# Is there a role for lithoplasty? Where and when

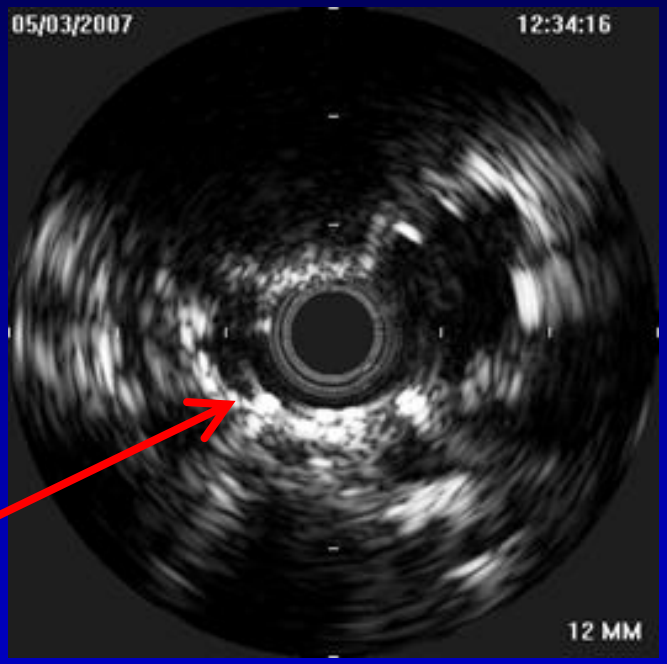
Lawrence A. Garcia, MD
*Chief, Section Interventional Cardiology and Vascular Interventions*
*Director, Vascular Medicine*
*St. Elizabeth's Medical Center*
*Tufts University School of Medicine*
*Boston, MA*

# 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 | • Abbott, Covidien/Medtronic |
| • Consulting (non-compensated) | • Covidien/Medtronic, Boston Scientific, Abbott |
| • Major Stock Shareholder/Equity | • Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular, Syntervention, Essential Medical |
| • Royalty Income | • None |
| • Ownership/Founder | • Innovation Vascular Partners |
| • Intellectual Property Rights | • None |
| • Other Financial Benefit | • None |

# *Shortcoming of SFA-Stents*




*Insufficient radial strength in calcified lesions*

# IN.PACT Global Long Lesion Imaging Cohort: Lesion/Procedural Characteristics

| | |
|---|---|
| Lesions (N) | 164 |
| **Lesion Type:**<br>de novo<br>restenotic (no ISR)<br>ISR | <br>83.2% (134/161)<br>16.8% (27/161)<br>0.0% (0/161) |
| **Lesion Length** | **26.40 ± 8.61 cm** |
| Total Occlusions | 60.4% (99/164) |
| Calcification<br>Severe | 71.8% (117/163)<br>19.6% (32/163) |
| RVD (mm) | 4.594 ± 0.819 |
| Diameter Stenosis (pre-treatment) | 90.9% ± 14.2 |
| Dissections: 0 | 37.9% (61/161) |
| A-C | 47.2% (76/161) |
| D-F | 14.9% (24/161) |

| | |
|---|---|
| Device Success [1] | 99.5% (442/444) |
| Procedure Success [2] | 99.4% (155/156) |
| Clinical Success [3] | 99.4% (155/156) |
| Pre-dilatation | 89.8% (141/157) |
| Post-dilatation | 39.1% (61/156) |
| Provisional Stent<br>- LL 15-25 cm:<br>- LL > 25 cm: | 40.4% (63/156)<br>33.3% (33/99)<br>52.6% (30/57) |

1. *Device success: successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP*
2. *Procedure success: residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site reported estimate was used)*
3. *Clinical success: procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge*

***Schienert, D EuroPCR 2015 presentation***

- Given that we treat lesions far and away more severe, calcified and longer than any pivotal trial
- We must answer the question is there a need for vessel preparation in anticipation of final therapy to include DCB or stent?
- Critically this answer is elusive given the data

# 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

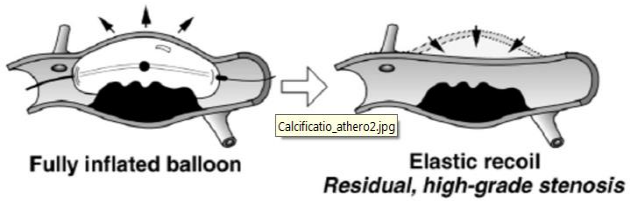
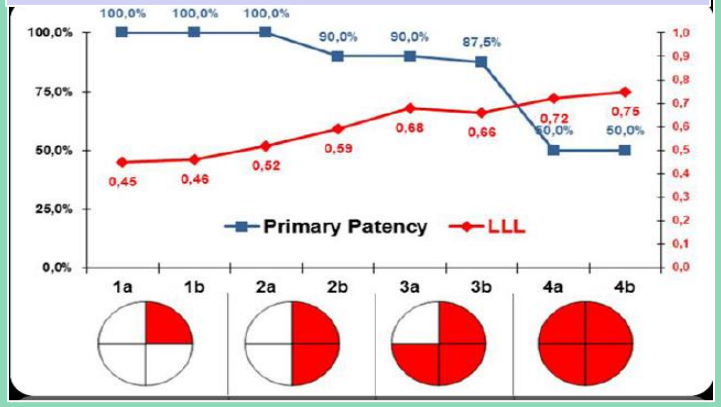



**Figure 12.1. Elastic Recoil After PTCA of Calcified Lesions**

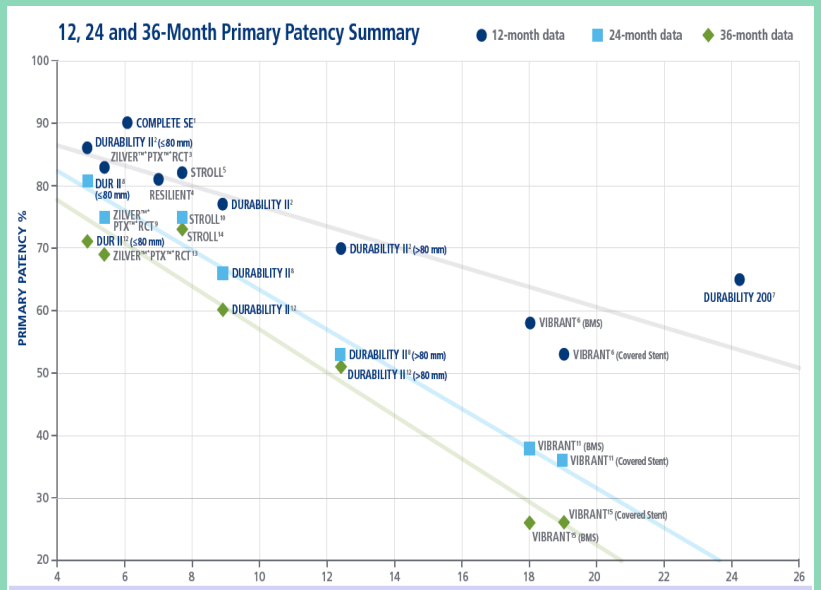
Rather than cracking the hard, calcified atheroma, PTCA causes stretching of the contralateral plaque-free wall segment and ineffective dilatation.

*Freed MS, Safian RD; Manual of Interventional Cardiology, Ch. 12, 245-254*

### Calcium May Limit Drug Effect[2]




## Longer Lesion Length



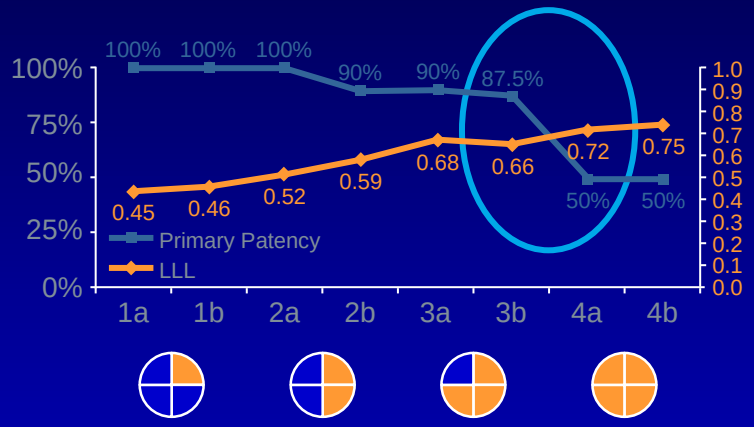

**Increased lesion length is an independent predictor of decreased patency[5].**

[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)

# Severe Calcium Acts as a Barrier to Biologic Uptake

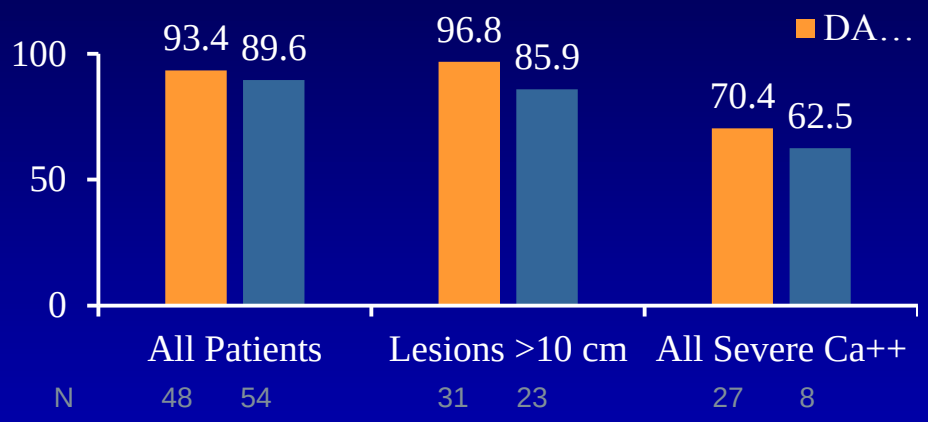
**Calcification may impair the antiproliferative effect of drug coated balloons (DCB) by likely acting as a physical barrier to drug penetration itself**

**12 Month Results[1]**




*Calcium distribution evaluation by CTA (circumferential) and DSA (longitudinal)*

**Key Study Outcome at 12 Months[2]**

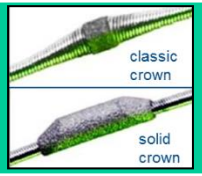
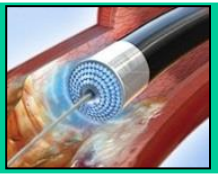



*Per Core Lab Assessment. "All Severe Ca++" group includes all patients treated with DAART therapy including randomized and non-randomized patients with severe calcium.*


[1]Fanelli F et al. Calcium Burden Assessment and Impact on Drug-Eluting Balloons in Peripheral Arterial Disease. Cardiovasc Intervent Radiol (2014) 37:898–907.

[2] Zeller, et al. Directional Atherectomy Followed by a Paclitaxel-Coated Balloon to Inhibit Restenosis and Maintain Vessel Patency: Twelve-Month Results of the DEFINITIVE AR Study. Circulation: Cardiovascular Interventions.2017 Sep;10(9). pii: e004848. doi:

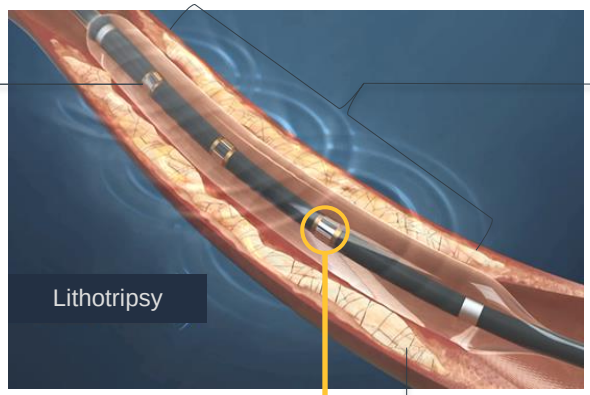
# Atherectomy Devices

| | 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.

# How IVL Works: An Overview

1 Integrated Balloon is inflated to a ***ultra-low pressure of 4 atm*** prior to activating emitters to ensure complete vessel wall apposition.




2 ***Emitters*** are the source of the Sonic Pressure Waves emitted at 1 pulse per second for 1 microsecond

3 ***Sonic Pressure Waves*** are emitted in the shape of a sphere, creating a field effect, thereby addressing calcium around the entire circumference and deep into the vessel wall

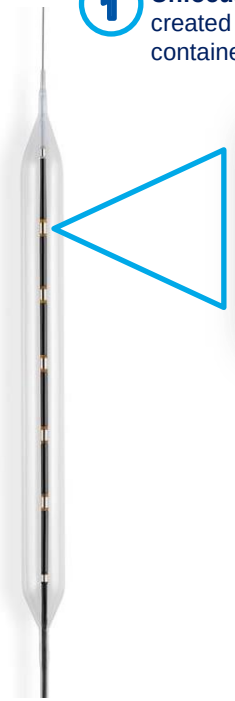
4 Sonic Pressure Waves transmit ***~50 atm of instantaneous pressure*** to the site of calcium, but pass through soft tissue

5 Sonic Pressure waves ***crack calcium***, softening vessel compliance. Fractured calcium remains inside the vessel wall.

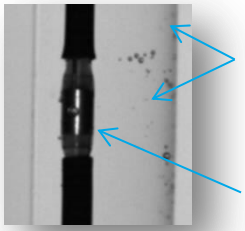
6 Softened vessel then able to be dilated at ***low pressure of 6 atm***, minimizing vessel trauma and complications.

# How Shockwave Creates Localized Lithotripsy

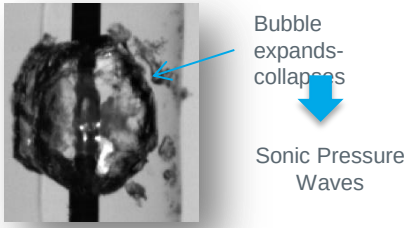
## High Speed Sonic Pressure Wave Created Safely Inside Integrated Balloon



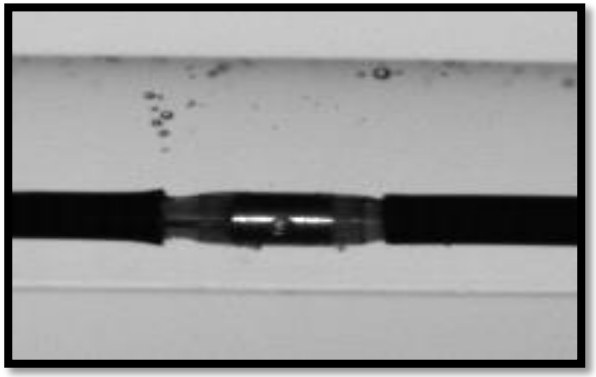
1 **Unfocused lithotripsy energy** is created at the emitters which are contained in a fluid filled coupler




2 Electrical energy is delivered to the emitter, initiating the steam bubble, which expand & collapses – creating **sonic pressure waves**.




***Video*: Actuation of Single Pulse (20µs/frame)**



# Peripheral IVL System: Clinical Programs

| DISRUPT PAD I | DISRUPT PAD II | DISRUPT BTK | DISRUPT PAD III | Observational Registry |
|---|---|---|---|---|
| Pre Market | Post Market | Post Market | Post Market | Post Market |
| Single Arm | Single Arm | Single Arm | Randomized | Single Arm |
| N = 35 | N = 60 | N = 20 | N = 400 | N = 1000 |
| 2014 | 2015 | 2017 | 2017 | 2017 |
| Study Completed | | | Enrolling | |

**Objective:** To study the safety and effectiveness of the IVL System in the treatment of *calcified*, stenotic femoropopliteal peripheral arteries.

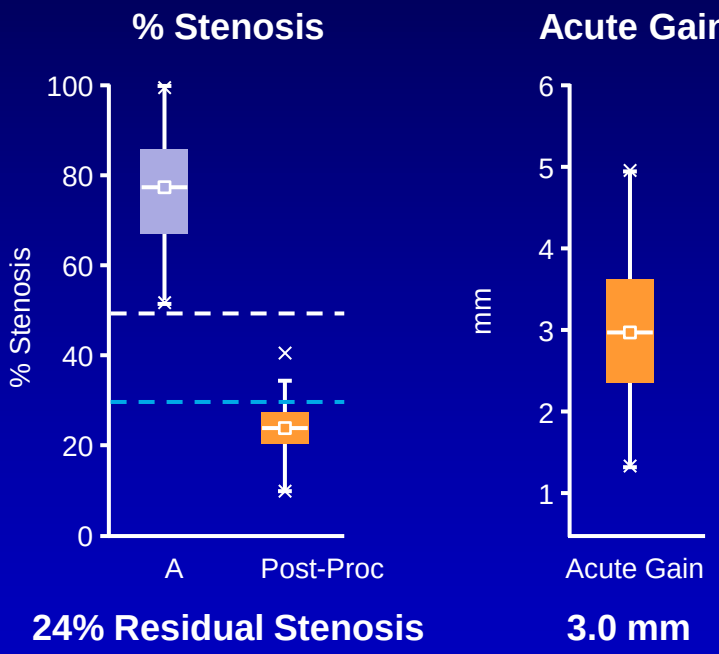
# Disrupt PAD II

**Only study to enroll this significant of calcium burden with severe calcification 85% (PARC) as determined by the core lab and an average length of calcium of 98.1 mm**

- Multi-center study, prospectively enrolling heavily calcified, stenotic fem-pop lesions
- Initial experience using IVL as a stand-alone treatment
- 8 centers in Europe and New Zealand
- 60 patients enrolled in 2015

| | Pre-Procedure N=60 |
|---|---|
| MLD (mm) | 1.2 ± 0.8 |
| % Diameter Stenosis | 78.1 ± 13.6 |
| RVD (mm) | 5.7 ± 0.7 |
| CTO | 16.7% (10) |
| Lesion Length (mm) | 78.6 ± 36.6 |
| Calcified Length (mm) | 98.1 ± 41.7 |
| Calcification by PARC¥ | |
| Moderate | 8.3% (5) |
| Severe | 85.0% (51) |

# Acute Angiographic Findings*




**24% Residual Stenosis**

**3.0 mm**

**High Acute Gain, Low Residual Stenosis, and Minimal Complications**

| | Post-Procedure N=60 |
|---|---|
| Dissections D†/E/F | 1.7% (1) |
| Perforations | 0% (0) |
| Abrupt Closure | 0% (0) |
| Slow/No Reflow | 0% (0) |
| Thrombosis | 0% (0) |

†Guidewire induced through recanalization of a CTO which was resolved with stent placement

*Core Lab Adjudicated

# Safety Results*

**A sustained low rate of safety events occurred following treatment with IVL**

**Primary Safety Endpoint**

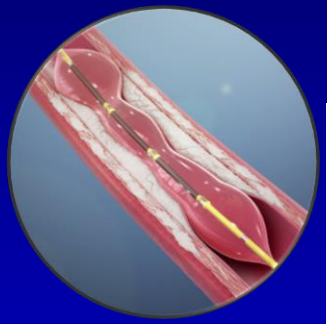
| | 30 Days N=59 | 12 Months N=57 |
|---|---|---|
| **Major Adverse Events (MAE)** | **1.7% (1)** | **1.8% (1)** |
| **Emergency surgical revascularization of target limb** | **0% (0)** | **0% (0)** |
| **Unplanned target limb amputation** | **0% (0)** | **0% (0)** |
| **Symptomatic thrombus or emboli** | **0% (0)** | **0% (0)** |
| **Perforations or Gr D dissections w/ interventions** | **1.7% (1)** | **1.8% (1)** |

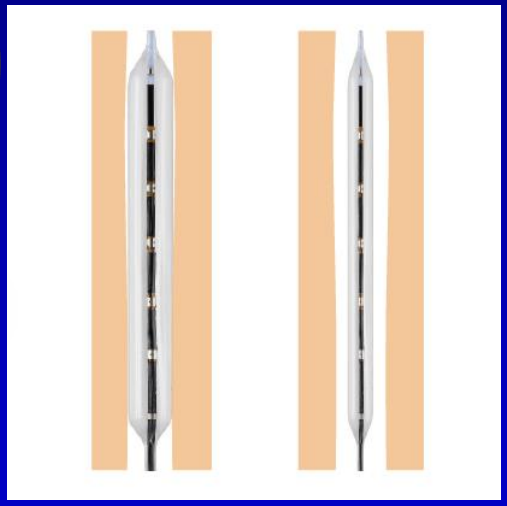
*Independent CEC Adjudicated

# Optimal Technique Optimizes Therapeutic Energy

**Oversize Device 10% vs RVD**

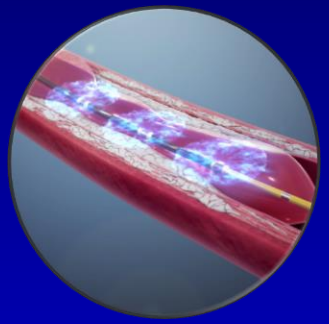
Wall apposition facilitates efficient energy transfer.
Optimized balloon sizing leads to improved patency

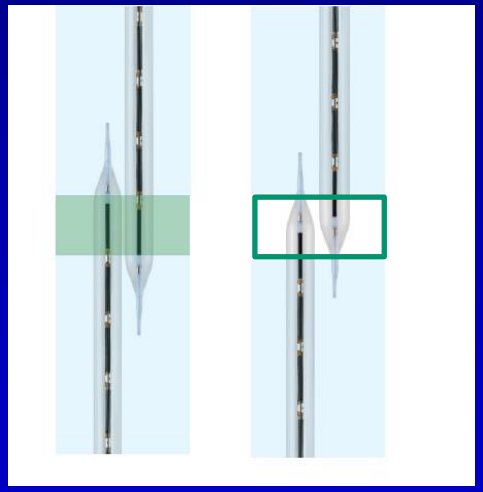





**Overlap Segments by 1 cm**

The sonic pressure waves create a spherical field effect that drops as the longitudinal distance from the emitters increases



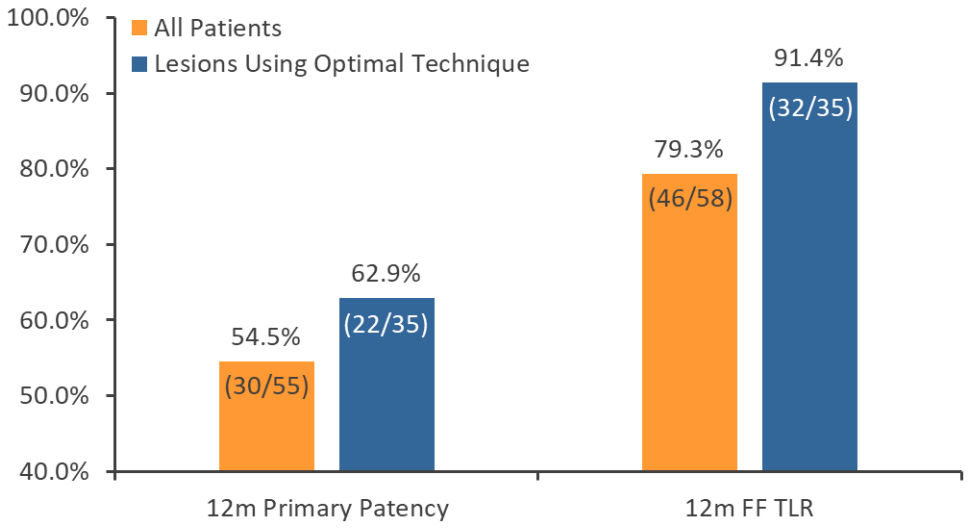


# 12-Month Patency*: Optimal Technique

**Optimal IVL technique was associated with significant improvement in clinical patency**

Primary patency: 54.5% for intent-to-treat versus 62.9% for those with optimal technique.

Clinically-driven TLR: 20.7% for intent-to-treat versus 8.6% for those with optimal technique.

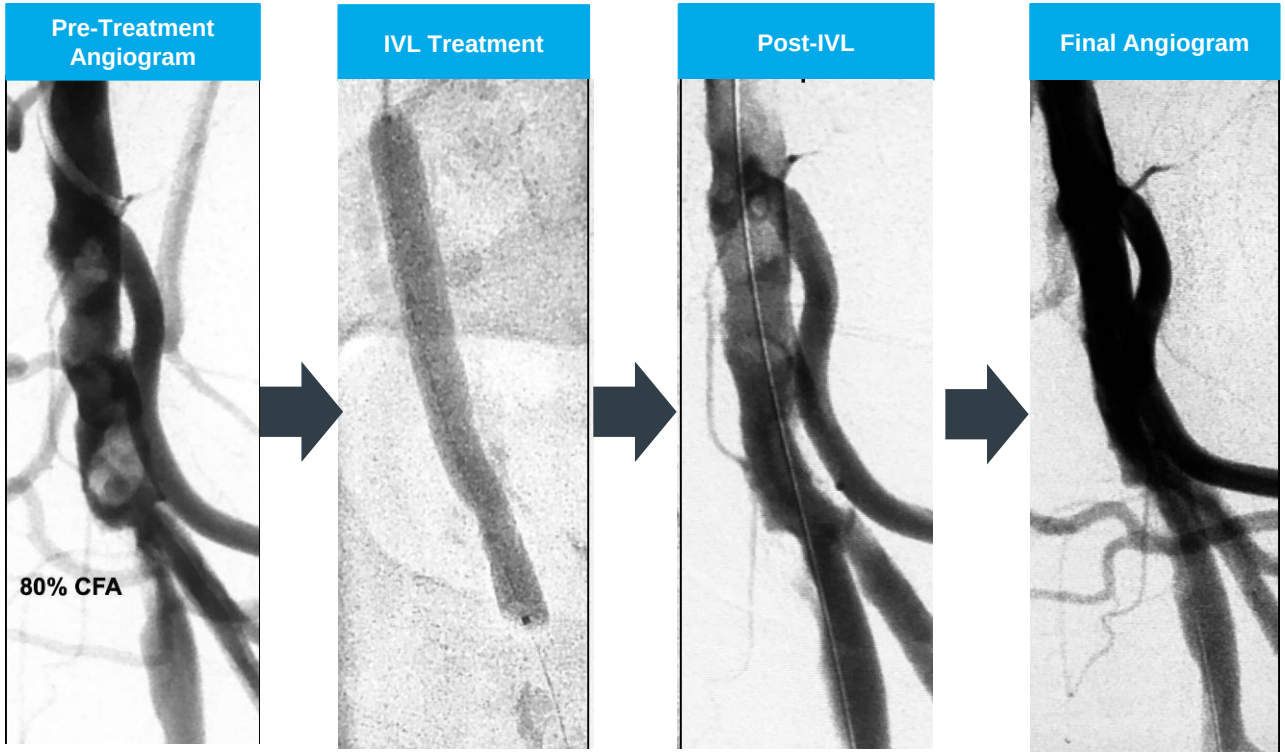



**Optimal technique** was defined as correct balloon sizing and avoidance of therapeutic miss.

**Primary Patency**: Freedom from CD-TLR and freedom from >50% restenosis as determined by duplex ultrasound

**Core Lab Adjudicated*

# Case Example: IVL + DCB




80% CFA stenosis

Severe calcification

6.5x60mm Peripheral IVL Catheter, 180 pulses

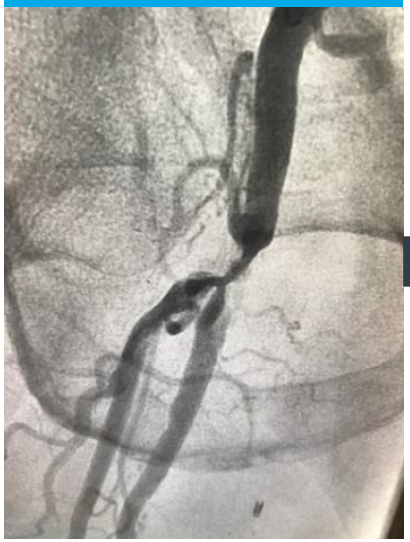
Final Angiogram Post-IVL & 6x60mm DCB



Case courtesy of: Dr Andrei Pop

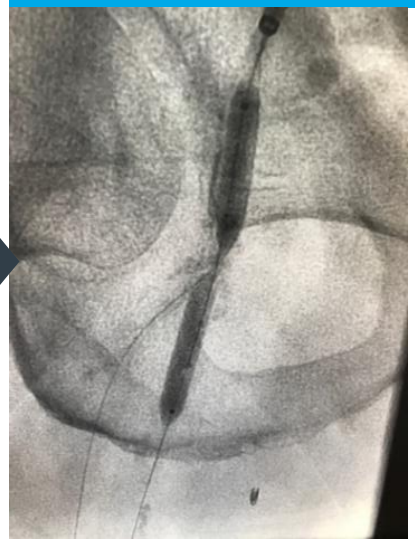
# Complex Calcified Common Femoral/Profunda Lesion

**Diagnostic Angiogram**



High surgical risk due to severity of calcium and lesion within the profunda

**IVL Procedural Angiogram**



IVL Treatment of CFA and Proximal SFA

IVL Treatment of Profunda with same IVL catheter

**Post IVL Treatment**

- No dissections, perforations, or emboli.
- No additional need for devices.
- Resolution of symptoms

Case courtesy of: Dr Nelson Bernardo

# Does vessel prep still matter?

- DCB's have dramatically changed the SFA landscape
  - Either the data suggests that up-front therapy is beneficial and durable in short and intermediate lesion lengths or that in surrogate fashion work for restenosis
  - Current meta-anlalysis needs resolution
- RCT data compel discussion and treatment strategies
  - ***Vessel prep remains a key element of benefit for many technologies***
  - Calcium remains a principal disruptor for final therapy
    - ***DISRUPT may answer this question***
- A "leave nothing behind" strategy appears to be the current trend for SFA therapy though no one group has shown the benefit beyond a modest SFA lesion length
- Lithoplasty appears well positioned for multiple applications and allow excellent vessel preparation in a myriad of anatomic locations