The Role of Lithotripsy in Solving the Challenges of Vascular Calcium

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Disclosure

Speaker name: Thomas Zeller

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I have the following potential conflicts of interest to report:

- [X] Consulting
- [ ] Employment in industry
- [X] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

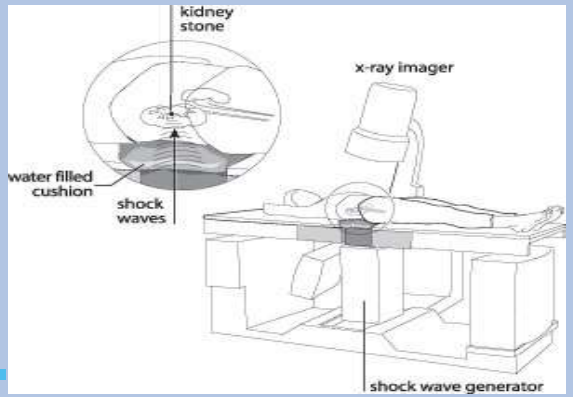
- [ ] I do not have any potential conflict of interest

Localized Lithotripsy to Treat Vascular Calcium

Lithotripsy

30 years of safety data
in kidney stone treatment

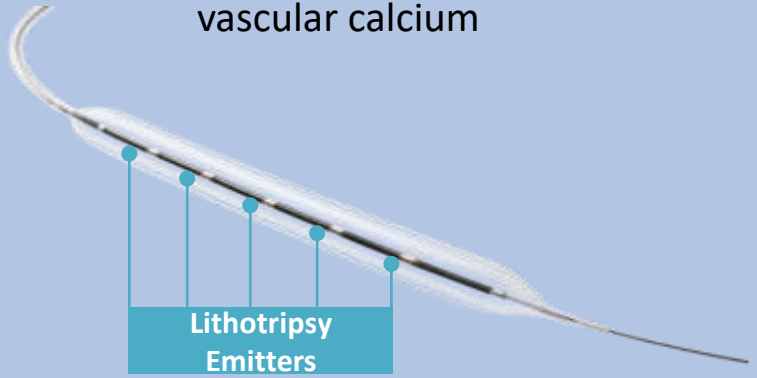
Sonic Pressure Waves preferentially impact hard tissue, disrupt calcium, leave soft tissue undisturbed



Lithoplasty Technology

Miniaturized and arrayed Lithotripsy Emitters for localized lithotripsy at the site of the vascular calcium

Optimized for the treatment of vascular calcium



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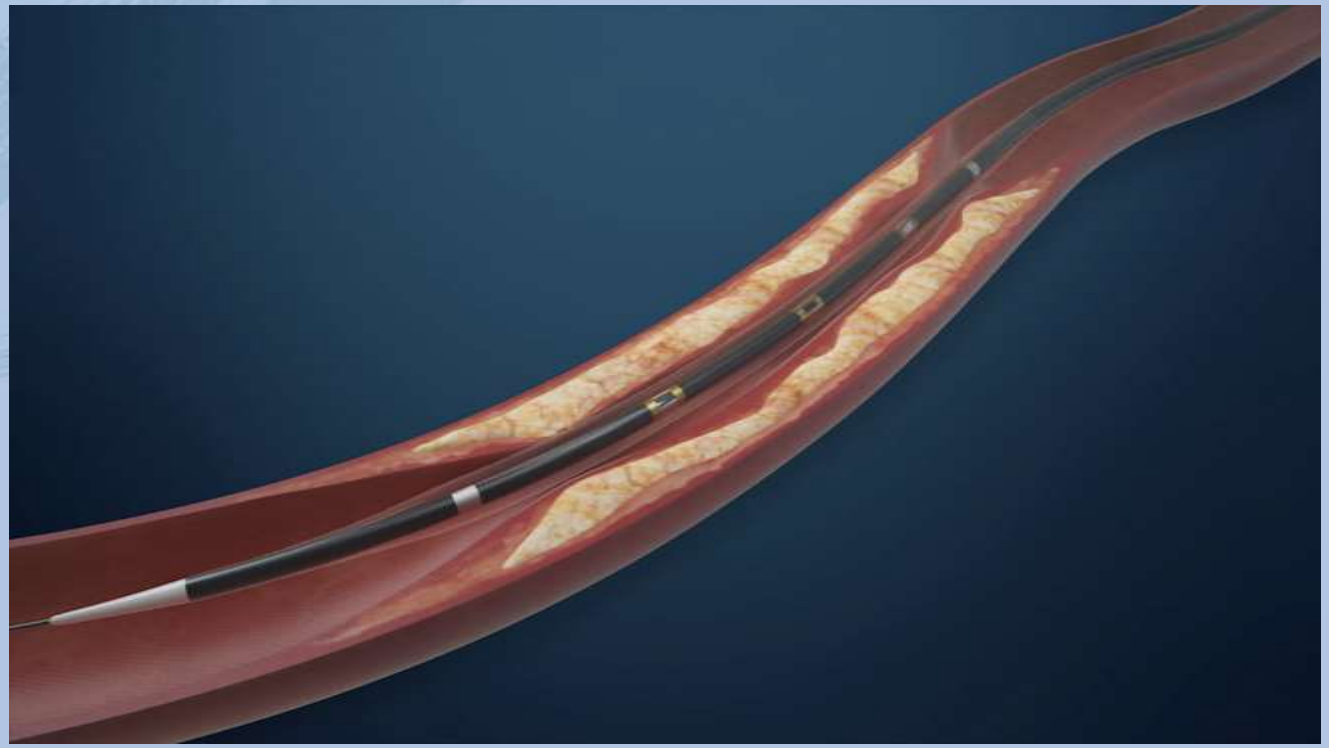
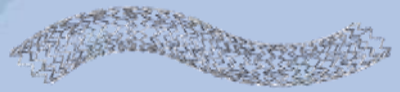
Shockwave Peripheral Intravascular Lithotripsy (IVL) System

IVL: *Hard on Hard Calcium, Soft on Soft Tissue*



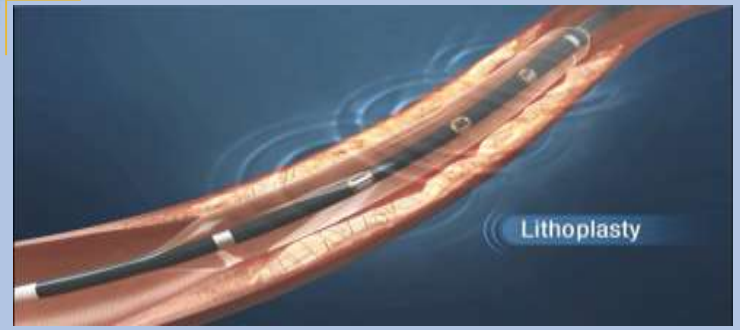
IVL: Primary & Adjunctive Therapy

EVAR
deployment in Calcium



DES
wall apposition

DCB
drug uptake in Calcium



TAVI
delivery through Calcium

BVS
deployment in Calcium

BVS = bioabsorbable vascular stents; DCB = drug coated balloons;
DES = drug eluting stents; EVAR = endovascular aneurysm repair;
TAVI = transcatheter aortic valve insertion

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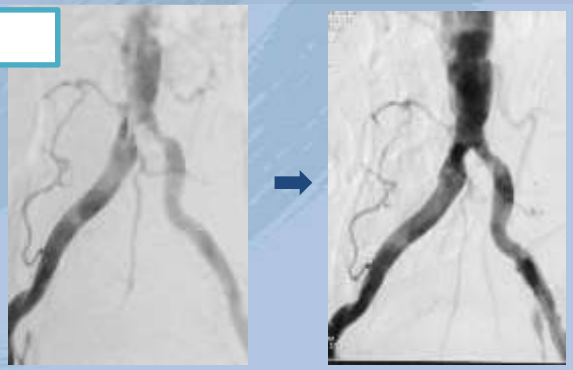
Peripheral IVL

Iliac

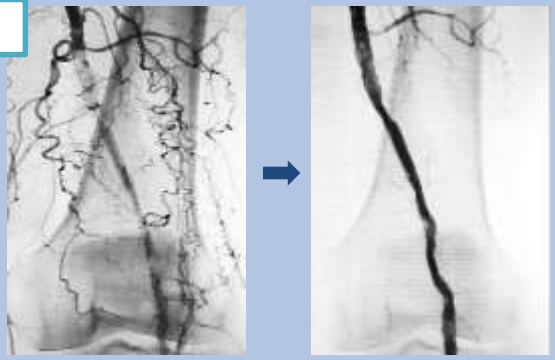


Pre IVL | Post IVL

CFA

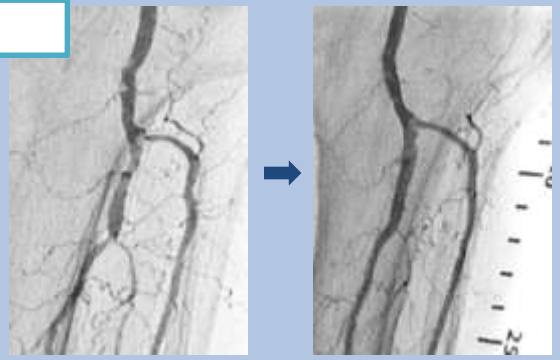
Pre IVL | Post IVL

SFA/POP



Pre IVL | Post IVL

BTK



Pre IVL | Post IVL

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Peripheral Lithoplasty System:
Clinical Programs

DISRUPT PAD I	DISRUPT PAD II	DISRUPT BTK	DISRUPT PAD III
Pre Market	Post Market	Post Market	Post Market
Single Arm	Single Arm	Single Arm	Randomized
N = 35	N = 60	N = 20	N = 334
Study Completed			Enrolling

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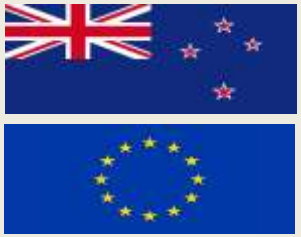
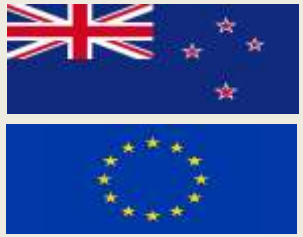
DISRUPT PAD Study: Femoropopliteal Disease



DISRUPT PAD I
35 subjects, 3 sites
Jan 2014 – Sep 2014



DISRUPT PAD II
60 subjects, 8 sites
Jun 2015 – Dec 2015

Objective: To study the safety and effectiveness of the Shockwave Medical Intrvascular Lithotripsy System in the treatment of calcified, stenotic infrainguinal peripheral arteries.

- Two-phase, prospective, non-randomized, multi-center study
- Monitoring with 100% source document verification
- Independent angiographic and duplex ultrasound core labs
- Independent clinical events committee

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DISRUPT PAD Study Design and Endpoints

Design

Key eligibility criteria

- Intermittent claudication: Rutherford Classification 2–4
- Ankle-brachial index ≤0.9
- SFA/Popliteal lesions ≥70% stenosis
- RVD 3.5–7.0 mm, ≤150 mm length
- Moderate and severe calcification by angiography

Study device

- Shockwave Medical Peripheral Lithoplasty Catheter
- Diameters: 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0 mm
- Length: 60 mm

Endpoints

Procedural

- Procedural success: <50% residual stenosis
- Exploratory endpoint: ≤30% residual stenosis

Follow up: 30 days, 6 Mo, & 12 Mo*

- Major adverse events
- Target lesion patency by DUS (stenosis <50%)
- Target lesion revascularization (TLR)
- Functional outcomes

DISRUPT PAD I/II:

Patient Demographics and Angiographic Findings

		DISRUPT PAD I/II N = 95
Patients Included	Rutherford 2	33.7% (32)
	Rutherford 3	65.3% (62)
	Rutherford 4	1.1% (1)
	Rutherford 5	-
Calcification	Moderate	44.2% (42)
	Severe	54.7% (52)
Angiographic Findings	RVD (mm)	5.3
	Lesion length	71.9
	Calcified length	92.5
	CTO	18.9% (18)

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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.

DISRUPT PAD I/II:
Safety & Effectiveness

		DISRUPT PAD I/II N = 95
Safety	Dissections	1% (1) Grade D or greater 1% (1) stent placed
	Embolization	0 Embolic Events 8% EPD Usage
	Perforations, abrupt closure, slow/no reflow or thrombosis	0 Complications
Effectiveness	Residual Stenosis	23.8%
	Acute Gain	2.9mm
Follow-Up	30 days	100% Freedom from TLR 100% Patency
	6 months	96.8% Freedom from TLR 76.7% Patency

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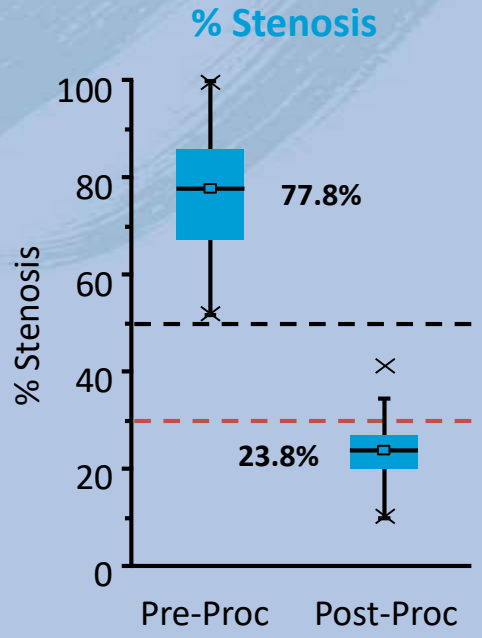
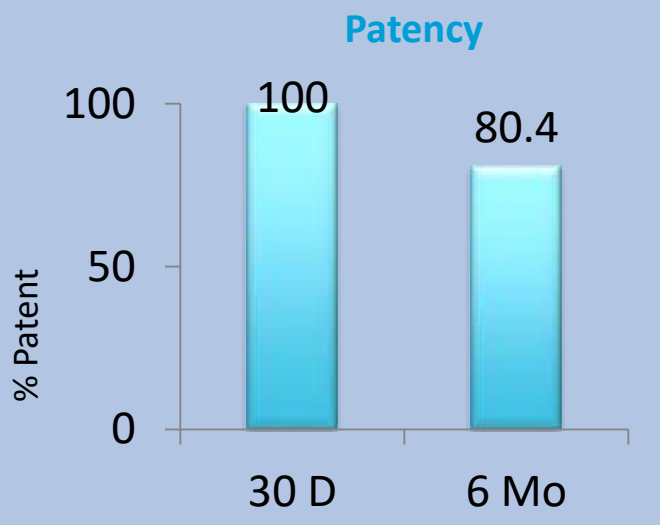
DISRUPT PAD & DISRUPT BTK categorized calcified lesions as per PARC definitions. Both studies utilized independent core labs and clinical events committees.
DISRUPT BTK data based on European studies.

DISRUPT PAD Effectiveness*

- 100% procedural success with a 24% residual stenosis
- Compelling 6 month results in a challenging lesion cohort





TLR	30 days	6 mo
	0.0%	3.2%

*By angiographic and DUS core labs

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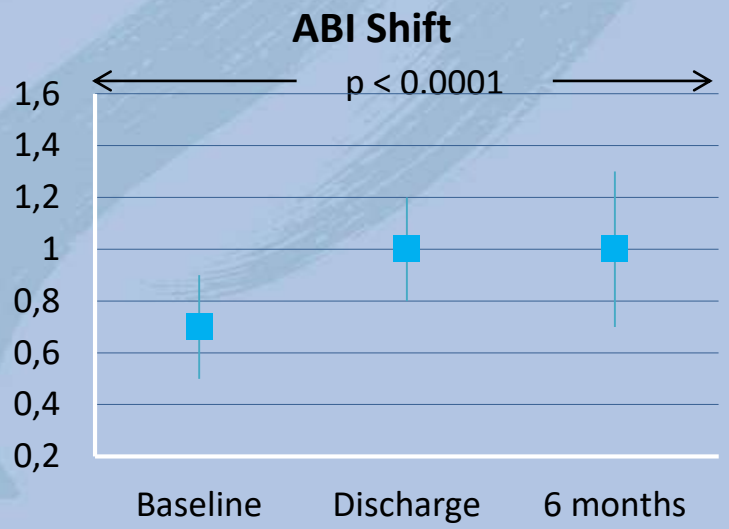
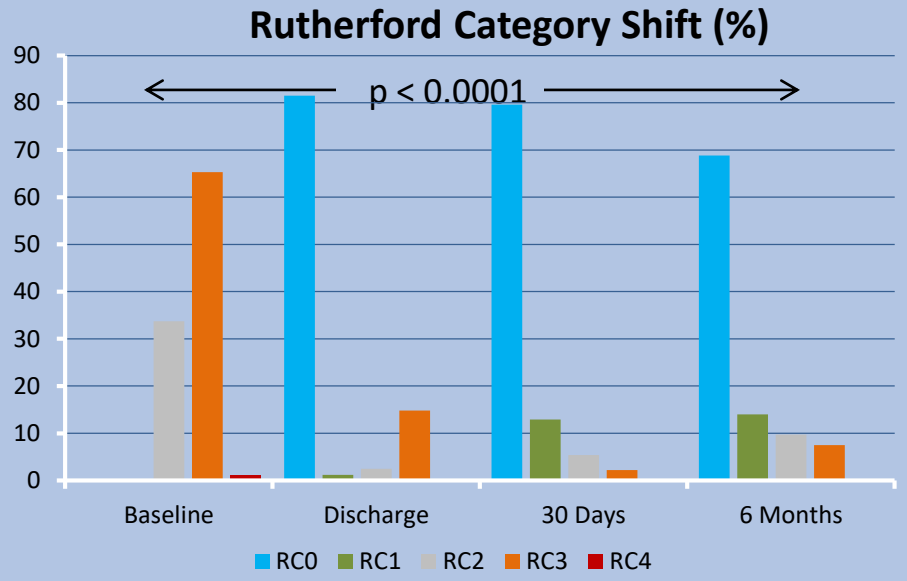
DISRUPT PAD Functional Outcomes

Sustained hemodynamic and Rutherford Category improvement



N	91	88	89



N	95	81	93	89

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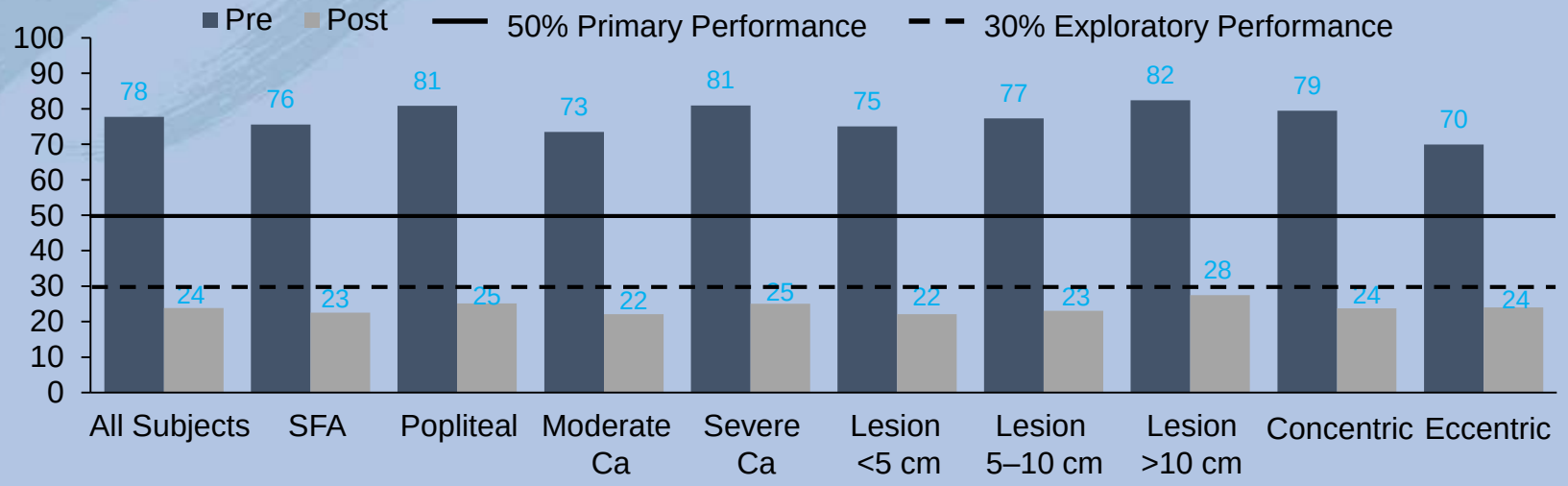
DISRUPT PAD Procedural Success by Subgroups

Pre and Post % Diameter Stenosis

Achieves consistent successful procedural outcomes in calcified lesions regardless of lesion complexity or location.



N	95	70	24	42	52	33	39	23	78	17

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IVL Case Example : Severely Calcified SFA Lesion

Diagnostic Angiogram

Heavily calcified sub-total SFA occlusion

Fluoroscopic Image

5.5 x 60mm IVL Catheter, 120 pulses

Procedural Angiogram

Post IVL

Final Angiogram

Post 6.0mm DCB treatment

Disrupt PAD III Study Design

Moderate and severely calcified femoropopliteal arteries
Rutherford 2 to 4
RVD 4-7, stenosis ≥70%,
Lesion length 5–18 cm occlusive or ≤10 cm CTO

Treatment arm (N=167)
Lithoplasty +
IN.PACT DCB

334 subjects
45 global sites
Randomization 1:1
24 months follow-up

Control arm (N=167)
PTA +
IN.PACT DCB

- **Study Design:** Randomized study of the Shockwave Medical Peripheral Intravascular Lithotripsy System with DCB versus standard balloon angioplasty with DCB to treat moderate and severely calcified femoropopliteal arteries (Disrupt PAD III).
- **Objective:** The objective is to assess the optimal therapy to dilate heavily calcified lesions with IVL versus traditional angioplasty, in achieving less than 30 % stenosis without the need for a stent. In addition, all patients who do not receive a stent will be treated with a drug-coated balloon.

DISRUPT BTK Study: Infrapopliteal Disease

Objective: To study the safety and performance of the Shockwave Medical Lithoplasty® 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)

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

DISRUPT BTK:
Safety & Effectiveness

		DISRUPT BTK N = 20 (21 lesions)
Safety	Dissections	0 Grade D or greater
	Embolization	0 Embolic Events
	Perforations, abrupt closure, slow/no reflow or thrombosis	0 Complications
Effectiveness	Residual Stenosis	26.2%
	Acute Gain	1.5mm
Follow-Up	30 days	100% Freedom from TLR 0% MAE (death, amp. or MI)

Brodmann, M. Presentation, CIRSE, 2017

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.

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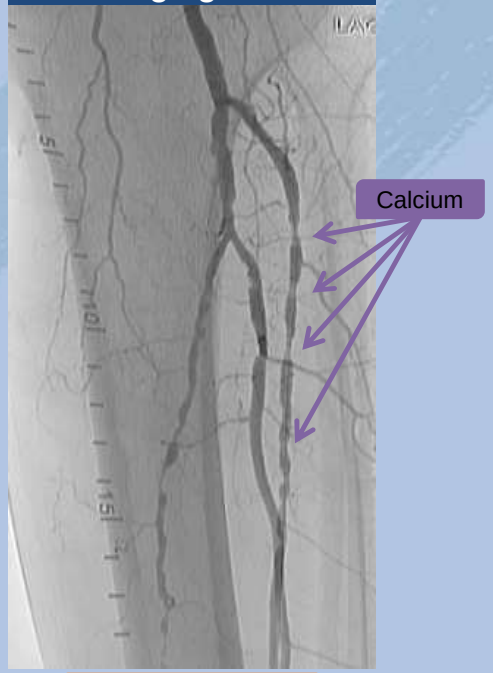
IVL Case Example: Anterior Tibial Lesion

Diagnostic Angiogram



65% Stenosis

IVL Catheter Image

3.5 mm IVL @ 4 atm

Case courtesy of: Prof Andrew Holden

Final Angiogram

21% Residual
1.6mm Acute Gain

Summary:
IVL is Uniquely Capable of Treating Vascular Calcium

- The **Disrupt PAD** trials have demonstrated that heavily calcified SFA/popliteal lesions can be **treated safely with compelling acute gain** and without the need for adjunctive tools like filters and specialty balloons.
- The **DISRUPT BTK** study demonstrated **excellent safety with consistent acute gain,** minimal stent utilization, along with low reported rates of recoil.
- IVL is proving safe and effective in treatment of heavily calcified **common femoral and iliac lesions** without the need for stenting.
- **Ongoing and future trials** are targeting even **broader clinical applications** for this platform technology for vascular therapy.

The Role of Lithotripsy in Solving the Challenges of Vascular Calcium

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