BTK Severe Ca++: Technical Challenges & Implications

Breakfast with Experts

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Severe Ca++: Technical Considerations & Clinical Implications

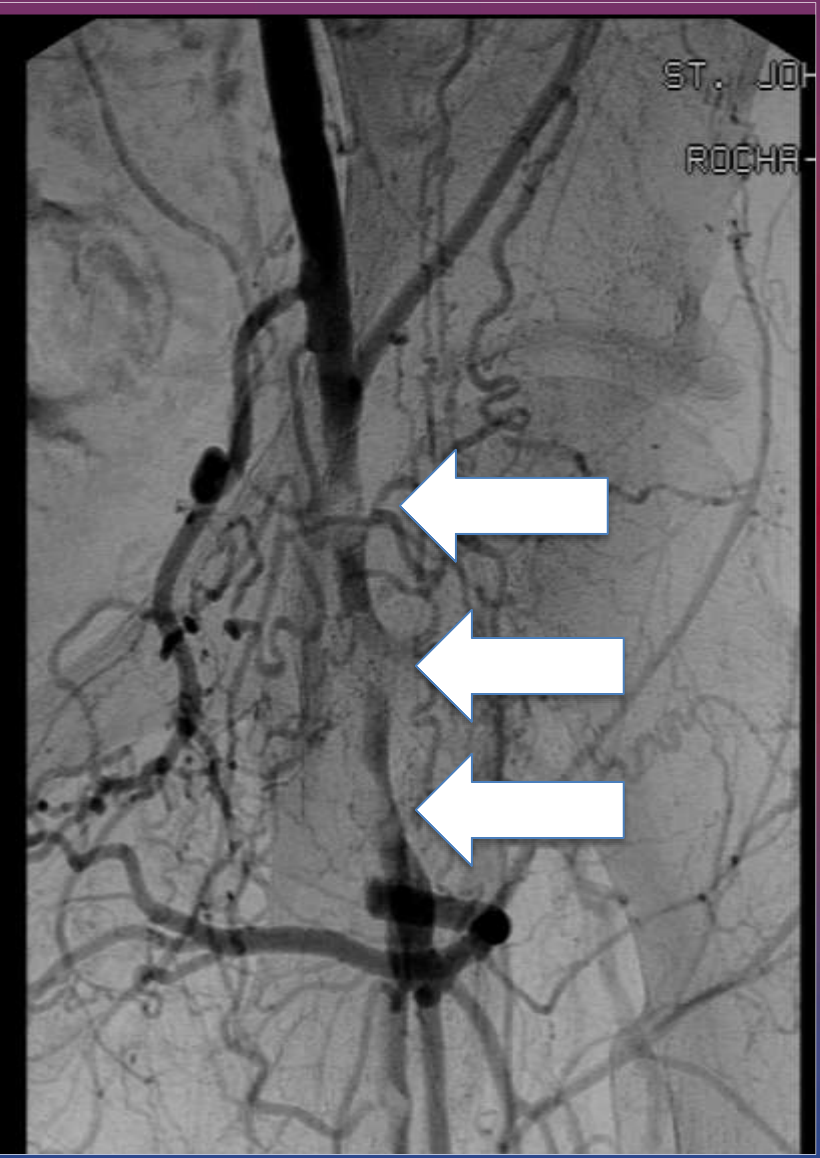
<u>Lecture Goals</u>: *A Call to Arms*

- **Review** the pathogenesis of vascular Ca++ and challenges to its classification
- **Discuss** current endovascular approaches to severe BTK calcification
- **Consider** the potential impact of severe vascular Ca++ on emerging technologies (i.e., DEBs)

What Would You Do?

- 67 yr old BF, s/p CABG, R CEA, DM with RC 4 Lt 1st toe pain
- Non-compressible ABIs; abnormal PVRs
- Up-stream left CFA and SFA angiography revealed the following:

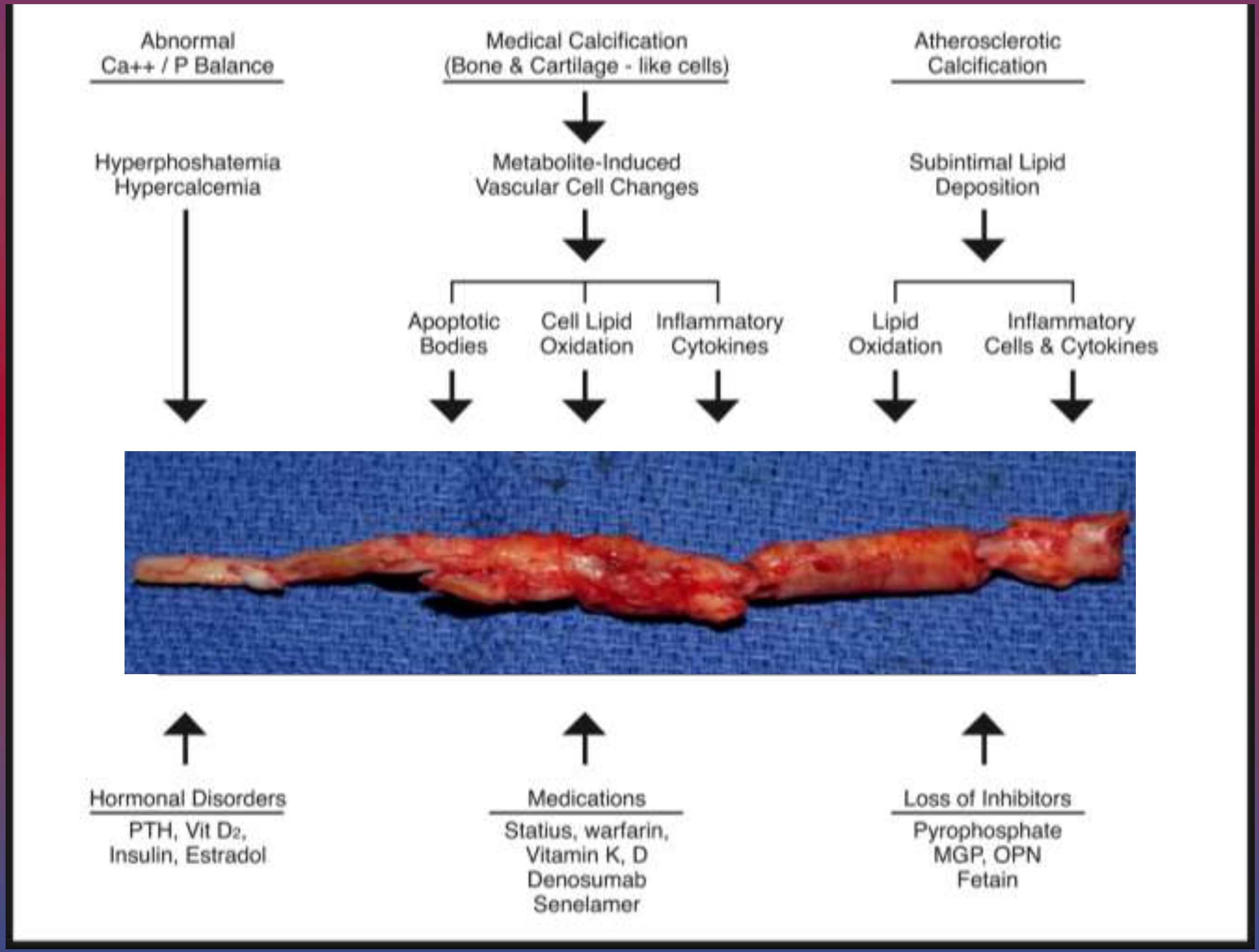
Severe Ca++ via DSA



WHAT Would YOU Do and WHY?

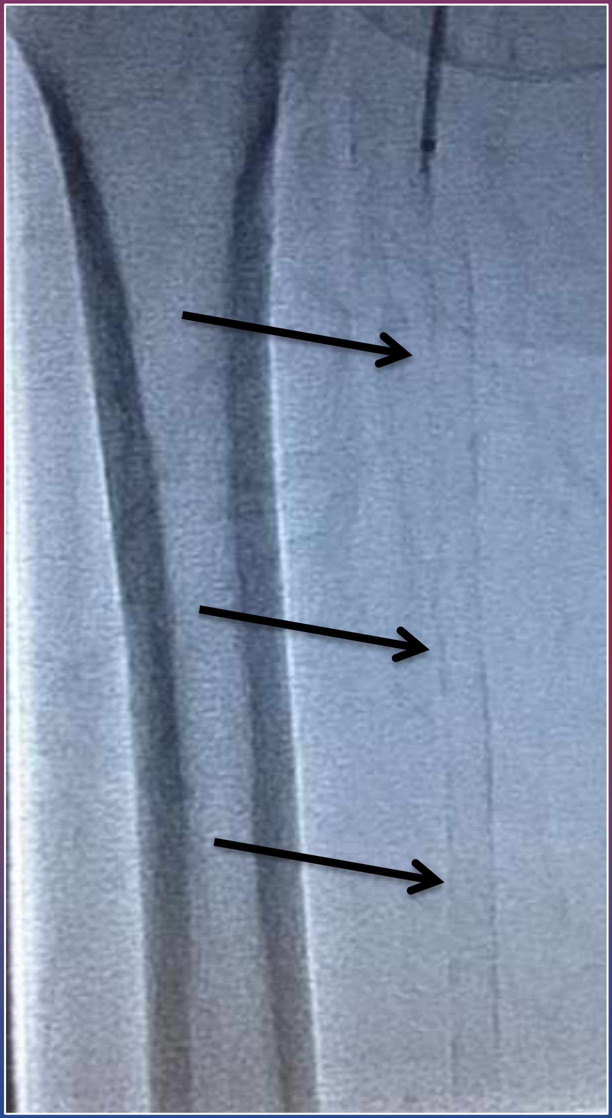
1. PTA + adjunct stenting
2. Primary nitinol stent implantation
3. Fox Hollow® atherectomy with DP + PTA
4. CFA endarterectomy + patch angioplasty

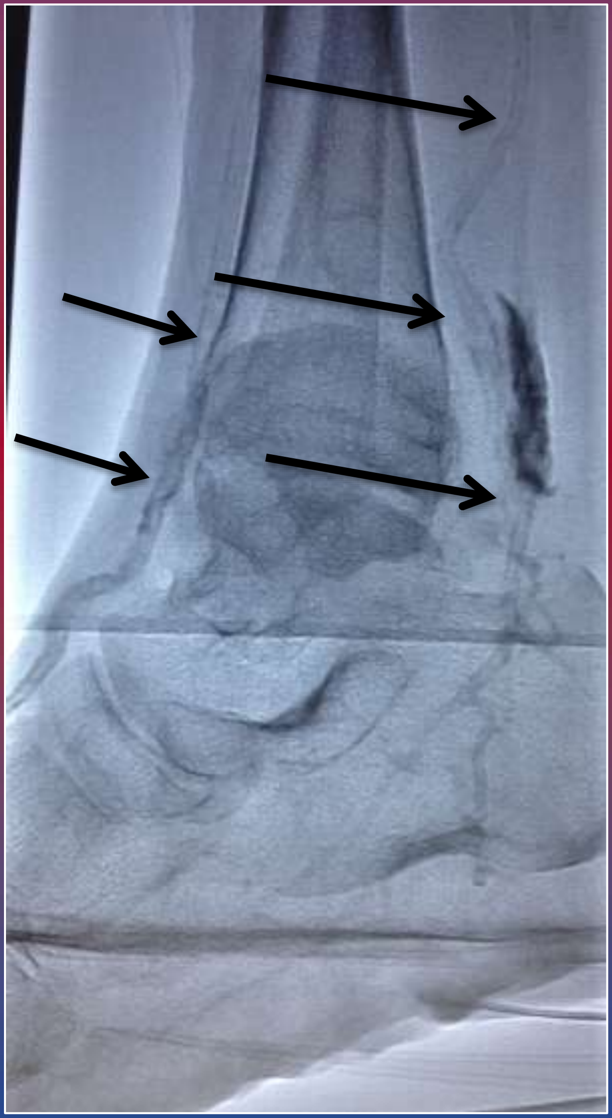
Vascular Calcification: It's Harder Than You Think!



Rocha-Singh CCI 2013

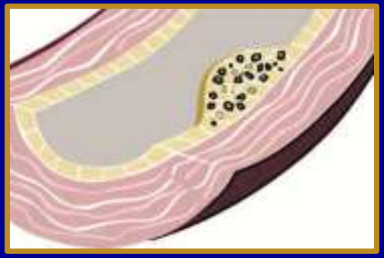
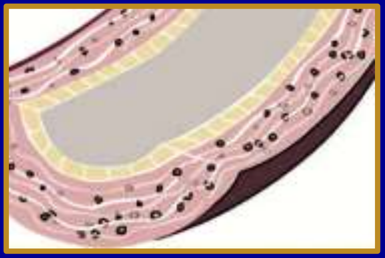
Severe BTK Ca++ in a 32 y/o Diabetic with ESRD





An Important Dichotomy:

Intimal vs. Medial Vascular Calcification

	Intimal calcification	Medial calcification
Calcification pattern	Atherosclerosis Focal, in plaques 	Arteriosclerosis or Mönckeberg’s sclerosis Generalized 
Risk factors	Dyslipidemia, hypercholesterolemia Lipid accumulation	Aging, diabetes, renal failure, osteoporosis, hypertension
Molecular mechanisms	Foam cell formation Inflammation Oxidative stress Apoptosis	Transdifferentiation of VSMCs into bone-like cells (osteoblast-chondrocyte and osteoclast-like cells) Ca, P, vitamin D metabolism Loss of calcification inhibitors (pyrophosphate, MGP, fetuin)
Consequences	Plaque formation: stenosis Plaque calcification: controversial effect on plaque stability, possibly relating to the localization of Calcification	Arterial stiffening: increased pulse pressure, elevated pulse wave velocity
Complications	Ischemia, infarction	Systolic hypertension, LVH

Question:
What is *'Severe'* Calcification?

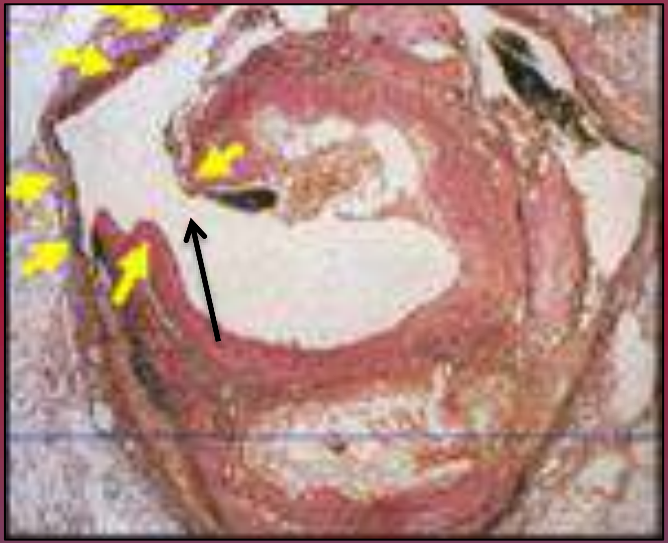
- Unlike the coronary bed, there is NO standardized, validated calcium scoring system tied to acute procedural, 30 d or long term (i.e., 12 mo.) clinical outcomes
- Most, if not all, US device regulatory trials exclude "severe" calcification
- However, medical conditions associated with severe vascular calcification are increasing…DM and CKD

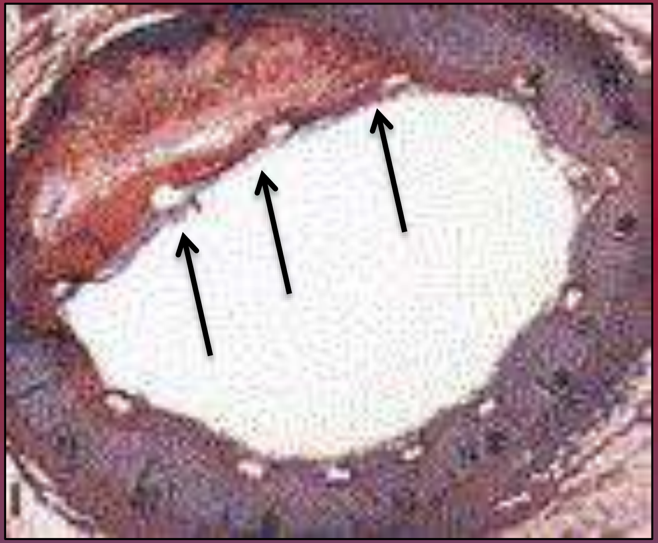
How Should Vascular Calcification Be Graded?

- By its fluoroscopic appearance?
- Its angiographic appearance?
- Its IVUS signature?
- By CTA?
- Or, retrospectively based on its acute and long term clinical outcomes?

The question remains unanswered

Impact of Ca++: Dissections, Incomplete Stent Expansion, ?Drug Penetration





BTK Vessel Recoil Post PTA

Tibial Artery Diameters at Baseline and Extent of Early Recoil in 30 CLI Patients Undergoing Tibial Balloon Angioplasty Stratified for Diabetic vs. Non-Diabetic Patients

	Total (n=30)	Diabetics (n=15)	Non-Diabetics (n=15)	p
RVD				
ATA, mm	2.60±0.69	2.51±0.68	2.65±0.74	0.95
PTA, mm	2.52±0.73	2.53±0.85	2.51±0.72	0.75
TPT / PA, mm	2.78±0.23	2.77±0.24	2.78±0.25	0.92
MLD at baseline				
ATA, mm	0.40±0.52	0.49±0.58	0.34±0.51	0.92
PTA, mm	0.16±0.30	0.15±0.30	0.17±0.34	0.80
TPT / PA, mm	0.05±0.12	0.02±0.04	0.11±0.21	0.003
MLD post BA				
ATA, mm	2.10±0.53	1.84±0.36	2.26±0.57	0.43
PTA, mm	1.85±0.45	1.63±0.09	2.08±0.56	0.006
TPT / PA, mm	1.98±0.55	1.82±0.54	2.29±0.52	0.83
MLD at 15 minutes				
ATA, mm	1.62±0.43	1.45±0.37	1.73±0.44	0.78
PTA, mm	1.38±0.38	1.11±0.13	1.65±0.36	0.09
TPT / PA, mm	1.33±0.36	1.20±0.34	1.59±0.27	0.56
Elastic recoil at 15 minutes				
ATA, %	27.0±9.8	28.1±10.1	26.4±9.1	0.59
PTA, %	29.0±8.3	35.1±10.6	22.9±7.5	0.02
TPT / PA, %	33.1±5.7	34.2±10.7	30.9±8.8	0.03

Continuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage).
RVD: reference vessel diameter, ATA: anterior tibial artery, PTA: posterior tibial artery, TPT: tibioperoneal trunk, PA: peroneal artery, MLD: minimal lumen diameter, BA: balloon angioplasty.

Baumann J Endo Ther 2014

What Do Emerging Data Tell Us About the Impact of Vascular Calcification on Clinical Outcomes?

Few peer-reviewed, core lab adjudicated data which ***specifically*** address the impact of "severe" Ca++ on acute/long-term clinical results...until the recent release of the IN.PACT DEEP BTK Trial of DEB v. PTA for CLI

Baseline Angiographic Characteristics

	DEB (N=239)	PTA (N=119)	*P*
Lesions (N)	351	181	*0.443*
Inflow			
impaired (≥50%, lab reported)	40.7% (96/236)	28.8% (34/118)	*0.035*
impaired (site reported)	25.1% (60/239)	22.7% (27/119)	*0.695*
restored (<30%, site reported)	96.7% (58/60)	100.0% (27/27)	*1.000*
Pedal-loop			
complete	5.4% (13/239)	7.6% (9/119)	*0.356*
incomplete	78.2% (187/239)	70.6% (84/119)	
no Pedal-loop	7.1% (17/239)	11.8% (14/119)	
N/A	9.2% (22/239)	10.1% (12/119)	
Target Vessel			
anterior tibial	39.9% (140/351)	42.0% (76/181)	*0.643*
posterior tibial	22.2% (78/351)	21.0% (38/181)	*0.825*
peroneal	25.1% (88/351)	26.5% (48/181)	*0.753*
TPT	18.8% (66/351)	16.6% (30/181)	*0.554*

	DEB (N=350)	PTA (N=181)	*P*
Calcium			*0.332*
none	35.1%	32.0%	
moderate	51.1%	57.5%	
heavy	13.7%	10.5%	
Thrombus	0.6%	0.0%	*0.550*
Aneurysm	0.3%	0.0%	*1.000*

~60-65% had 'moderate' or 'severe' vessel wall Ca++ as adjudicated by a core lab

Baseline Angiographic Characteristics

	DEB (N=239)	PTA (N=119)	*p*
RVD (mm±SD)	**2.46 ± 0.69**	**2.41 ± 0.56**	***0.304***
Target Lesion			
Mean length (cm ± SD)	**10.2 ± 9.1**	**12.9 ± 9.5**	***0.002***
%DS (% ± SD)	**83.9 ± 16.9**	**86.6 ± 15.7**	***0.078***
Occlusion (%)	**38.6%**	**45.9%**	***0.114***
MLD (mm ± SD)	**0.42 ± 0.49**	**0.34 ± 0.43**	***0.075***
Pre-dilatation	**90.5% (325/359)**	**36.0% (68/189)**	***<.001***
Infl. time (sec±SD) [1]	**166.0 ± 138.4**	**137.7 ± 111.3**	***0.010***
(max) Infl. P (atm±SD)	**9.5 ± 2.4**	**10.3 ± 4.6**	***0.010***

	DEB (N=239)	PTA (N=119)	*p*
Post-dilation	**10.3% (37/359)**	**8.5% (16/189)**	***0.488***
Stenting	**3.9%**	**2.6%**	***0.446***
Procedural complications [2]	**9.7% (23/238)**	**3.4% (4/119)**	***0.035***
Distal embolization	**2.8% (9/319)**	**0.6% (1/169)**	***0.176***
Post proc dissections	**12.3% (42/342)**	**19.2% (34/177)**	***0.046***
Technical Success [3]	**93.2% (331/355)**	**88.4% (167/189)**	***0.051***
Device Success [4]	**98.0% (348/355)**	**96.3% (182/189)**	***0.224***
Procedural Success [5]	**98.3% (234/238)**	**100.0% (119/119)**	***0.155***

1. **Total Inflation:** time of treatment device per device
2. **Excluding post-procedure dissections**
3. **Technical Success:** Successful vascular access and completion of the endovascular procedure and immediate morphological success with ≤ 50% residual DS by Angio
4. **Device Success:** exact deployment of the device according to the IFU as documented with suitable imaging modalities and in case of DSA, in at least 2 different imaging projections
5. **Procedural Success:** combination of technical success, device success and absence of procedural complications

Angio Cohort Outcomes

12-month Outcomes [1]	DEB	PTA	*p*
Mean Lesion Length (mm±SD)	59.1 ± 41.7	79.7 ± 74.6	0.060
Binary (50%) Rest. Rate (%)	41.0% (25/61)	35.5% (11/31)	0.609
Occlusion Rate (%)	11.5% (7/61)	16.1% (5/31)	0.531
Longitudinal Restenosis (%) [2]	62.7 ± 56.2	93.2 ± 60.8	0.167

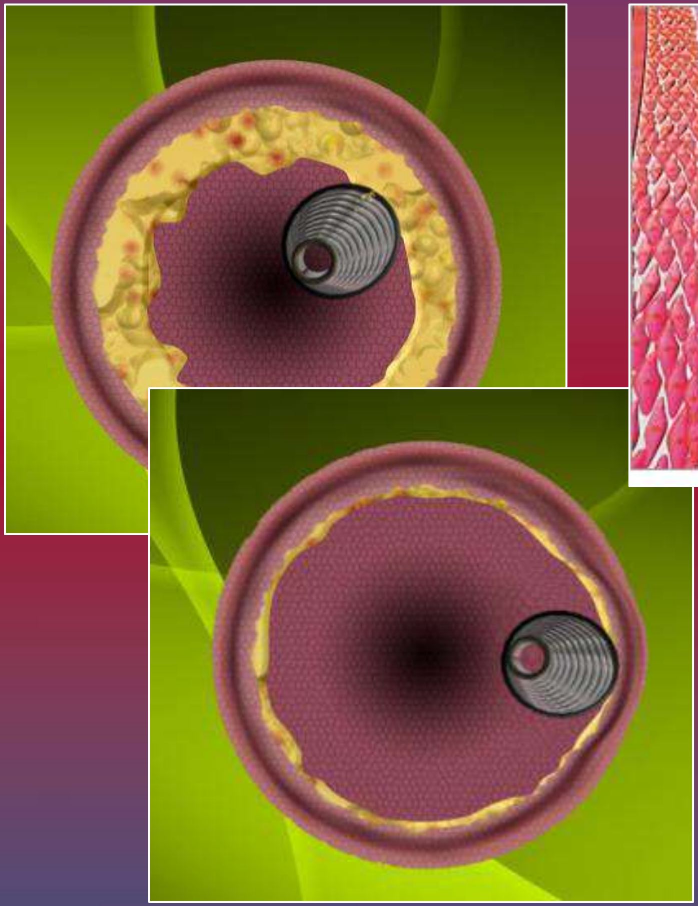
Revalidated Lumen Loss [3]	DEB	PTA	*p*
12-month LLL (mm, mean ± SD)	0.51 ± 0.66	0.60 ± 0.97	0.654

1. Angio Cohort, Corelab adjudicated. Angiogaphic Imaging 12-month FU compliance = 70.9% (DEB) vs. 71.4% (PTA)
2. Mean % of stenosis length vs. treated lesion length ± SD (Angiographic Cohort, ITT)
3. As evaluated by additional angiographic core laboratory (Beth Israel Deconess Medical Center, Boston, MA) to confirm earlier analysis

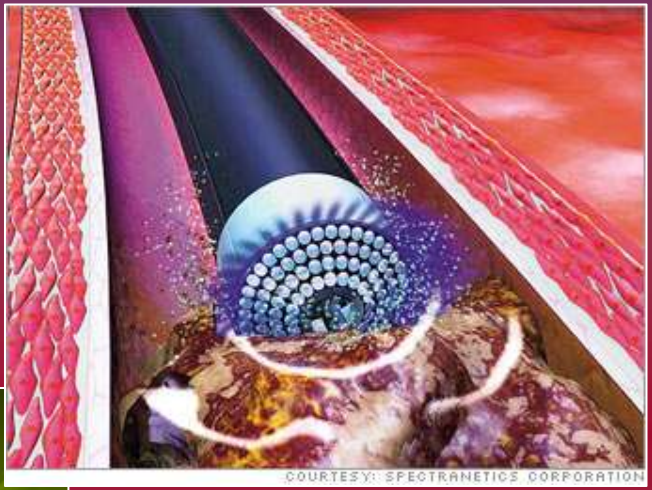
The Potential of Atherectomy

- There is no pre-defined requirement of endoprosthesis use
- Adjunct technology use or ‘stand alone’ use is possible
- Side-branches are generally preserved
- “Vessel wall preparation” concept is a re-emerging
- Unfortunately, few technologies have addressed ‘severe’ Ca++ head-on in well designed trials/registries

Atherectomy Devices: A Few Samples



CSI Diamond Back 360

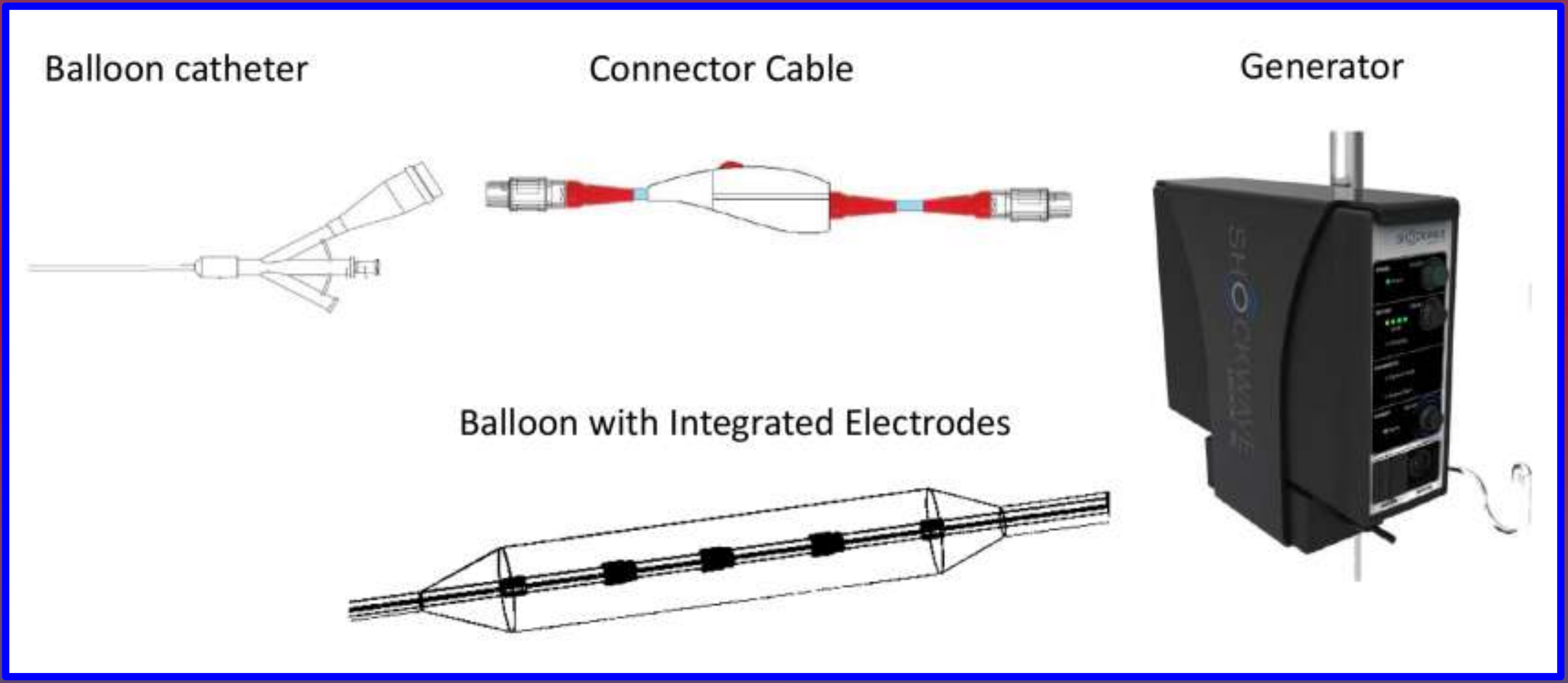


Spectranetics
TurboElite

Pathway JetStream

On the Horizon: Calcified Plaque Modification?

Shockwave Lithoplasty™ System



Calcified Plaque Modification?

Powerful impact outside the balloon

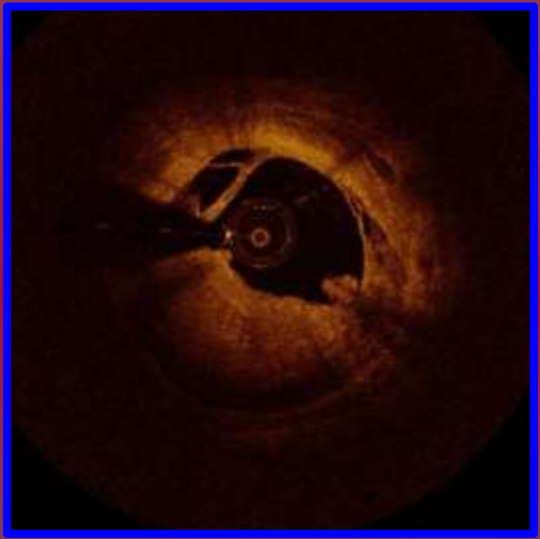
Very effective at low pressure

Impact travels *through* balloon wall

Effective at *sub-nominal* pressure

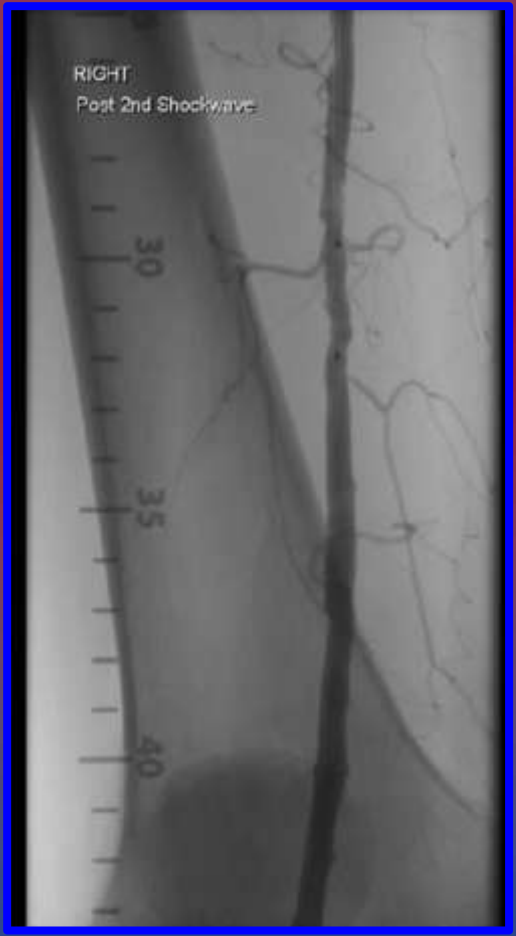
Sample FIM Results

Reference Pre-Treatment



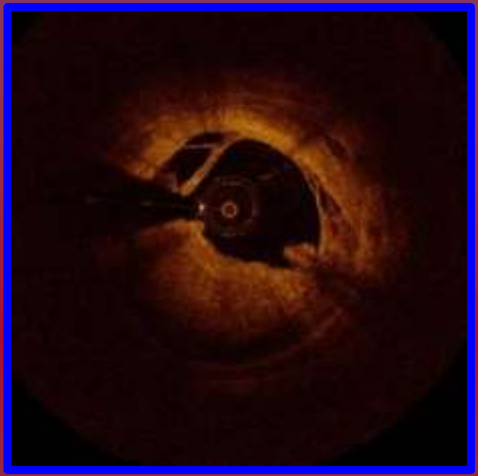
Reference Pre-Treatment

Post Lithoplasty™ @ 0.5 atm, *<u>before dilation</u>* to reference



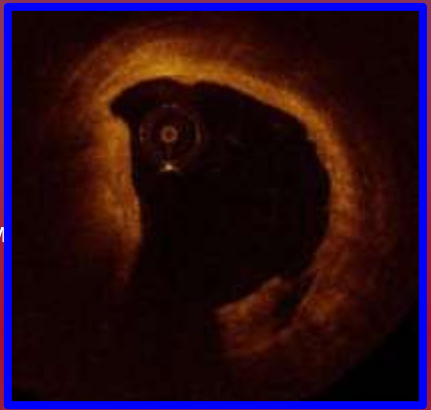
Sample FIM Results

Reference Pre-Treatment

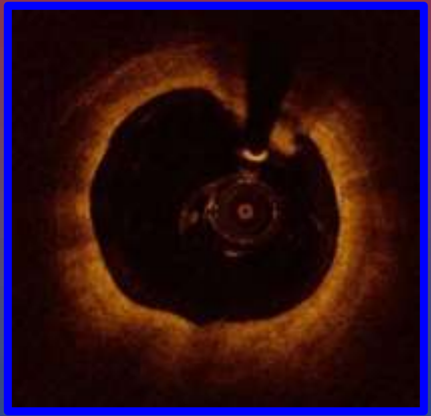


Lithoplasty™ @0.5atm

Post Lithoplasty™ @0.5atm, *before dilation* to reference



Post Lithoplasty™ @0.5atm, post dilation to reference



Post Lithoplasty™, Post Dilation @ 6.0atm

The Clinical Challenge of Severe Vascular Calcification

- Severe vascular Ca++ is ***NOT*** going away…
- Prospective, adjudicated, device-specific clinical outcomes are needed to assist in optimizing patient selection for specific endovascular/surgical approaches
- The potential impact of severe Ca++ on emerging technologies requires our careful attention and further study.