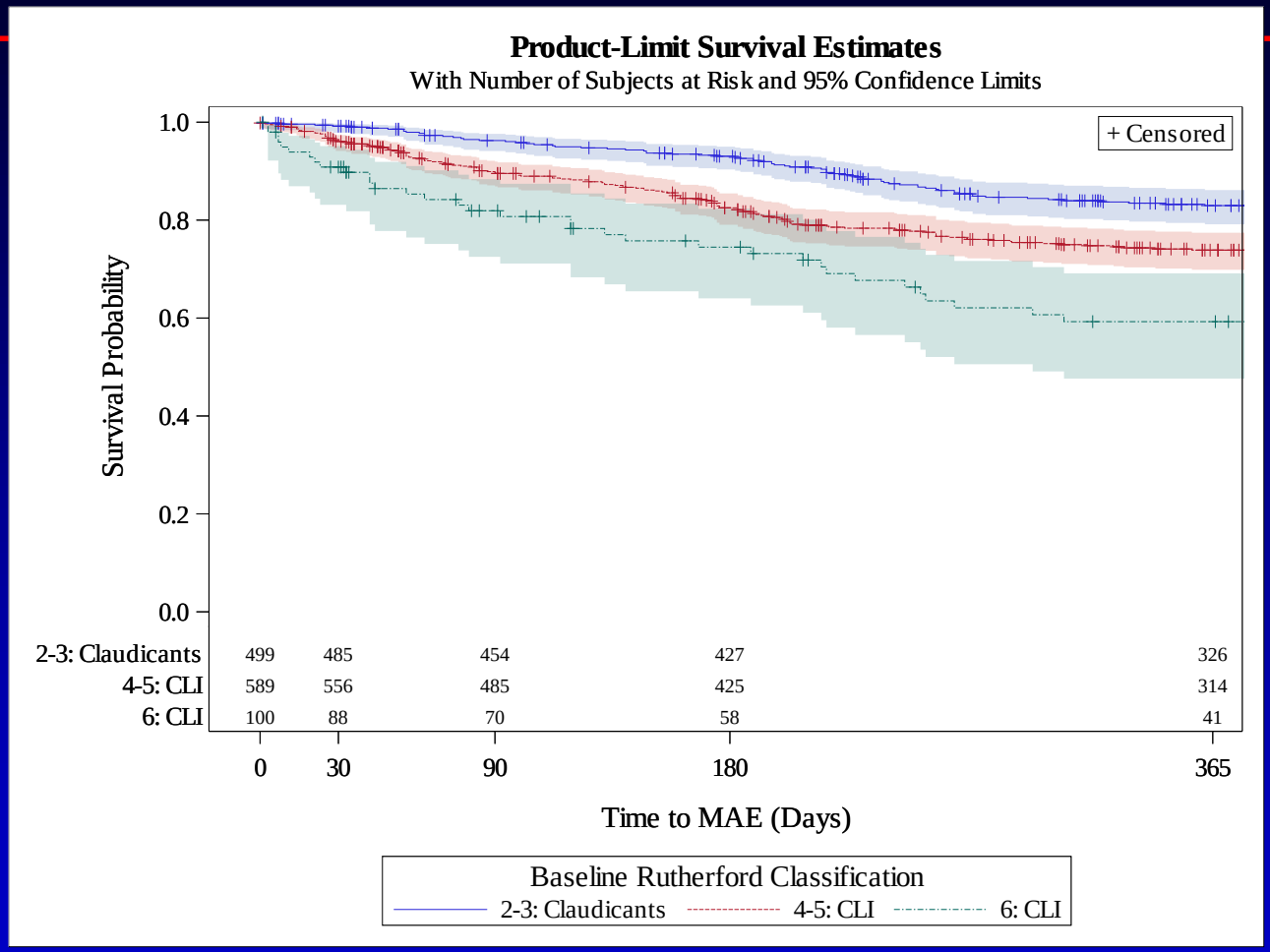
Core Lab reported lesions (Lesions with reported values may be less than total number of lesions treated in each arm).
23-May-2017 Data

Comparison between Rutherford categories significant ($p<0.05$)

LIBERTY Freedom from Major Adverse Events (MAEs)

Considering comorbidities, high freedom from MAE at 1-year, indicating even RC6 subjects can benefit from PVI.



MAE: Death to 30 days, Major amputation, TVR

LIBERTY 360: Prospective, observational, multi-center study to evaluate procedural and long-term clinical and economic outcomes of endovascular device interventions in patients with symptomatic lower extremity PAD (N=1,204 Subjects)

Kaplan-Meier method used to obtain estimate of freedom from MAE.
Greenwood's method used to obtain the 95% confidence interval for the estimate.
23-May-2017 Data

Atherectomy devices

- Pantheris (Avinger) above knee trial
- Phoenix (Volcano) above and BTK data registry
- Anecdotal BTK data

DISRUPT BTK Study: Infrapopliteal Disease

Objective: *To study the safety and performance of the Shockwave Medical Peripheral Intravascular Lithotripsy System in the treatment of calcified, stenotic infrapopliteal peripheral arteries.*

Design

Key eligibility criteria

- Rutherford category 1-5 infrapopliteal disease
- Infrapopliteal lesions ≥50% stenosis
- RVD 2.5–3.5 mm, ≤150 mm length
- Moderate and severe calcification by angiography

Endpoints

Procedural

- Primary Effectiveness: Acute reduction in % diameter stenosis

Follow up: 30 days

- Major adverse events (Death, MI, TLR, amputation)

DISRUPT BTK:
Patient Demographics and Angiographic Findings†

Baseline Characteristics	N = 20
Age, years, mean ± SD	79±9.6
Male Gender, % (n)	70.0% (14)
Diabetes, % (n)	40.0% (8)
Hypertension, % (n)	95.0% (19)
Hyperlipidemia, % (n)	75.0% (15)
Renal Insufficiency, % (n)	40.0% (8)
Coronary Artery Disease, % (n)	40.0% (8)
Current or Former Smoker, % (n)	25.0% (5)
Rutherford Class, % (n)	
RC 3	20.0% (4)
RC 4	5.0% (1)
RC 5	75.0% (15)

†Core lab adjudicated

Pre-procedure	N=21 lesions, 19 subjects
Tibio-peroneal trunk	9.5% (2)
Anterior tibial	38.1% (8)
Posterior tibial	38.1% (8)
Peroneal	9.5% (2)
Popliteal artery below knee	4.8% (1)
Reference vessel diameter, mm, mean ± SD (range)	3.2 ± 0.6 (2.4-4.8)
Lesion length, mm, mean ± SD (range)	52.2 ± 35.8 (13.8-144.0)
Calcified length, mm, mean ± SD (range)	72.1 ± 37.6 (12.4-172.6)
Calcification, % (n)	
Moderate	52.4% (11)
Severe	47.6% (9)
Mean luminal diameter, mm, mean ± SD (range)	.9 ± 0.6 (0.0-1.9)
Diameter stenosis, %	72.6%

Moderate Calcification: densities noted only prior to contrast injection. Severe Calcification: radiopacities noted prior to contrast injection generally involving both sides of the arterial wall

DISRUPT BTK data based on European studies.

DISRUPT BTK:
Safety & Effectiveness†

Endpoint	% (n)
Primary Safety Endpoint: MAE rate @ 30 days	0% (0/20)
Primary Effectiveness Endpoint: Acute reduction in % stenosis	46.5% (19/19*)
Secondary Endpoint: Post-IVL residual stenosis of ≤50%	100% (19/19*)

*In 1 patient, the IVL catheter was unable to cross

†Core lab adjudicated

Final Procedure	N=21 lesions, 19 subjects
Mean luminal diameter, mm, mean ± SD (range)	2.4 ± 0.5 (1.5-3.6)
Diameter stenosis, %	26.2%
Diameter stenosis reduction, %	46.5.%
Acute gain, mm, mean ± SD (range)	1.5± 0.5 (0.7-2.3)
Dissection	4.8.% (1)
Perforation	0% (0)
Distal embolization	0% (0)
Thrombus	0% (0)
No reflow	0% (0)
Abrupt closure	0% (0)

DISRUPT PAD & DISRUPT BTK categorized calcified lesions as per PARC definitions. Both studies utilized independent core labs and clinical events committees.
DISRUPT BTK data based on European studies.

Conclusions

- Arterial compliance is an issue for many if not all endovascular procedures
- Many devices available to alter vessel compliance
- Arterial outcomes appear (registry data) improved (primary patency, MALE) with upfront atherectomy for tibial circulation
- No data to date to suggest atherectomy improves amputation free survival
- Other devices on the horizon may afford similar outcomes
  - Costs remain a question
- More data clearly needed on these cost consuming strategies
- DCB data mixed and moderately positive at 6 months