Treatment of Heavily Calcified Lesions

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Disclosure Statement of Financial Interest

- Ajay J. Kirtane
  - Institutional research grants to Columbia University from Medtronic, Boston Scientific, Abbott Vascular, CSI, Abiomed, CathWorks, Siemens

Detection and frequency of coronary calcification

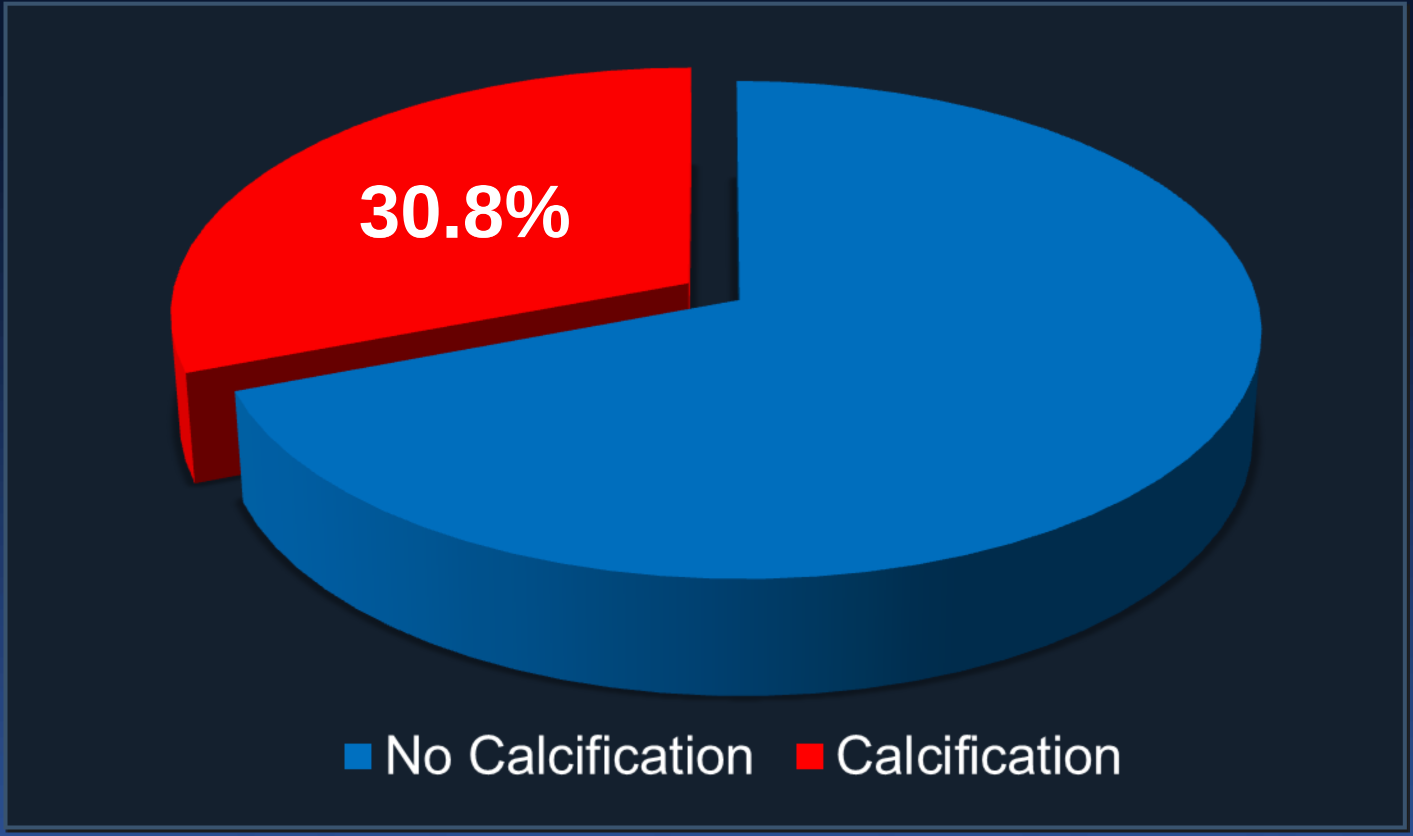
Frequency of angio core lab moderate-severe calcification in 13 DES studies

(despite being an exclusion criterion in most studies)

RAVEL	23.3% (27/116)
SIRIUS	17.1% (91/531)
E-SIRIUS	16.1% (28/174)
C-SIRIUS	12.0% (6/50)
TAXUS IV	18.3% (121/660)
TAXUS V	32.5% (185/570)
TAXUS VI	29.7% (65/219)
ENDEAVOR II	23.7% (140/590)
ENDEAVOR III	17.9% (78/436)
ENDEAVOR IV	33.2% (513/1546)
SPIRIT II	31.4% (91/290)
SPIRIT III	27.8% (277/997)
COMPARE	38.5% (693/1799)
Pooled	**29.0% (2,315/7,978)**

ADAPT-DES (11 center all-comers registry):
Site-reported Mod/Sev Calcification

N = 8,582 pts

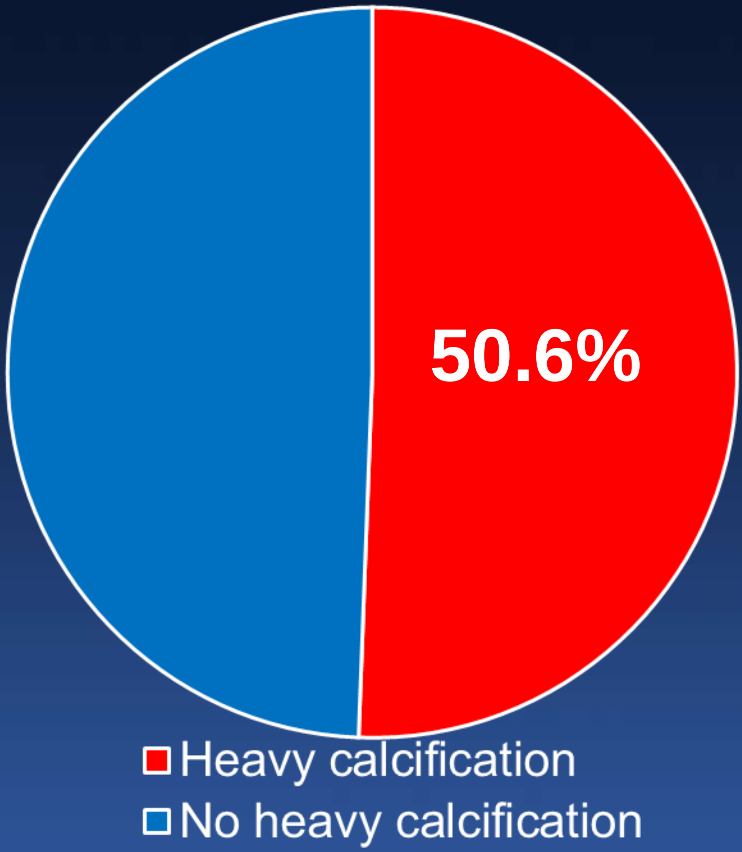


Généreux et al, Int J Cardiol 2017

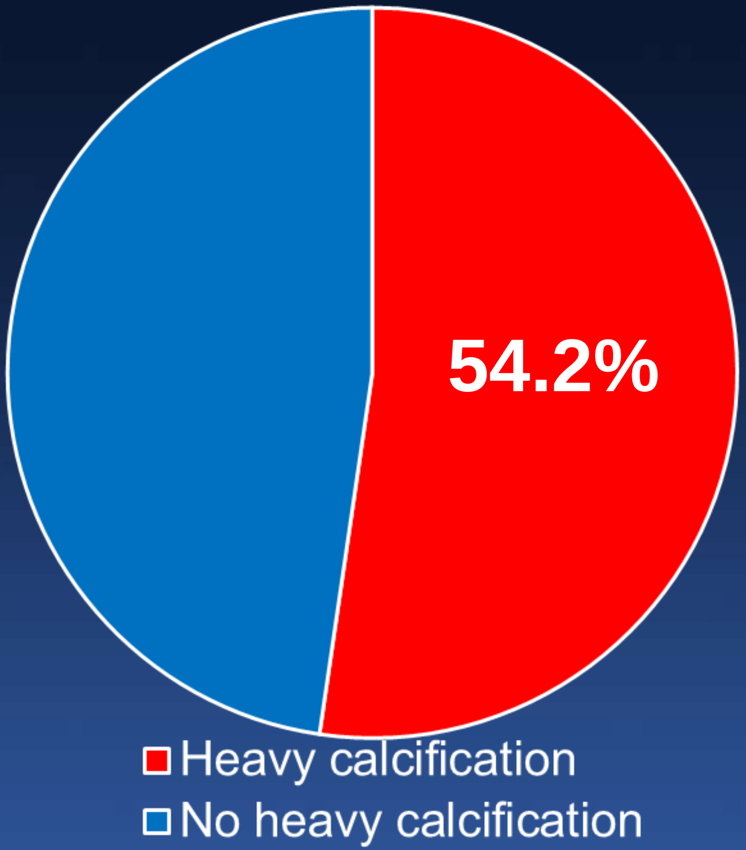
Frequency of "heavy" calcification in the SYNTAX trial: Randomized + Registry

N=2,636 pts with LM or 3VD

PCI (n=1,095)



CABG (n=1,541)



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Farooq et al. J Am Coll Cardiol 2013;61:282–94

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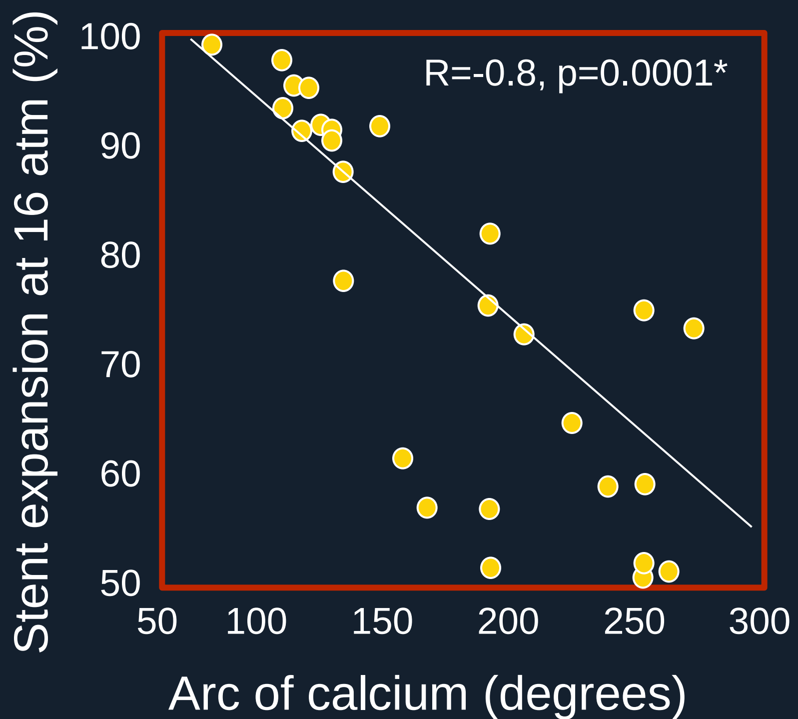
Implications of coronary calcification

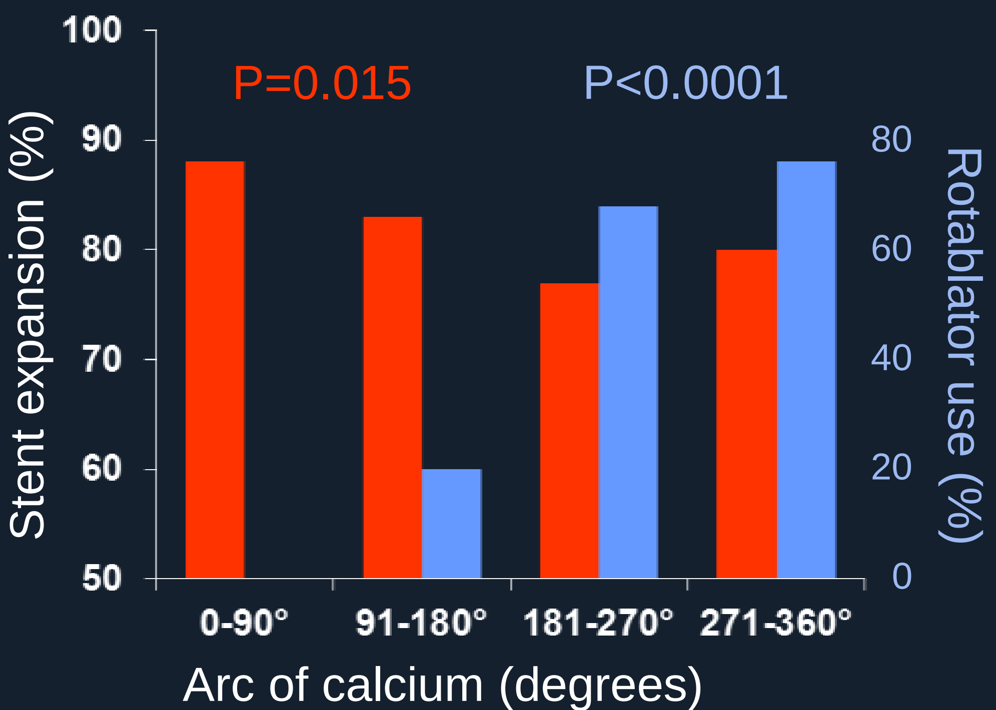
Implications of coronary calcification

- ***Coronary calcification results in:***
  - Impaired stent delivery, decreased stent expansion, increased malapposition and stent asymmetry
  - Increased procedural complications (edge dissections and perforations)
  - Increased rates of stent thrombosis and restenosis

Stent Expansion in Calcified Lesions



*There was a similar, albeit less strong, correlation after 20 atm inflation (r=-0.58, p=0.0007)



Vavarunakis et al. Catheter Cardiovasc Interv 2001;52:164-172
Hoffmann et al. Eur Heart J 1998;19:1224-31

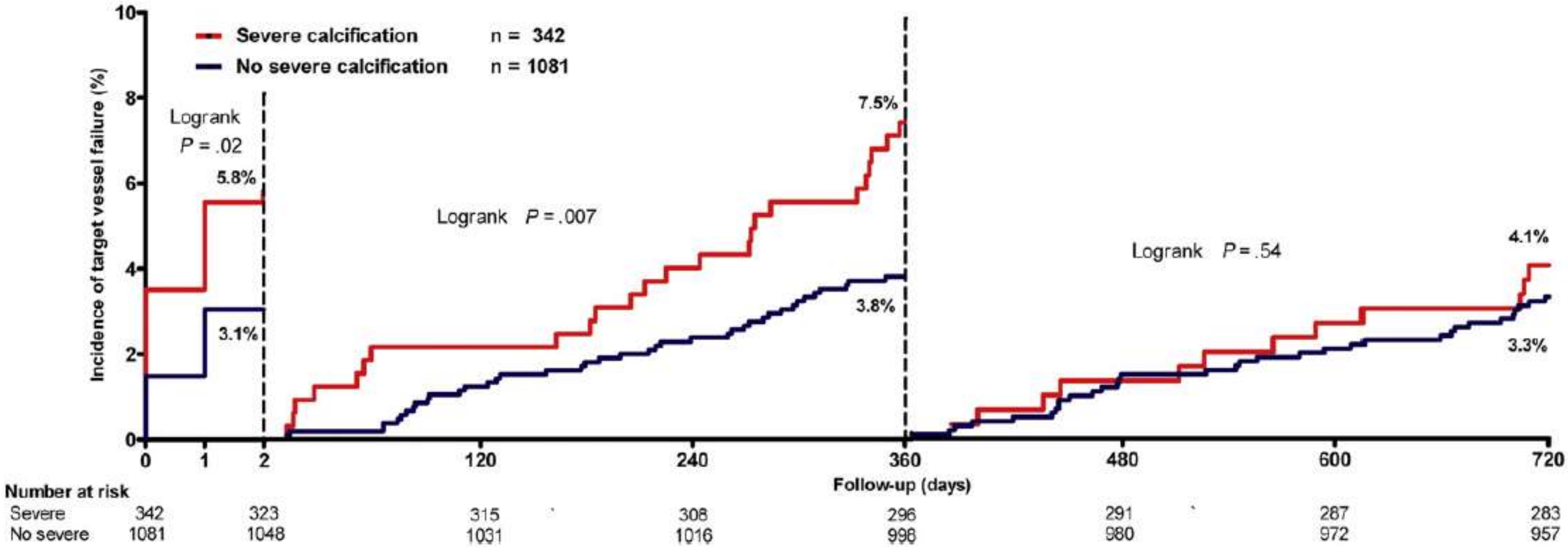
ADAPT-DES (N=8,582): Calcification and 2-Year Events

	Calcification		Unadjusted P value	Adjusted HR [95% CI]	Adjusted P value
	No (n=5,938)	Yes (n=2,644)			
TVF	14.2%	18.1%	<0.0001	1.23 [1.09, 1.39]	0.0008
MACE	5.6%	8.3%	<0.0001	1.47 [1.22, 1.76]	<0.0001
Death	3.5%	4.8%	0.003	1.15 [0.90, 1.46]	0.26
CV death	2.3%	2.8%	0.09	1.09 [0.80, 1.48]	0.60
MI	4.0%	6.4%	<0.0001	1.61 [1.30, 1.99]	<0.0001
Clinically-driven TVR	9.5%	10.4%	0.16	1.10 [0.94, 1.29]	0.24
Stent thrombosis	0.9%	1.1%	0.32	1.49 [0.92, 2.43]	0.11

Généreux et al, Int J Cardiol 2017

TWENTE and DUTCH PEERS (TWENTE II): Impact of Severe Calcification with 2nd Generation DES

1,423 pts with stable angina; 342 with severe calcification (24%)



At 2 years, TVF was 16.4% vs. 9.8%, p=0.001
predominantly driven by events in the first 48 hours and up to 1 year

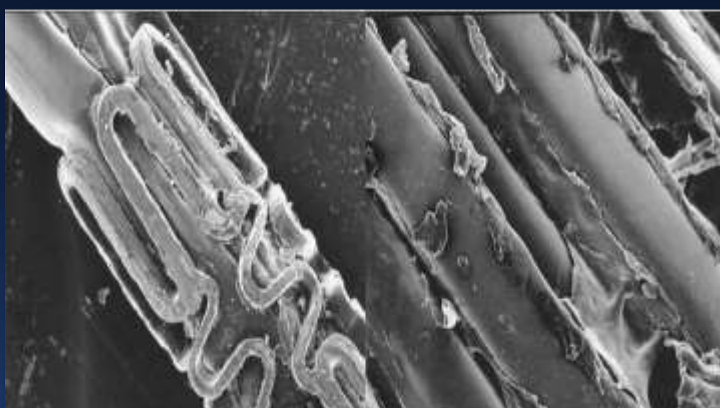
Of note, 2 year definite ST was 1.8% vs. 0.4%, p=0.02

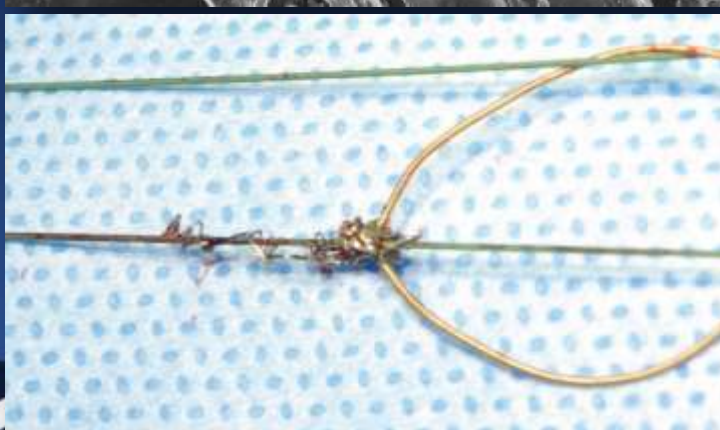
Treatment of coronary calcification

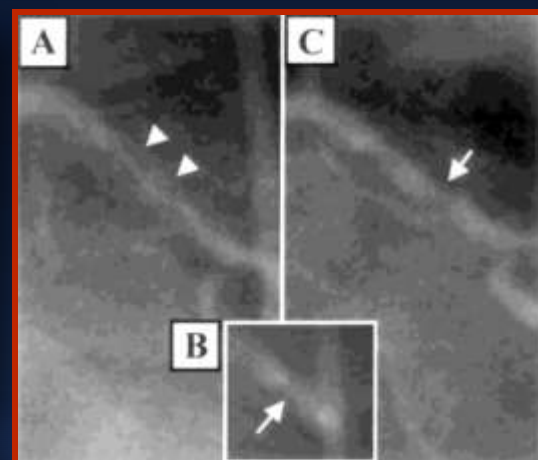
Why is Appropriate Lesion Preparation for Coronary Calcification Important?

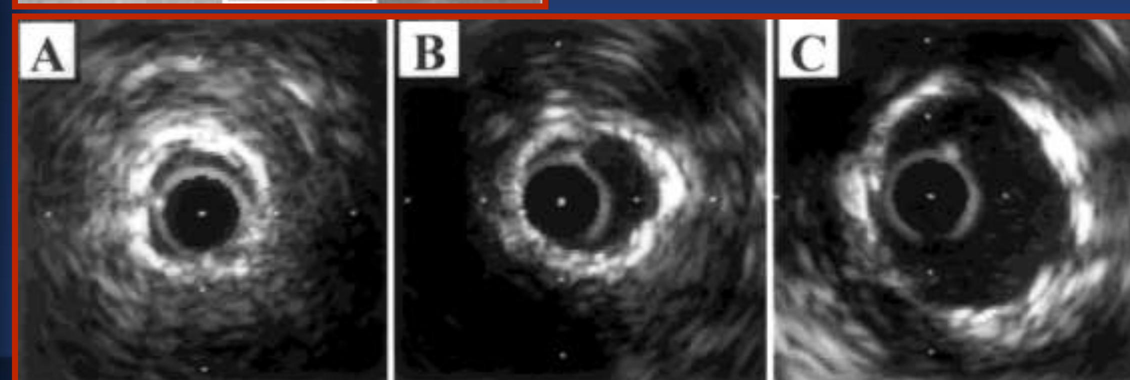
Lesion calcification:

- May impair stent delivery or expansion
- May abrade polymers off DES









Stentablation
Kobayashi et al.
CCI
2001;52:208-11

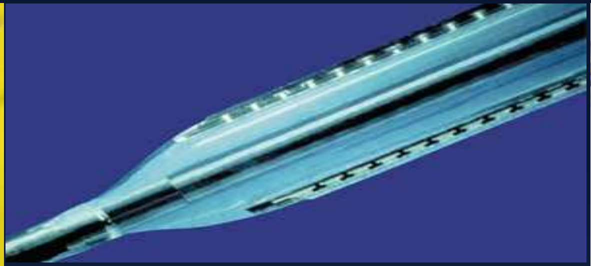
Lesion Preparation =
Lumen Expansion + Plaque modification

- *Facilitates procedural success* when treating calcified/complex lesions
  - enables lesion access for balloons and especially stents
- *Plaque modification*: changing lesion compliance
  - minimizes vessel “trauma” (severe dissections)
  - creates a larger MLD

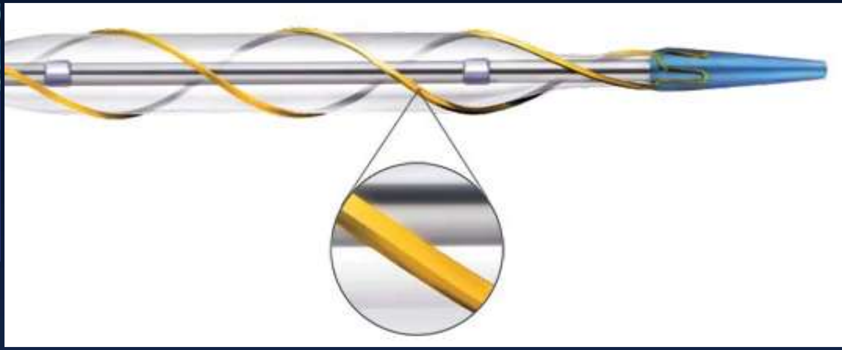
Treatment of Calcified Lesions: Options

NC balloons

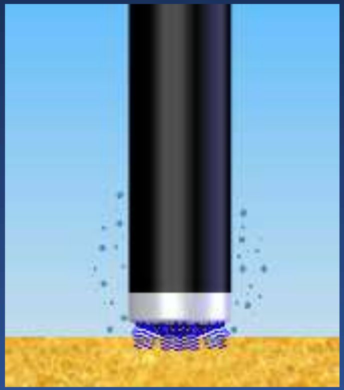
Cutting balloon



Angiosculpt

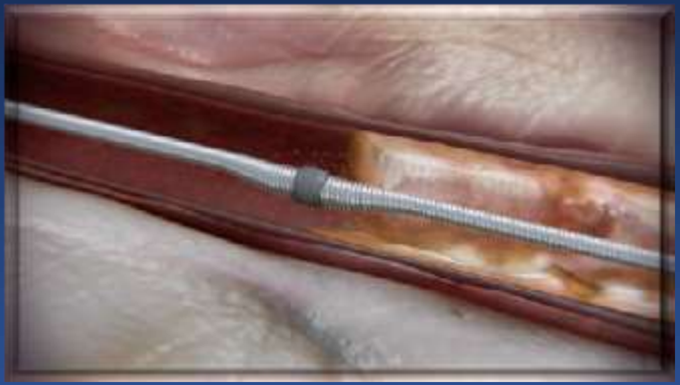


Laser



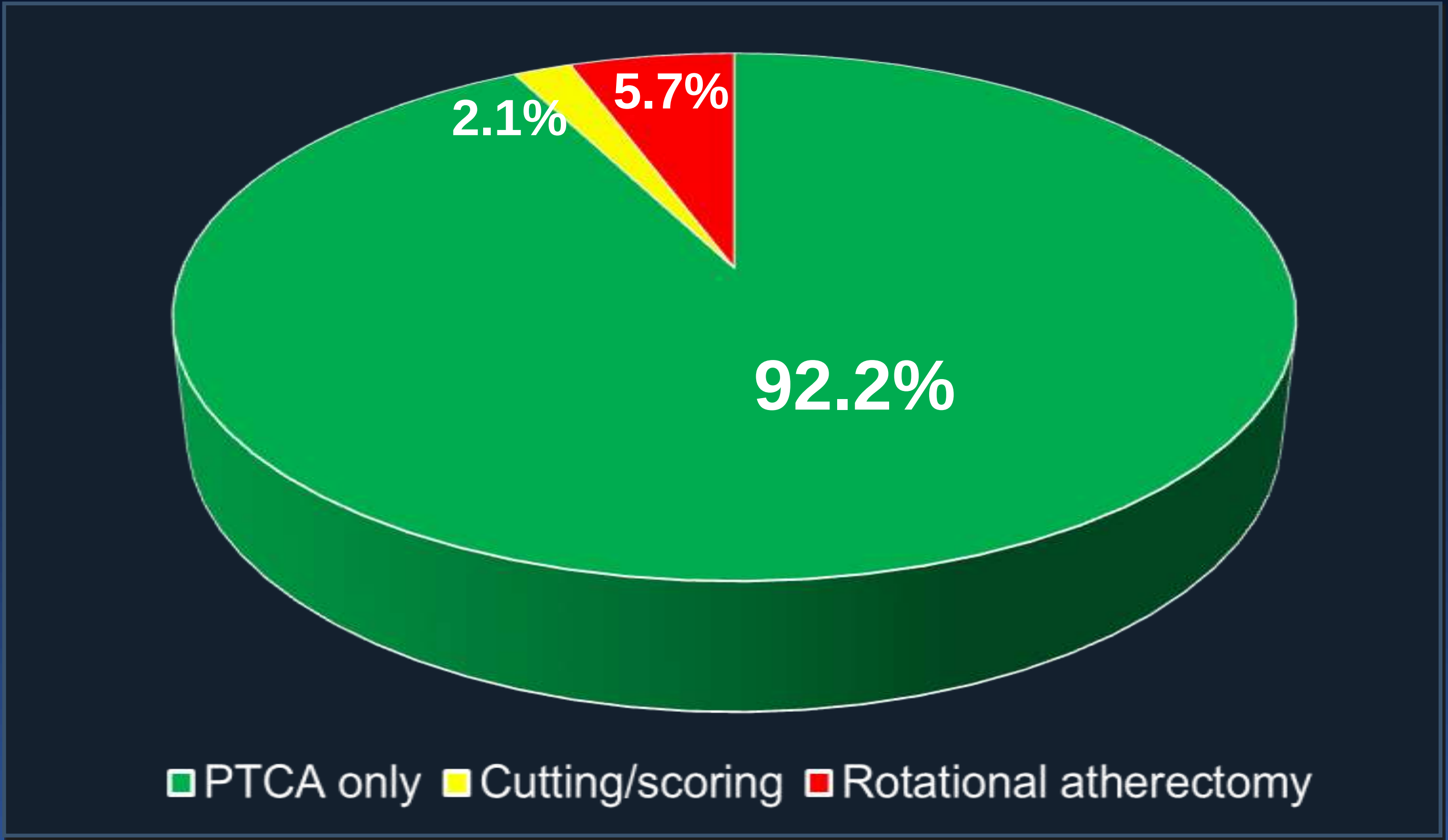
Rotational atherectomy

Orbital atherectomy



ADAPT-DES (11 center all-comers registry):
Calcified lesion preparation

N = 2,644 patients



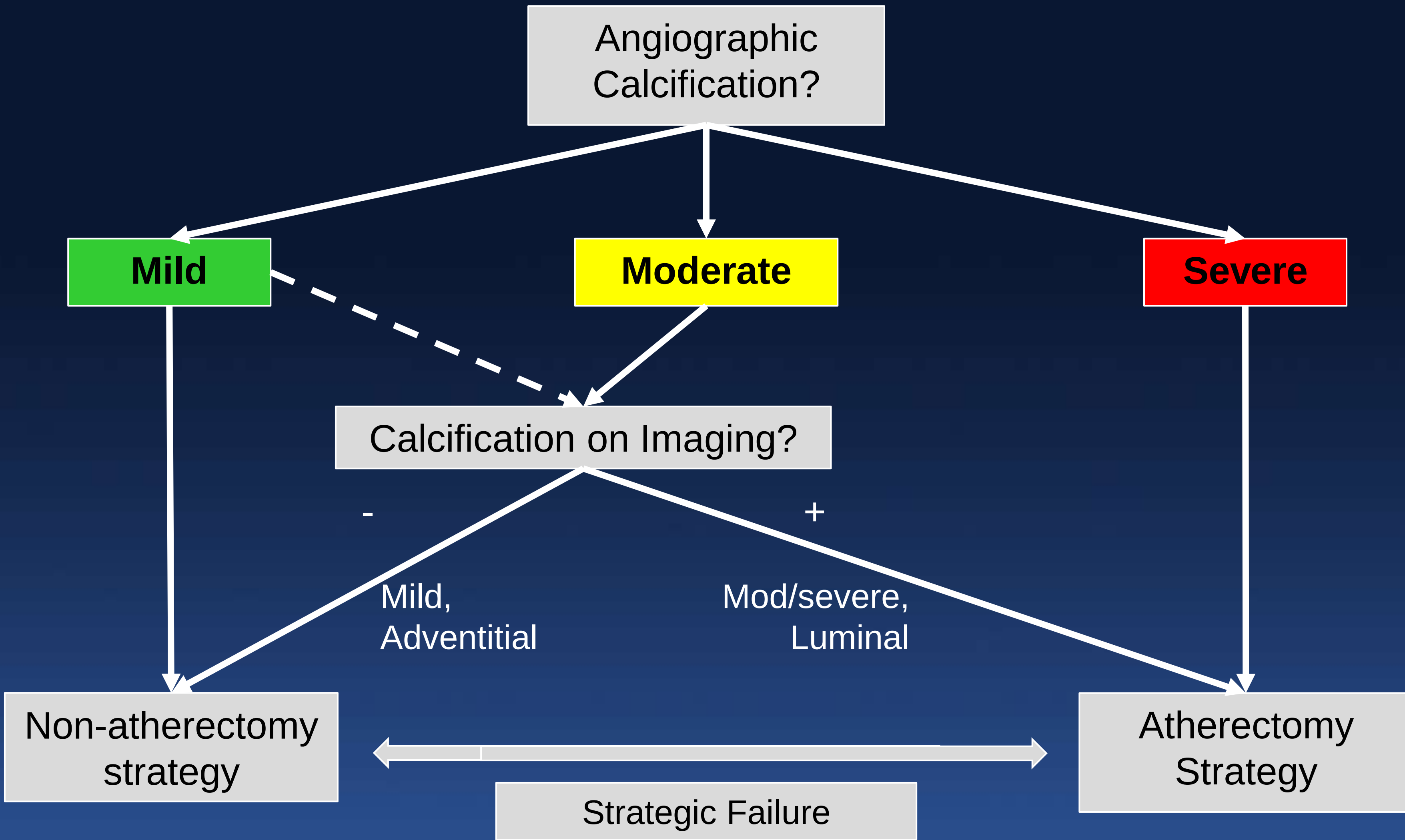
Généreux et al. Int. J. Cardiol 2017

Treatment of Calcified Lesions: PCI guidelines

Device	ACCF/AHA/SCAI 2011	ESC/EAPCI 2014
Cutting/scoring balloon angioplasty	• Might be considered to avoid slippage induced coronary artery trauma during PCI for in-stent restenosis or ostial lesions in side branches (**Class IIb-C**) • Should not be performed routinely during PCI (**Class III-A**)	May be useful in highly calcified, rigid ostial lesions (also applies to scoring).
Rotational atherectomy	• Reasonable for fibrotic or ***heavily calcified lesions*** that might not be crossed by a balloon catheter or adequately dilated before stent implantation (**Class IIa-C**) • Should not be performed routinely for de novo lesions or in-stent restenosis (**Class III-A**)	Might technically be required in cases of tight and calcified lesions, to allow subsequent passage of balloons and stents.
Laser angioplasty	• Might be considered for fibrotic or moderately calcified lesions that cannot be crossed or dilated with conventional balloon angioplasty (**Class IIb-C**) • Should not be used routinely during PCI (**Class III-A**)	(Laser not mentioned for calcification)

Levine GN et al. JACC 2011;58:e44-122
Windecker S et al. EHJ 2014;35:3541-619

Strategy for Approaching Calcified Lesions



Adapted from Tomey et al, JACC CV Intv 2014

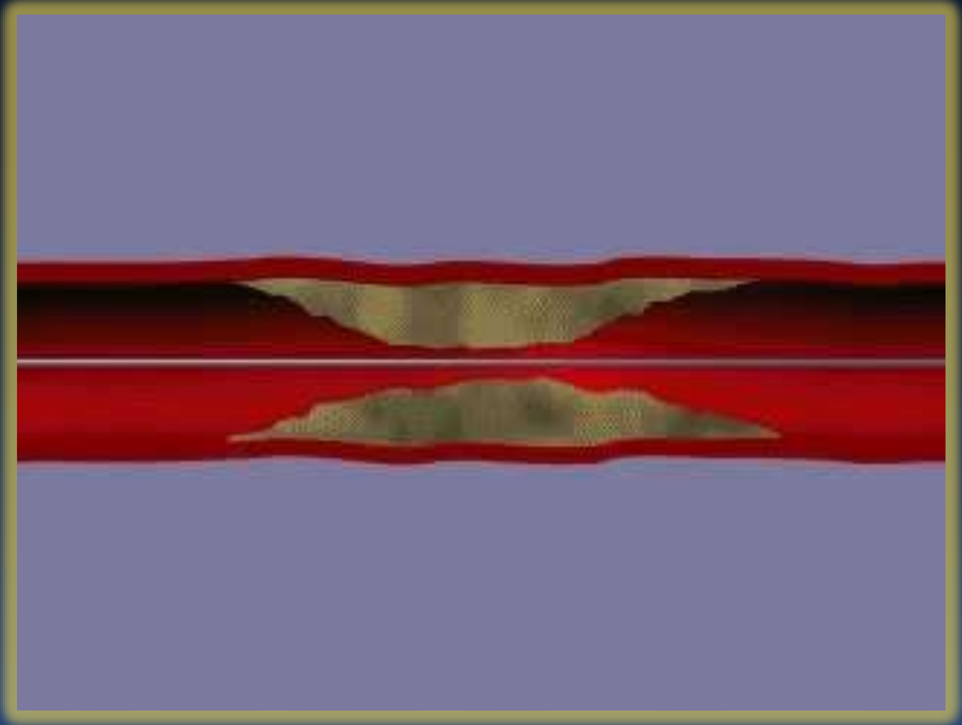
Rotablator Rotational Atherectomy System

FDA approved May 1993

Rotablator Rotational Atherectomy System

TECHNICAL CONSIDERATIONS

- **Single burr with burr-to-artery ratio of 0.5 to 0.6**
- **Rotational speed of 140,000 to 150,000 rpm**

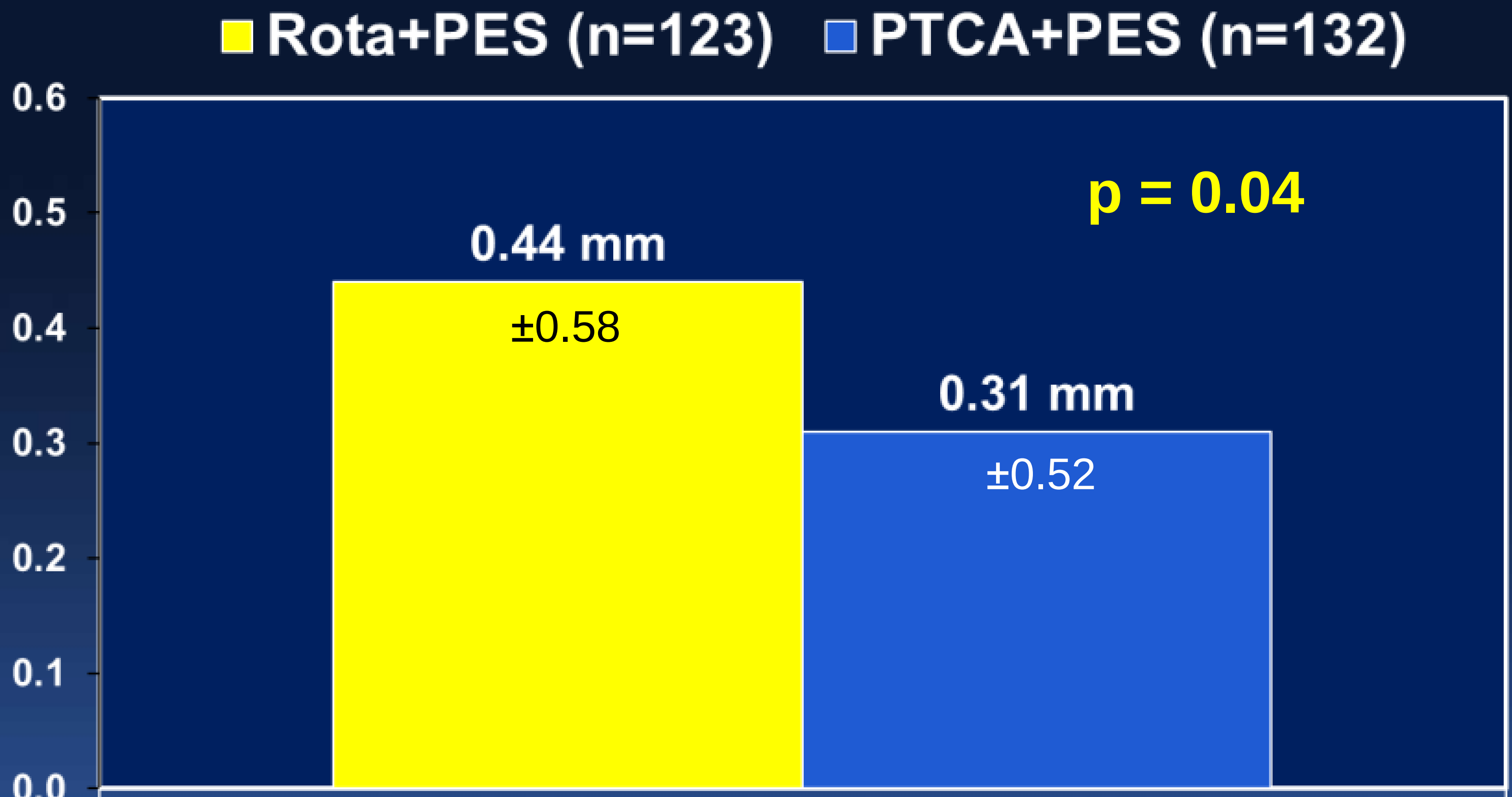


OPERATOR TECHNIQUE

- **Gradual burr advancement using a pecking motion**
- **Short ablation runs of 15 – 30 sec**
- **Avoidance of decelerations > 5,000 rpm**
- **Final polishing run**

ROTAXUS: Primary Endpoint

In-Stent Late Lumen Loss at 9 Months



Restenosis = 12.2% vs. 12.9%, P=0.89

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Abdel-Wahab M et al. JACC CV Interv 2013;6:10-19

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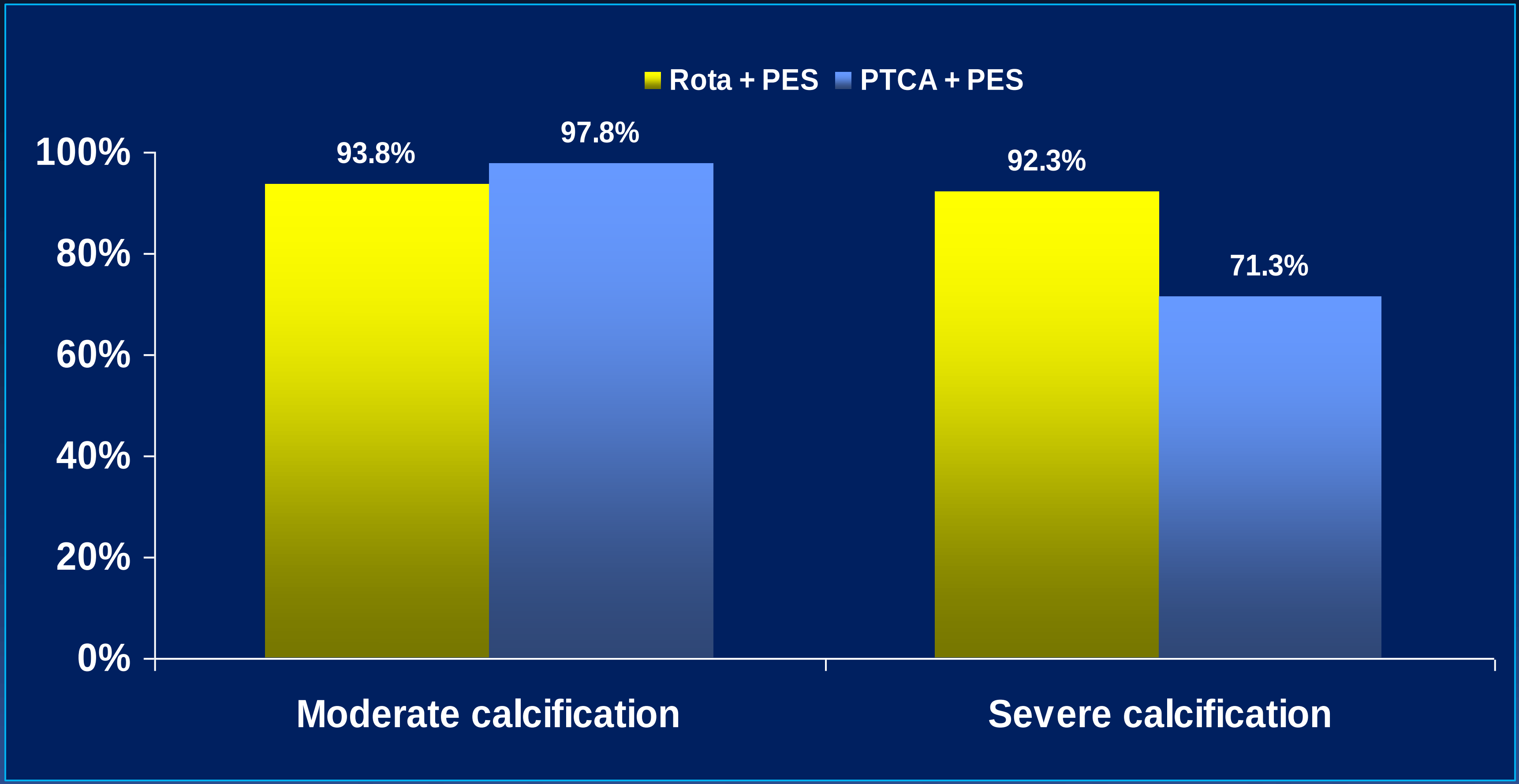
ROTAXUS: Strategy Success according to calcification



Abdel-Wahab M et al. JACC CV Interv 2013;6:10-19

ROATE: Provisional RA Sub-analysis

A potential risk of RA following balloon dilatation

Provisional RA
309 patients (349 lesions)

- **Device delivery failure** — 226 patients (73.1%)
- **Balloon expansion failure** — 83 patients (26.9%)

Device delivery failure		Balloon expansion failure
7.1%	In-hospital MACE	16.9%
	P=0.01	
6.2%	In-hospital MI	14.5%
	P=0.02	

Kawamoto et al, CCI 2016

DIAMONDBACK 360: Coronary Orbital Atherectomy System

Device Features
- Simple device setup
- Microsecond feedback to changes in loading
- 135cm usable length

Eccentric diamond coated crown

Electric motor powered handle

Power on/off switch
- 8 cm axial travel

On-handle speed control
- Low (80K) and High Speed (120K)

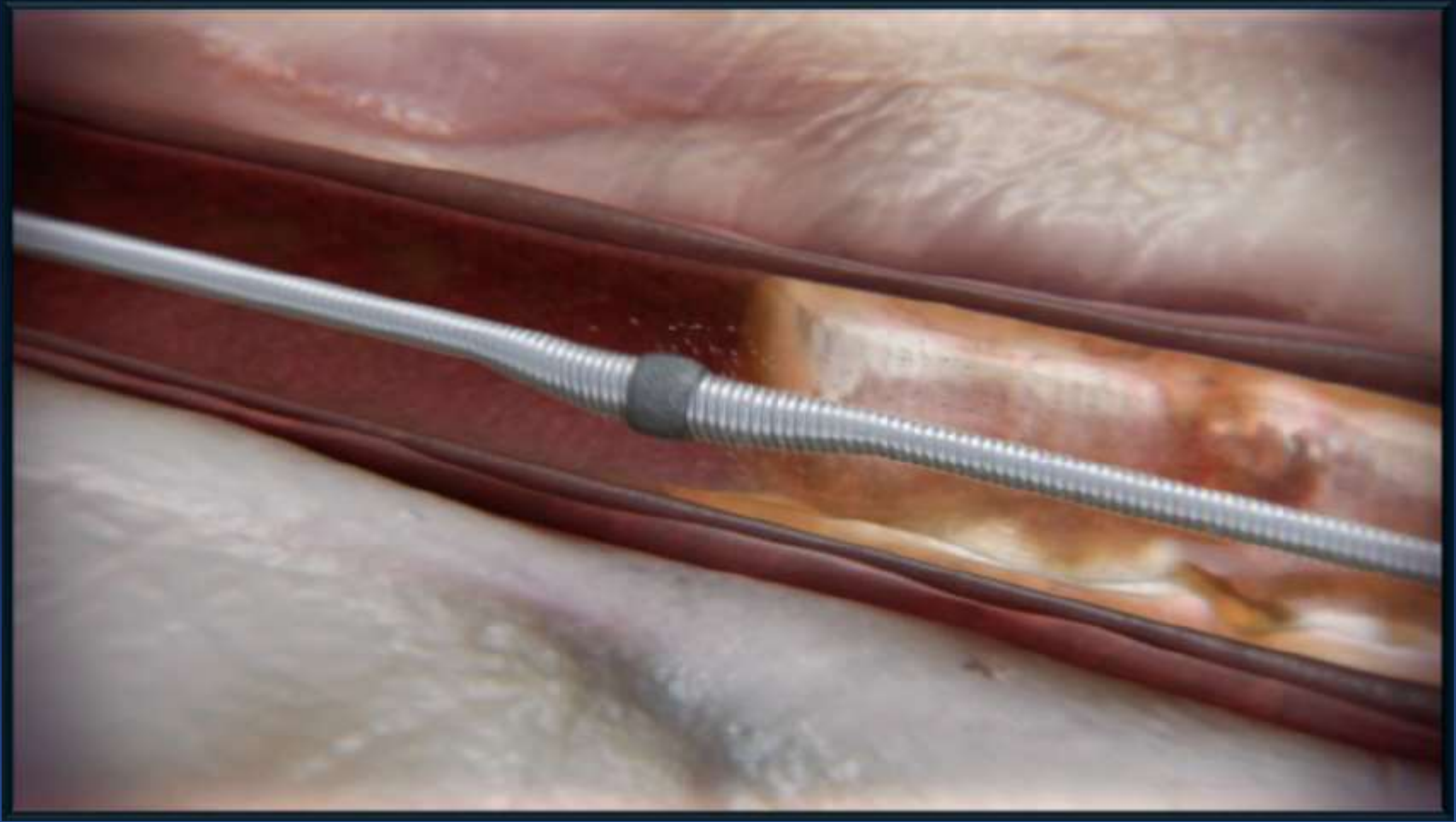
6Fr Guide Compatible

0.012" Viper Wire

Saline Infusion Pump
- Mounts directly on to an IV pole
- Provides power
- Delivers fluid
- Includes saline sensor

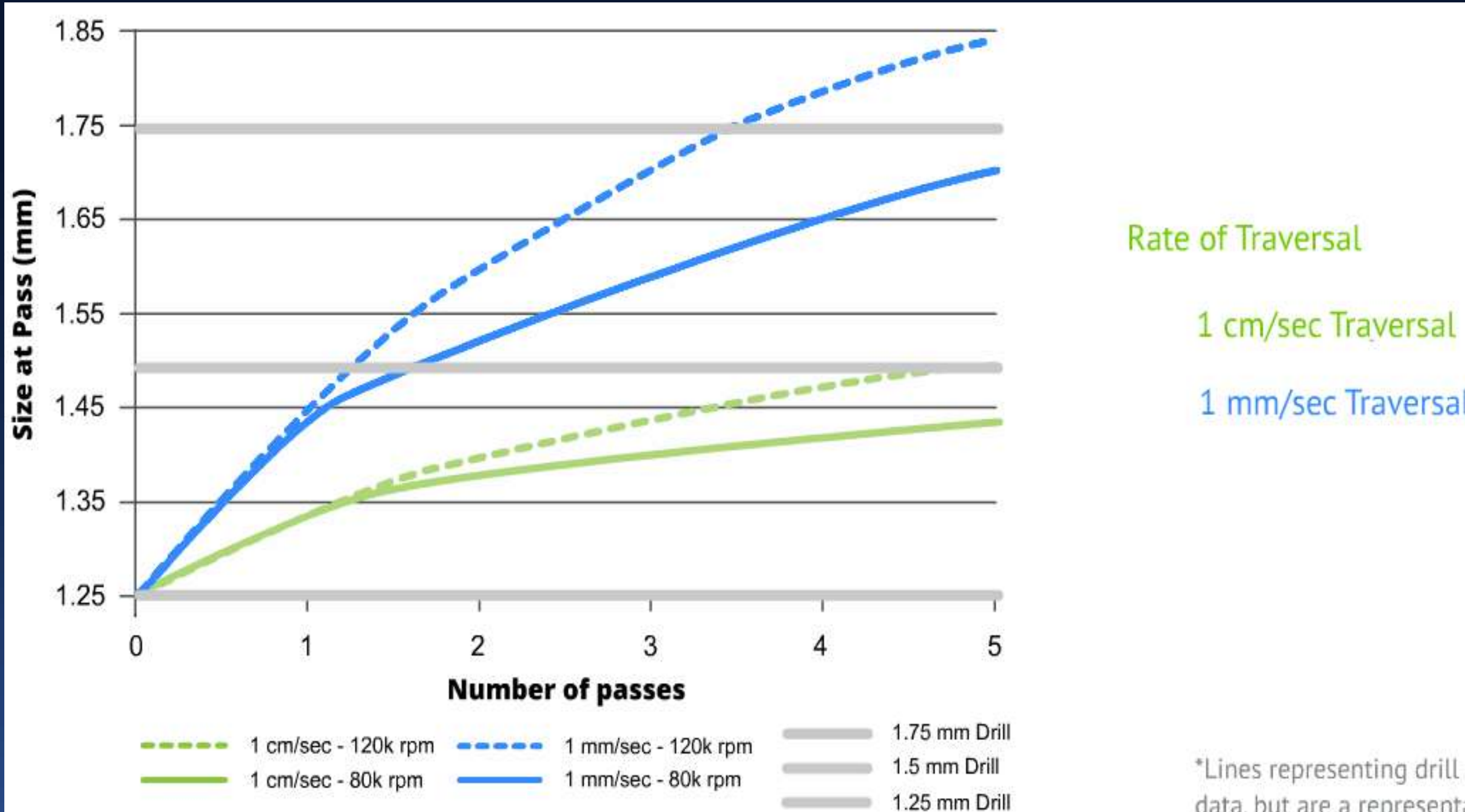
ViperSlide® Lubricant
- ViperSlide reduces friction during operation
- 20ml ViperSlide per liter of saline

OAS: Mechanism is Differential Sanding



Orbital Atherectomy is Time-Dependent

Orbit in a Carbon Block Model System

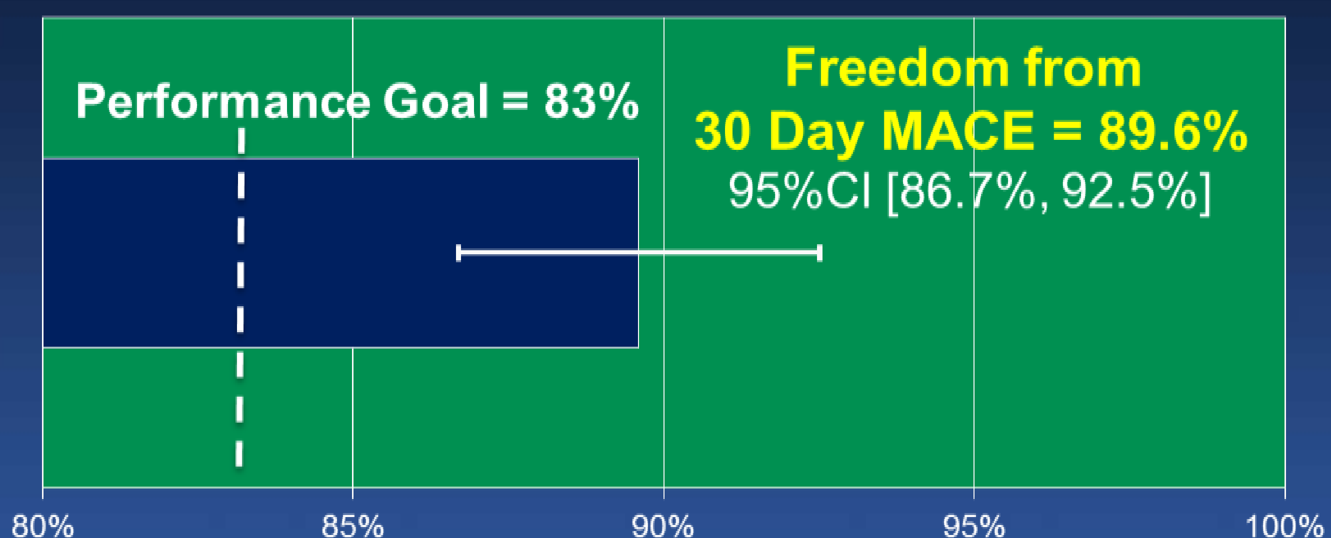


*Lines representing drill are not based on data, but are a representation to illustrate lack of luminal gain over time

ORBIT II: Single arm study in severely calcified lesions (n=443 at 49 US sites)

1° safety endpoint: 30 day MACE = 10.4%

Cardiac death:	0.2%
MI (CK-MB >3x ULN):	9.7%
- Non Q-wave	8.8%
- Q-wave	0.9%
TVR/TLR:	1.4%

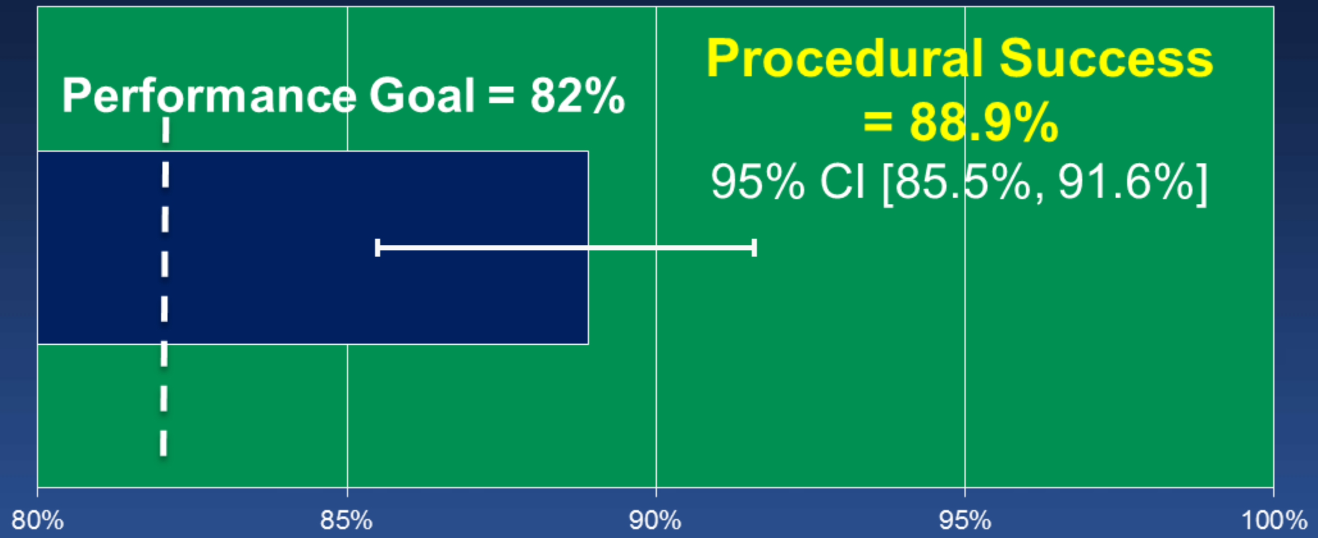


Chambers JW et al. JACC CV Interv. 2014;7:510-8

ORBIT II: Single arm study in severely calcified lesions (n=443 at 49 US sites)

1° efficacy endpoint: Procedural success (stent delivery with DS <50% without in-hospital MACE) = 88.9%

Successful stent delivery:	97.7%
DS <50%:	98.6%
In hospital MACE:	9.8%



ORBIT II: Single arm study in severely calcified lesions (n=443 at 49 US sites)

Clinical Outcomes

Variable	In-Hospital	30-Day	1-Year
MACE	43 (9.8)	46 (10.4)	72 (16.4)
Death	2 (0.5)	2 (0.5)	19 (4.4)
- Cardiac death	1 (0.2)	1 (0.2)	13 (3.0)
MI (≥3x CK-MB)	41 (9.3)	43 (9.7)	43 (9.7)
- Non–Q-wave MI	38 (8.6)	39 (8.8)	39 (8.8)
- Q-wave MI	3 (0.7)	4 (0.9)	4 (0.9)
MI (≥10x CK-MB)	9 (2.1)	9 (2.0)	9 (2.0)
TLR	0 (0.0)	3 (0.7)	20 (4.7)
TVR	3 (0.7)	6 (1.4)	25 (5.9)
ARC def/prob ST	1 (0.2)	1 (0.2)	1 (0.2)

Chambers JW et al. JACC CV Interv. 2014;7:510-8
Généreux PG et al. Am J Cardiol 2015 ;115:1685-90

Relative Advantages of OAS and RA

OAS (0.012" wire)	RA (0.009" wire, 2 choices)
• Quick set-up • Faster learning curve • Hemodynamic stability (less slow flow?) • Single device for all lesions (e.g. larger lumen Rx via 6 Fr) • Distal/multiple lesions	• Front cutting for severe stenoses (subtotal/total/subintimal) • Aorto-ostial lesions • Severe angulation (with more wire bias/ less risk of perforation?) • ISR/underexpansion • Very large vessel needing 2.0 mm+ burr

Either can be used in most cases of severe calcium!

ECLIPSE

ECLIPSE Clinical Trial

Evaluation of Treatment Strategies for Severe **C**a**L**cif**I**c Coronary Arteries: Orbital Atherectomy vs. Conventional Angioplasty **P**rior to Implantation of Drug Eluting **S**t**E**nts

~2000 pts with severely calcified lesions; ~60 US sites

Randomize 1:1

Orbital Atherectomy Strategy	Conventional Angioplasty Strategy
(1.25 mm Crown followed by non-compliant balloon optimization)	(conventional and/or specialty balloons per operator discretion)
2nd generation DES implantation and optimization	2nd generation DES implantation and optimization

1° endpoints: 1) Post-PCI in-stent MSA (N~400 in imaging study)
2) 1-year TVF (all patients)

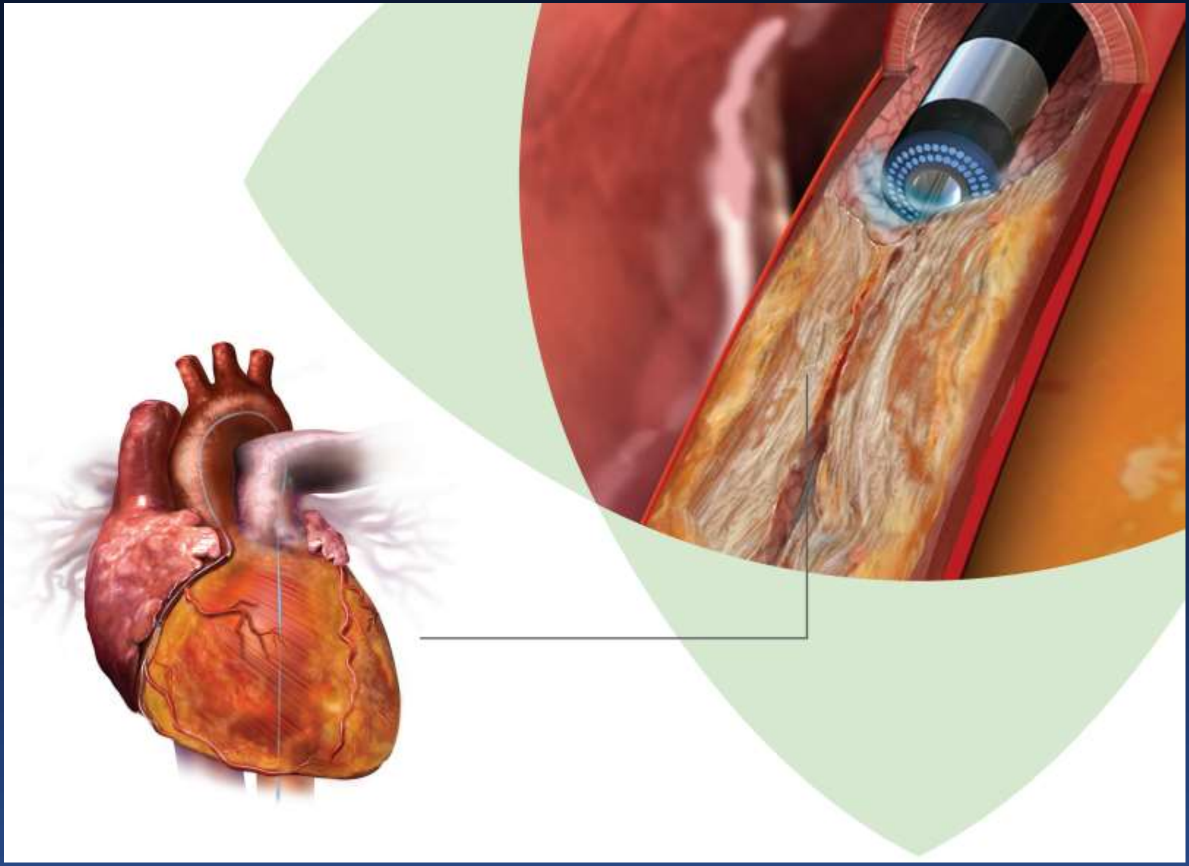
2° endpoint: Procedural Success (stent deployed w/RS<20% & no maj complications)

Principal investigators: Ajay J. Kirtane, Philippe Généreux; **Study chairman:** Gregg W. Stone
Sponsor: Cardiovascular Systems Inc.

Laser Atherectomy

Indications

- Total Occlusions: traversable by wire
- In-Stent Restenosis: 316L Stents
- SVG
- Moderately Calcified
- Failed Balloon
- Ostial Lesions
- Long Lesions



Shockwave Lithoplasty (Investigational)

Balloon Sizes

Diameter	Length
2.5 mm	12 mm
2.75 mm	12 mm
3.0 mm	12 mm
3.25 mm	12 mm
3.5 mm	12 mm
3.75 mm	12 mm
4.0 mm	12 mm

Lithotripsy delivery: 4 atm
Nominal: 6 atm
RBP: 10 atm

0.014" guidewire compatible
6F sheath compatibility

Summary and Conclusions I

- The presence and extent of lesion calcification is angiographically under-appreciated
- Moderate/severe lesion calcification is associated with greater rates of death, MI, TLR and stent thrombosis compared to non-calcified lesions
  - *When treating heavily calcified lesions, be prepared for increased complications!*
- During PCI of calcified lesions, IVUS and OCT are useful to determine the extent of calcification and to optimize stent results (MSA, geographic coverage and edge issues)

Summary and Conclusions II

- Scoring and cutting balloons are useful in mild and some moderately calcified lesions to improve vessel compliance, facilitating stent delivery and expansion
- Atherectomy provides effective lesion “decalcification” but has not (yet) been proven to improve clinical outcomes when used routinely in calcified lesions prior to DES
- *Specific calcium-based strategies should currently be used when device delivery and/or adequate stent expansion are unlikely to be achieved by conventional balloon pre-dilatation alone*