

Vascular Calcium: New Pre-Clinical Models and New Treatment Solutions

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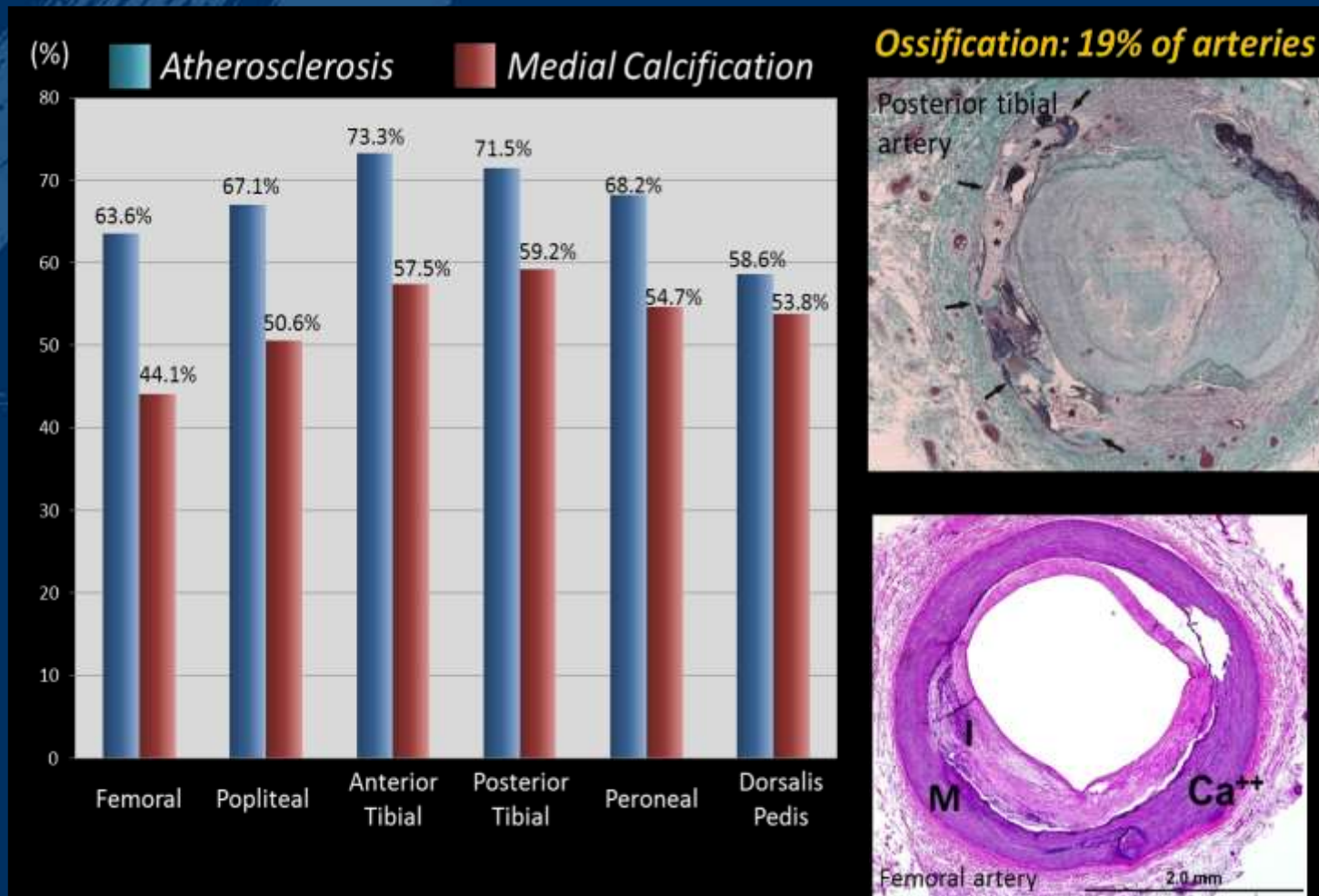
Disclosure Statement of Financial Interest

Within the past 12 months, the Skirball Center for Innovation have received grants and research support with the organization(s) listed below:

Grant/Research Support: Abbott Vascular, Amaranth Medical, Amber Medical, Amgen, Baylis, BIO2 Medical, Bristol-Myers, Boston Scientific, Cagent Vascular, Caliber Therapeutics, Cephea, Columbia Medical, Corindus Vascular, Celyad, Freudenberg Medical, Intact Vascular, JenaValve, Keystone Heart, LimFlow Medical, LoneStar Heart, Marvel Medical, Medtronic, Meril Life Sciences, MicroVention, Motus GI, Navigate Cardiac Structures, New York University, OrbusNeich Medical, SoundBite Medical, Spectranetics, Toray Industries, Vetex Medical, Volcano (Philips), Zimmer Biomet

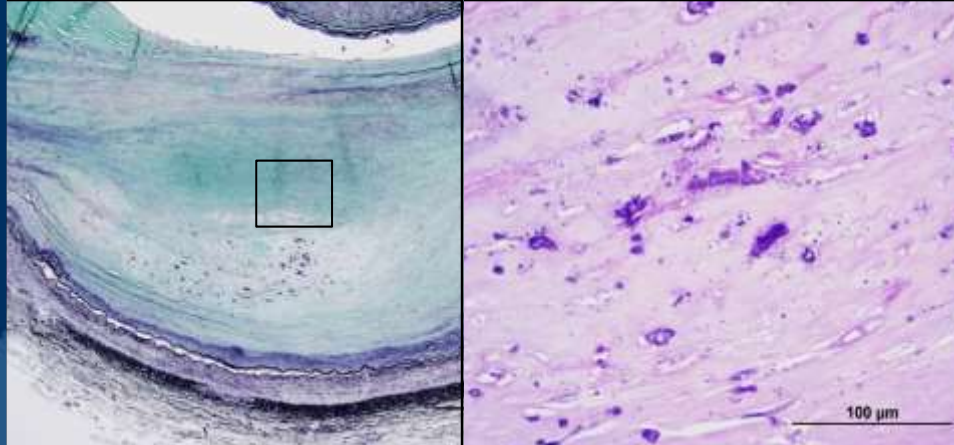
Calcium Correlates with Atherosclerosis Severity and Increases in the BTK Territory

Pathology Evaluation in CLI Patients Undergoing Amputation

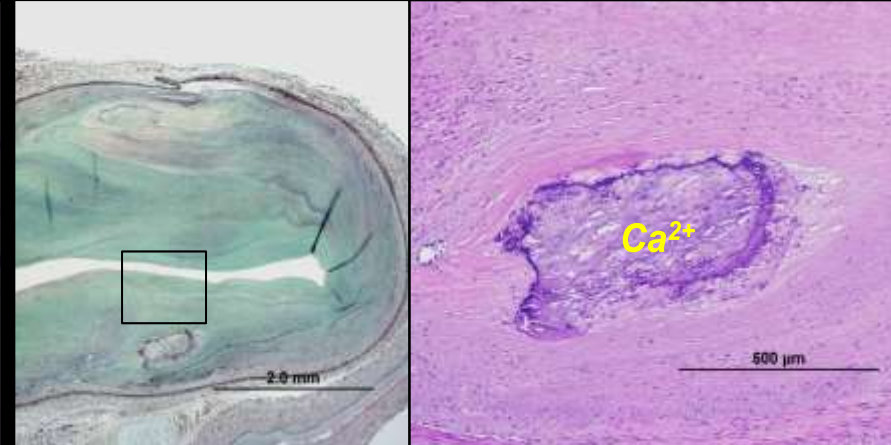


Types of Calcification in PVD

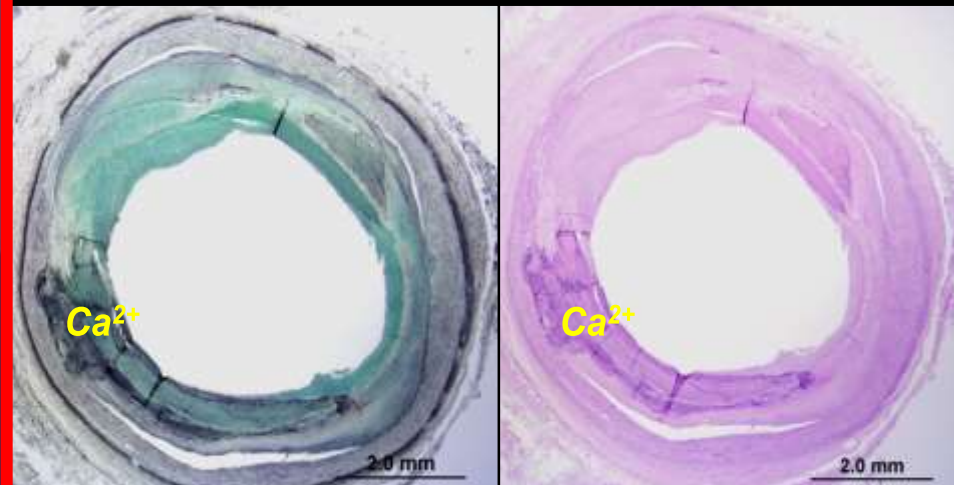
Microcalcification



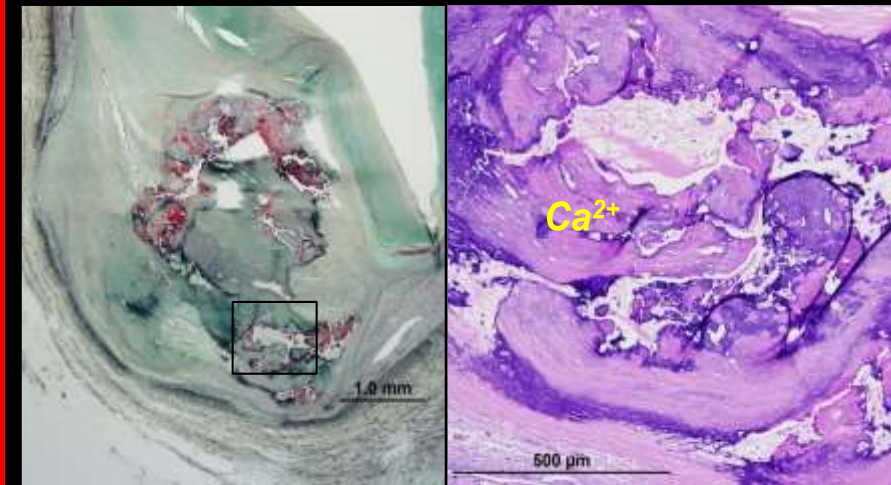
Fragmented calcification



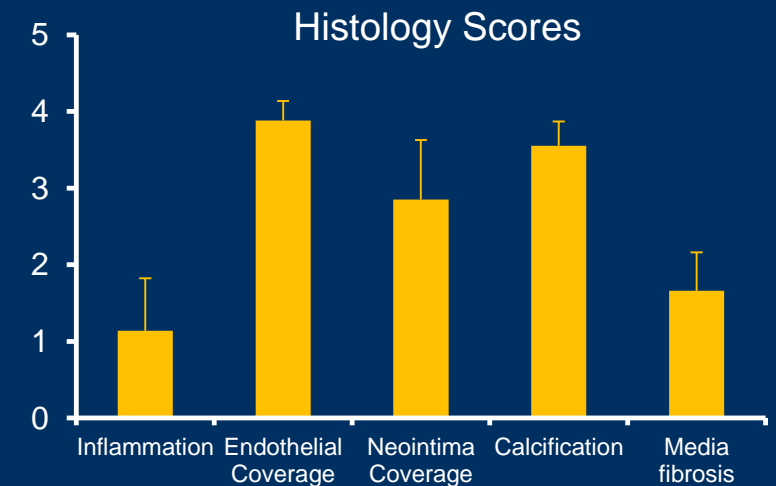
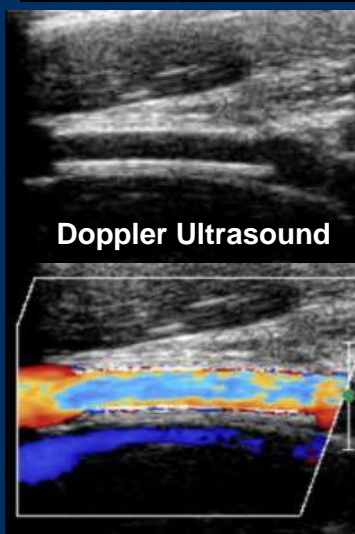
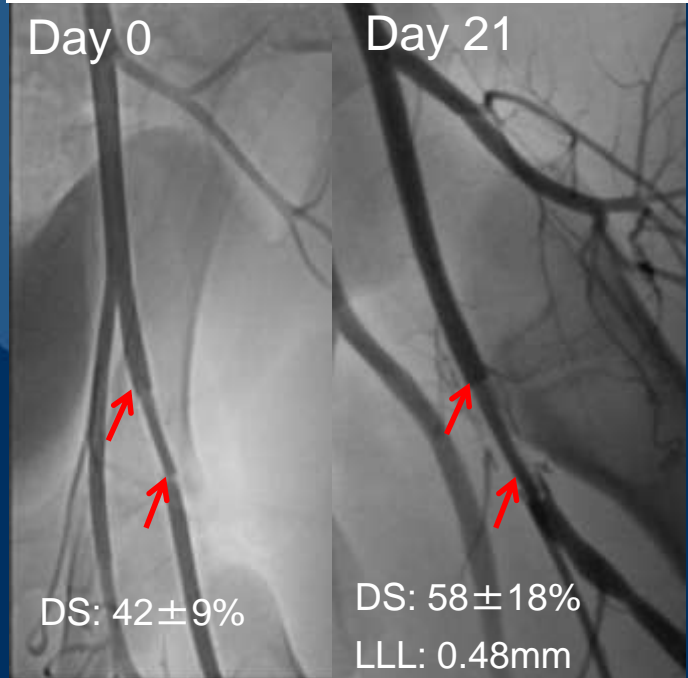
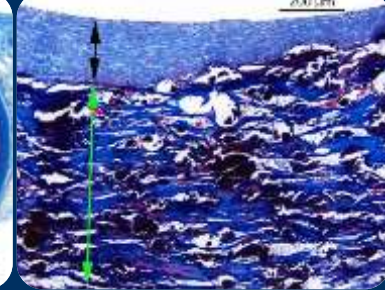
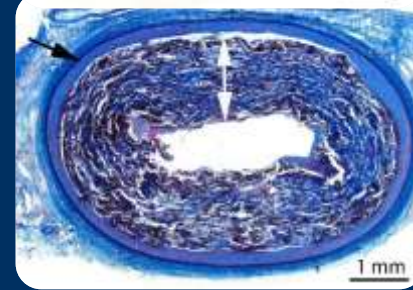
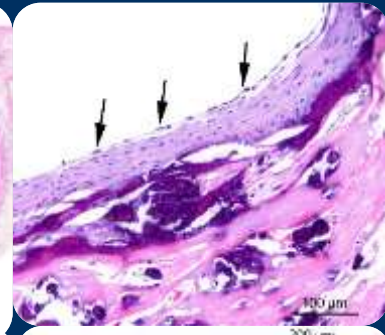
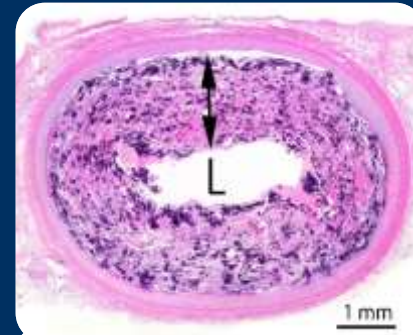
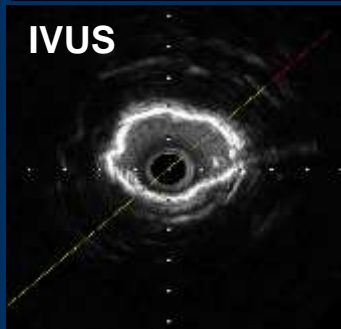
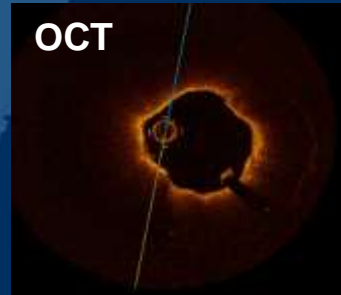
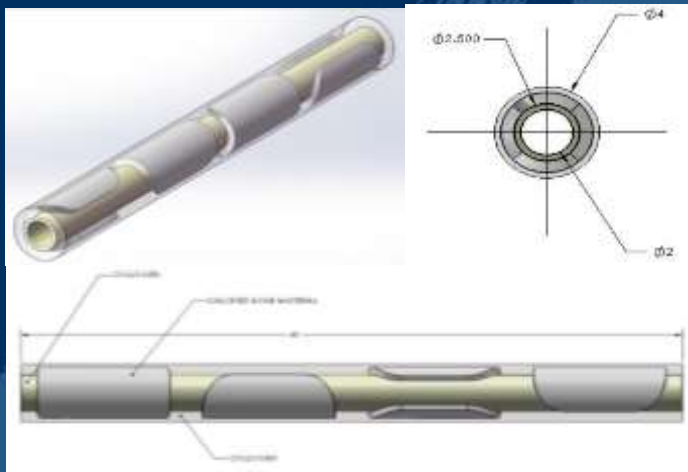
Sheet calcification



Nodular calcification

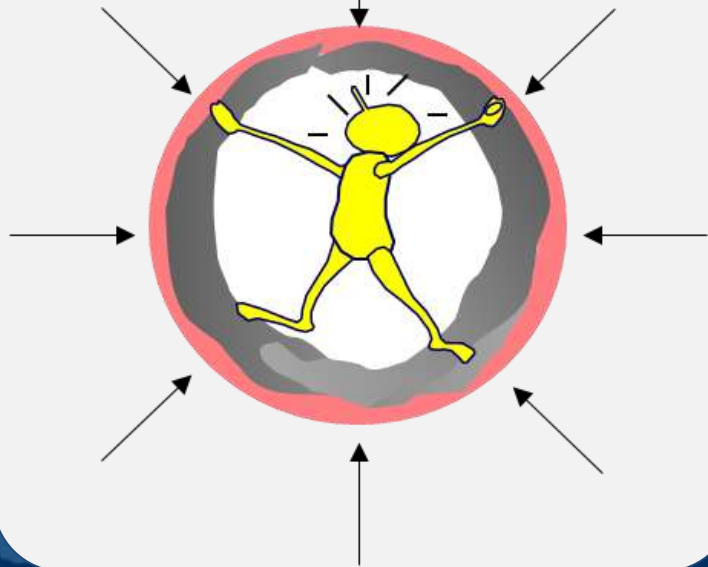


Novel Porcine Model of Calcific SFA Stenosis for the Evaluation of Endovascular Therapies

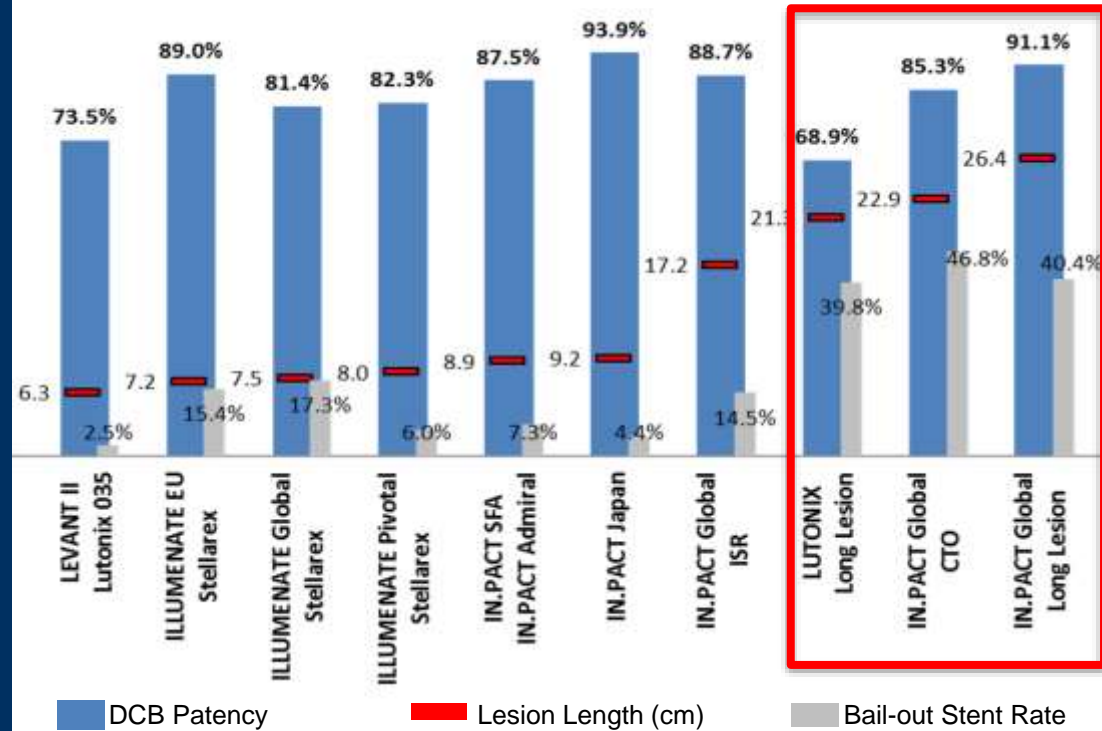


Severe Vessel Calcification: Reduced Vessel Compliance and Stent Use

Reduced Vessel Compliance



12-mo Primary Patency Rates
[and mean lesion lengths (cm); Core Lab-Adjudicated]



1. Rosenfield K, et al. New Engl J Med 373:145-53 (2015).
2. Presented by Brodmann M, AMP, Chicago, US 2016.
3. Presented by Zeller T, LINC, Leipzig, Germany 2017.
4. Presented by Lyden S, TCT Washington DC, US 2016.
5. IN.PACT™ Admiral Instructions for Use, M052624T001_Rev1F_EN, Figure 10.

6. MDT-2113, IN.PACT Japan, presented by Iida O, LINC, Leipzig, Germany 2017.
7. Presented by Brodmann M, VIVA Las Vegas, US 2015. * 14.5% reflects provisional stent rate during DCB treatment of 100% in-stent restenosis cohort.
8. Lutonix™ 035 Instructions for Use, BAW 1387400r3 Section 10.5.
9. Presented by Tepe G, Charing Cross London, 2016.
10. Presented by Scheinert D, EuroPCR Paris, 2015.

Severe Vessel Calcification: Reduced Tissue Permeability and Drug Delivery

Reduced Tissue Permeability



Barrier to Drug Absorption

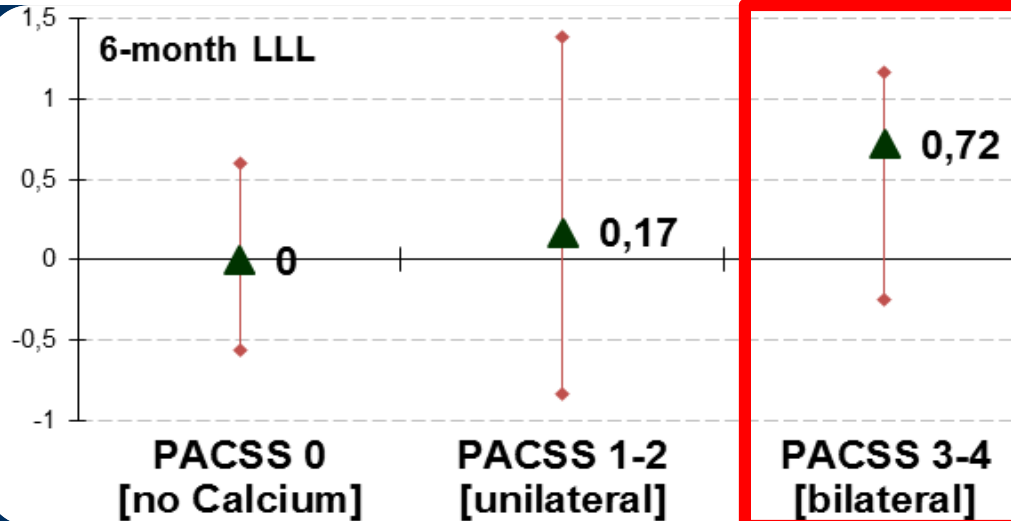
Clinical Investigation

JOURNAL OF
ENDOVASCULAR
THERAPY

Drug-Eluting Balloon Therapy for Femoropopliteal Occlusive Disease: Predictors of Outcome With a Special Emphasis on Calcium

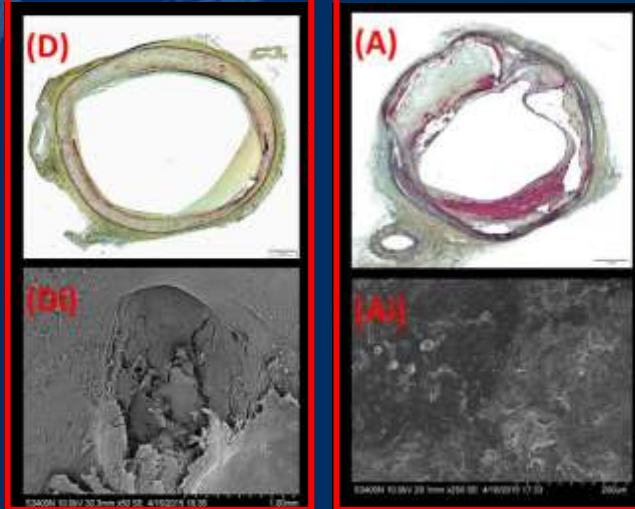
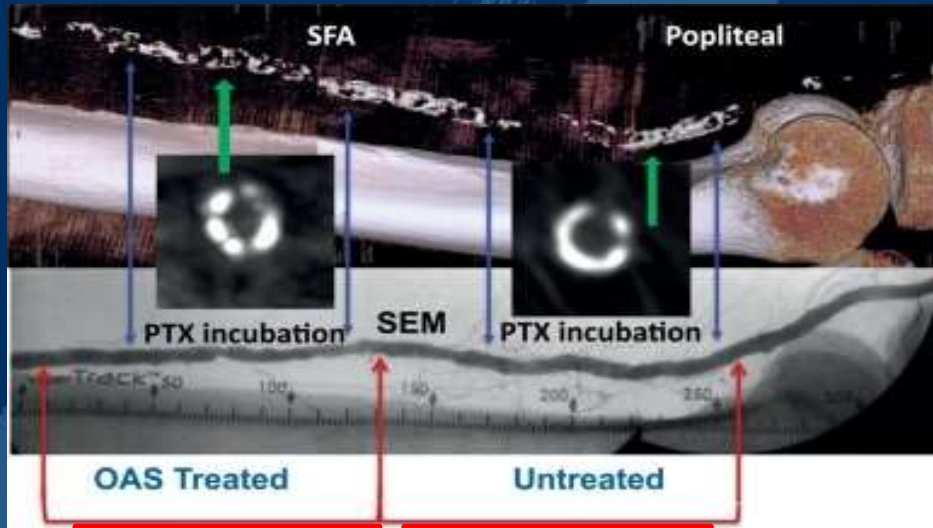
Journal of Endovascular Therapy
2015, Vol. 22(5) 727-733
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sagepub.com/journalsPermissions.nav
DOI: 10.1177/1526602815600156
www.jevt.org
SAGE

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Imma Fischer, PhD³, Peter Pfaffinger, MD¹, Elias Noory, MD²,
and Thomas Zeller, MD³



Severity of lesion calcification is associated with increased LLL after treatment with DCB

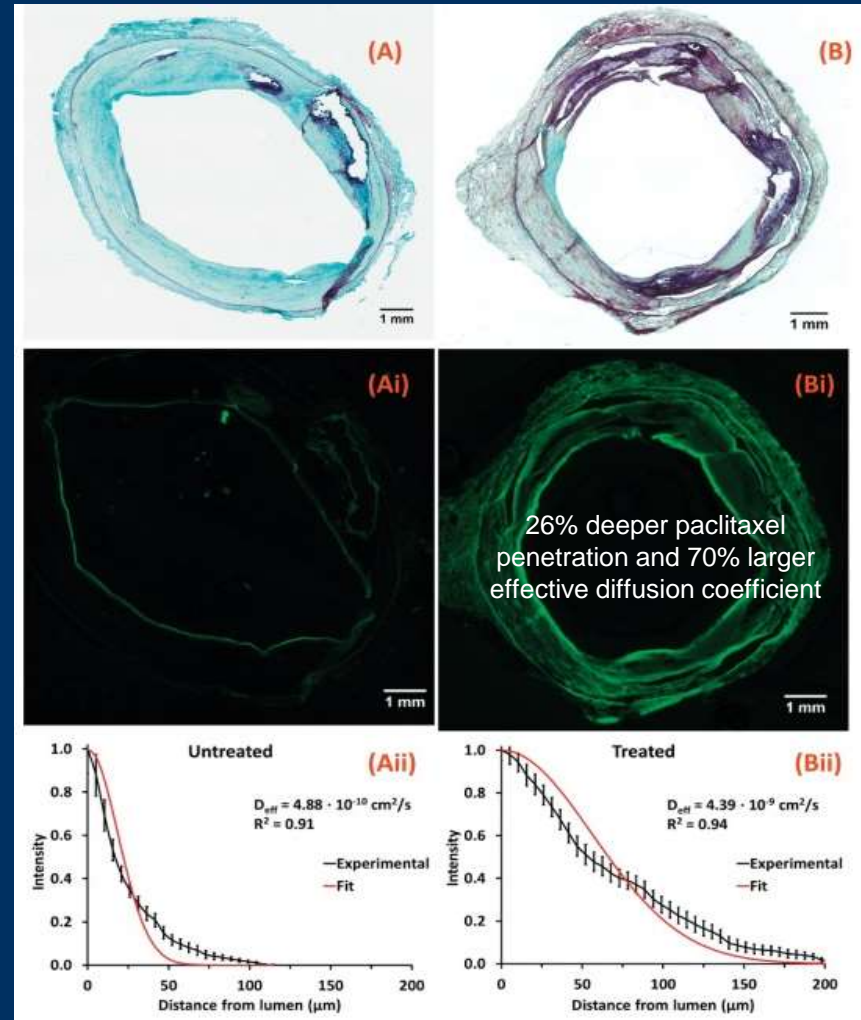
Calcified Plaque Modification Alters Local Drug Delivery in the Treatment of Peripheral Atherosclerosis



OAS Treated SFA segments exhibited decreases in plaque thickness and circumferential arc

Drug Distribution

Control OAS-Treated

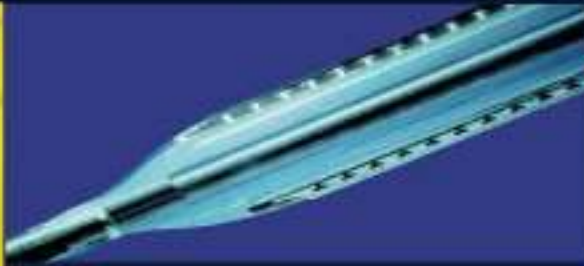


Therapeutic Options to Vascular Calcification

NC balloons



Cutting balloon



Angiosculpt



Laser



Rotational atherectomy



Orbital atherectomy

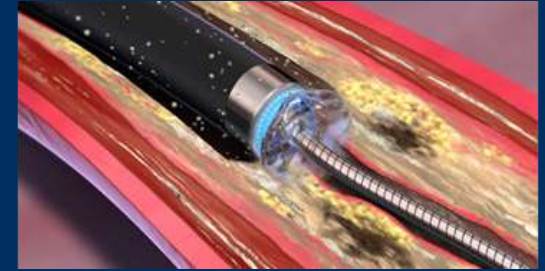


Debulk or Disrupt or **Debulk AND Disrupt?**

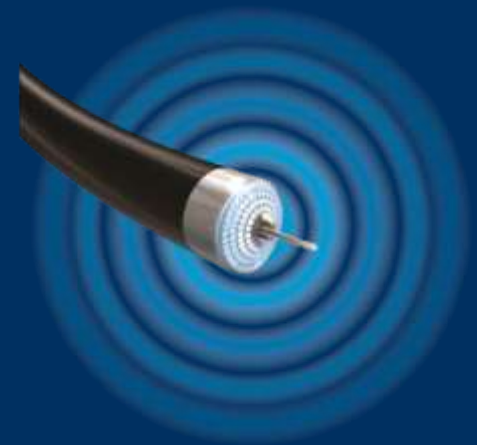
Laser Mechanism of Action (Turbo Power)

With Each Pulse (*Hertz = 40-80 pulses/second*)

1. Light is Absorbed, Breaking Molecular Bonds



2. Laser Induces Acoustic Pressure Wave
 - DISRUPTS Hard Plaque

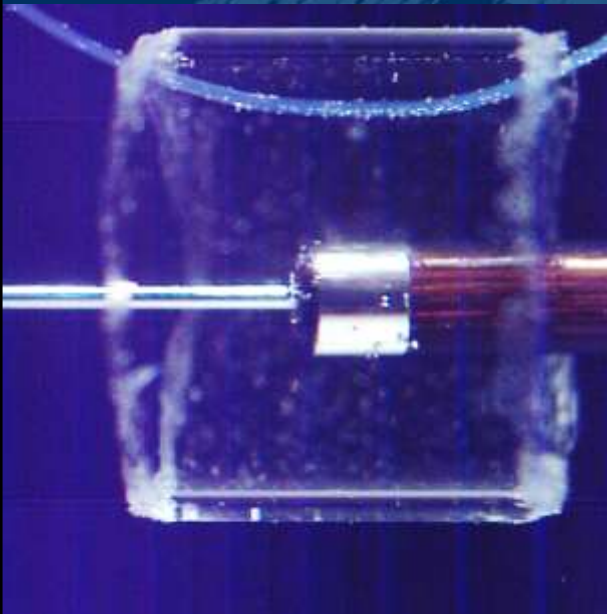


3. Hydraulic Vapor Bubble Expands and Collapse
 - DEBULKS Mixed Morphologies

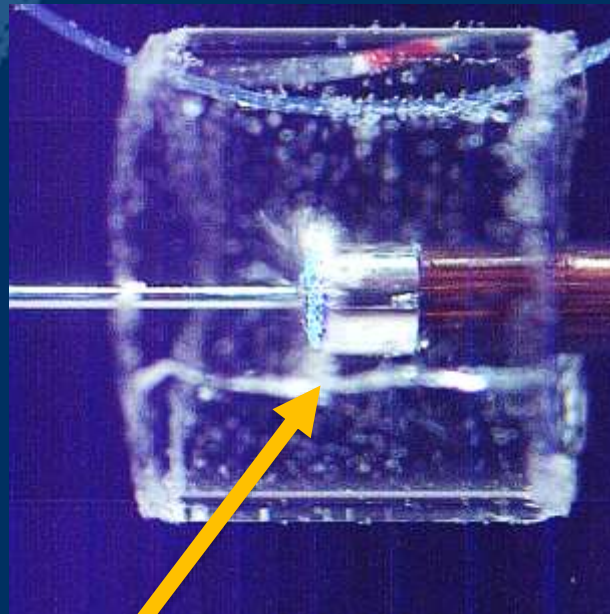


Bench Top Testing: Power of Acoustic Pressure Wave

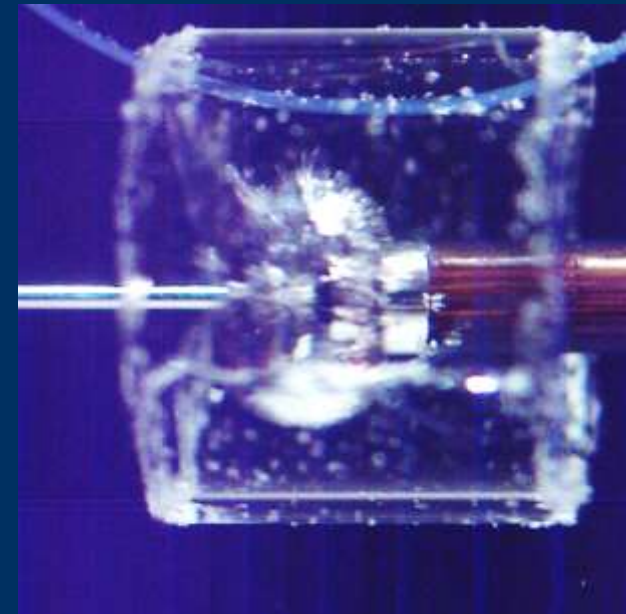
Laser Mechanism of Action



Pre-Laser Pulse



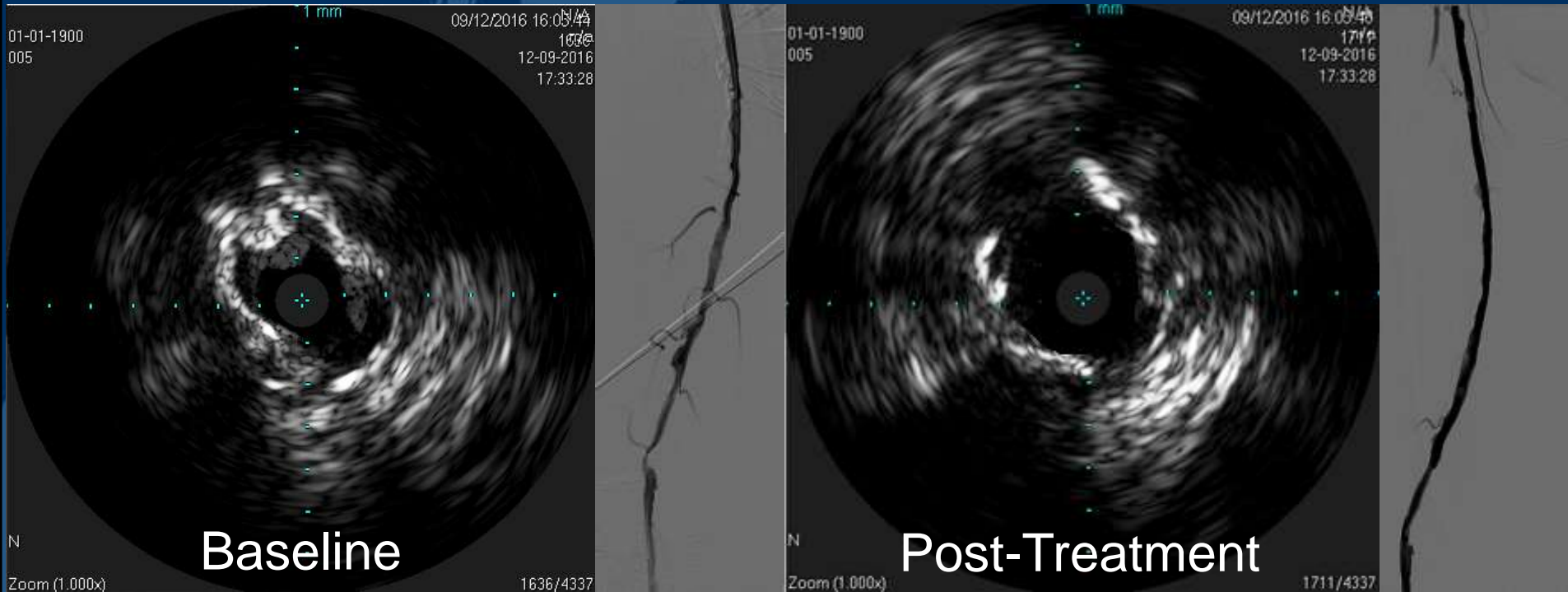
Laser Pulse
Crack Propagation



Bubble Formation

2.0 Turbo Elite Pulsed in Glass Tube

Laser Mechanism of Action in Humans



- Modify lesion from the tip with no moving parts
- Laser delivery is directional/rotational
- Rotation reduces “dead space” and may increase ablation capabilities
- More deliverable in calcific lesions

Images courtesy of Dr. George Adams

Conclusions

- Calcium is universally present in PVD; significant variability exist in regards to severity and location
- Calcium is a marker of disease severity and its presence correlates to worse peri-procedural and long term outcomes
- Circumferential superficial LAMINAR calcium may the biggest issue (as a barrier for drug delivery)
- Disrupting calcium (via different mechanisms) has been proposed to be beneficial to improve clinical outcomes
- Laser technology offers unique combination of calcium disruption and plaque debulking
- Clinical evidence warranted to support this hypothesis

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