Directional atherectomy (DA) plus DCB to treat long, calcified femoropopliteal artery lesions:

The REALITY study

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Disclosures

Thomas Zeller, MD

- Consultant: Boston Scientific Corp., CSI, Gore & Associates, Medtronic, Veryan, Philips-Intact Vascular, Shockwave, Bayer, Vesper Medical, VentureMed, ANT
- Grant/Research Support: Bard Peripheral Vascular, Veryan, Biotronik, Cook Medical, Gore & Associates, Medtronic, Philips, Terumo, TriReme, Shockwave, Med Alliance, Intact Vascular, B. Braun, CSI, Boston Scientific, University of Jena, Pluristem, Philips, PQ Bypass
- Major Stock Shareholder: QT Medical
- Honoraria: Abbott Vascular, BIBA Medical, Biotronik, Boston Scientific Corp., Cook Medical, Efemoral, Gore & Associates, Medtronic, Philips-Spectranetics, Shockwave, Veryan

REALITY STUDY[1]

Objective and Design

Study Objective

Evaluate the effectiveness of the HawkOne™ directional atherectomy system followed by the IN.PACT™ Admiral™ drug coated balloon to debulk moderate and severely calcified femoropopliteal artery atherosclerotic lesions.

- Primary Endpoints:
  - Effectiveness: Primary Patency at 12 months[2]
  - Safety: Freedom from Major Adverse Events (MAE) through 30 days[3]
- Primary Investigators: Dr. Krishna Rocha-Singh, Dr. Brian DeRubertis & VIVA Physicians

Study Design & Oversight

- 102 subjects enrolled at 13 sites in the US & Germany
- Prospective, non-randomized, single-arm study
- Angiographic and duplex ultrasound (DUS) core lab adjudicated
- Change in maximal luminal plaque area adjudicated by an independent intravascular ultrasound (IVUS) core lab

1. Sponsored and conducted by VIVA Physicians; funded by Medtronic.
2. Primary patency defined as freedom from restenosis (DUS peak systolic velocity ratio >2.4) and CD-TLR, defined as any reintervention to the target lesion due to a return of symptoms and/or ankle-brachial index (ABI) decrease of 20% or > 0.15 when compared with the post index procedure baseline ABI.
3. Major Adverse Events (MAE) defined as flow-limiting dissections (D-F), vessel perforation(s) requiring bare metal stents or stent-grafts implantation, unplanned major amputation, intra-procedure distal atheroembolization and CD-TVR.

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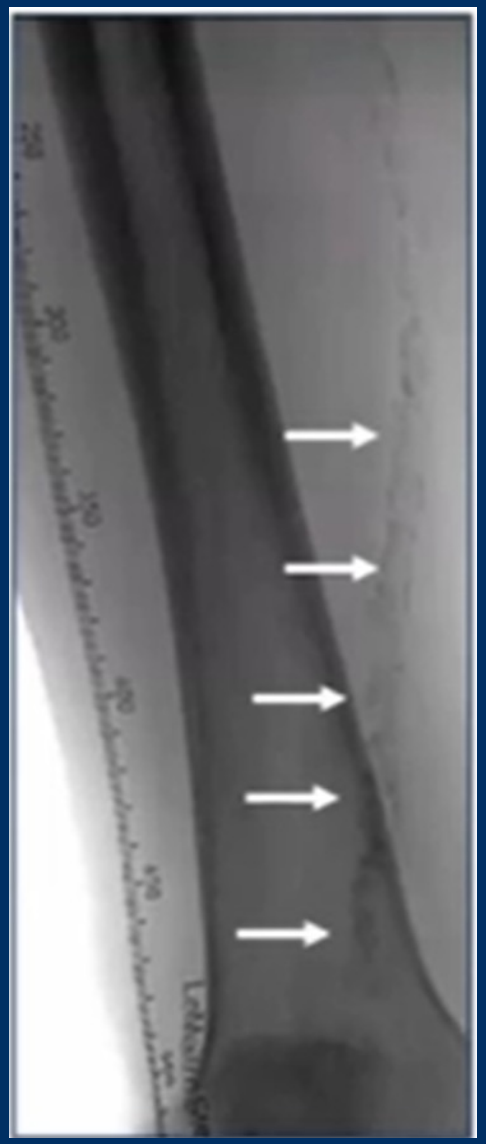
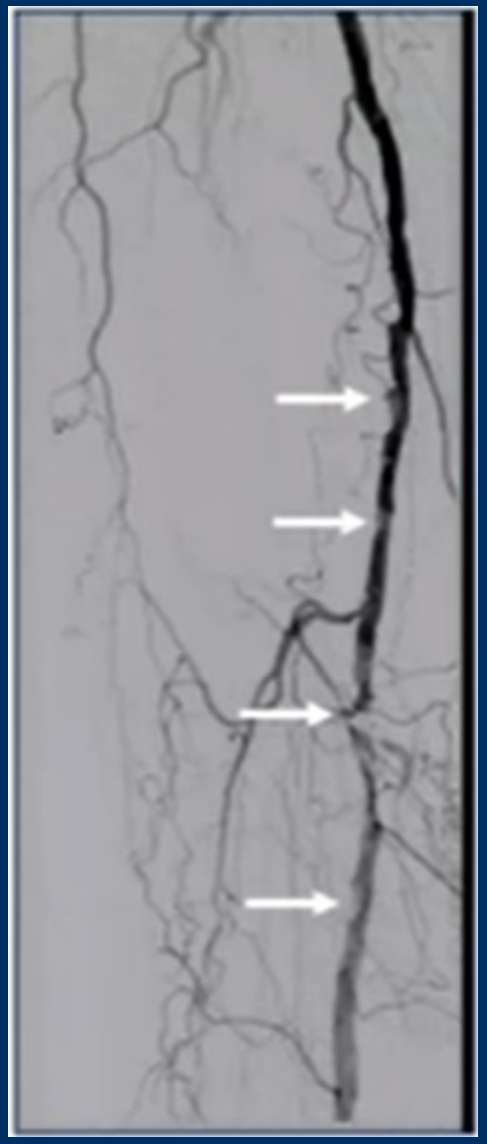
REALITY INCLUSION CRITERIA

Defining “Complex” Lesion Morphologies

- Femoropopliteal lesion lengths: 8-36 cm
- Long chronic total occlusion lengths: >10cm
- Bilateral vessel wall calcification **required** in all lesions





Images courtesy Krishnan Rocha-Singh, MD

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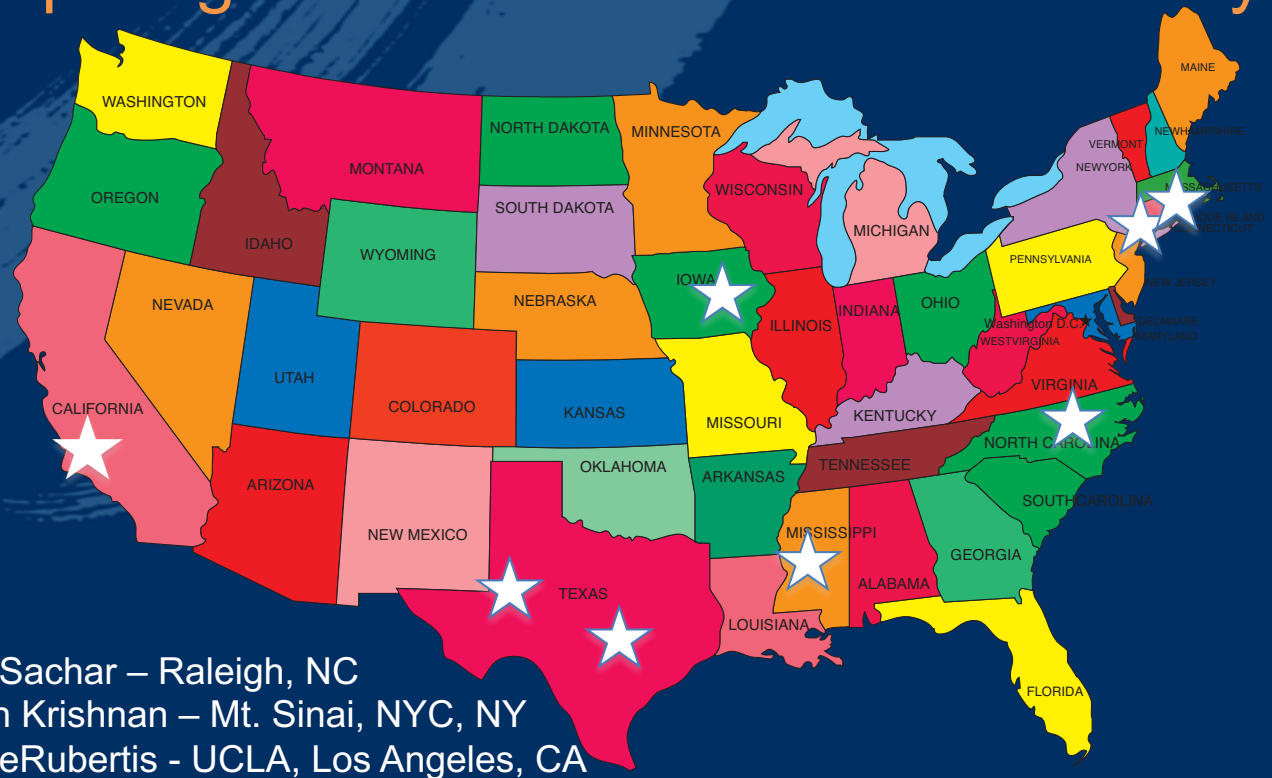
REALITY STUDY

Participating Sites from the US and Germany



- Dr. Ravish Sachar – Raleigh, NC
- Dr. Prakash Krishnan – Mt. Sinai, NYC, NY
- Dr. Brian DeRubertis - UCLA, Los Angeles, CA
- Dr. Lawrence Garcia - Boston, MA
- Dr. Eric Scott – Iowa Methodist, IA
- Dr. John Winscott – University of Mississippi
- Dr. Samir Germanwala – Longview, TX
- Dr. Roger Gammon – Austin, TX
- Dr. Miles McClure – Saginaw, MI

- Dr. Thomas Zeller - Bad Krozingen
- Dr. Giovanni Torsello - Munster
- Dr. Claus Nolte-Ernsting - Mulheim
- Dr. Erwin Blessing - Karlsbad

REALITY STUDY

Patient Flow

400 Screened Patients

298 Patients did not meet Inclusion/Exclusion Criteria

102 Eligible Patients

- 4 Deaths
- 1 Target limb amputation
- 6 Withdrew
- 4 Lost to F/U

Eligible for Follow-up:

- 30-day F/U 100 patients
- 6-month F/U 97 patients
- 12-month F/U 92 patients

Rocha-Singh KJ, et al. Catheter Cardiovasc Interv 2021 Jun 3. doi: 10.1002/ccd.29777.

REALITY STUDY

Clinical & Lesion Characteristics

Key Baseline Clinical Characteristics	N=102
Age (years); ± SD	69.6 ± 9.7
Sex (male)	65.7%
Hypertension	89.2%
Hyperlipidemia	81.4%
Diabetes Mellitus	53.9%
History of Coronary Artery Disease	61.8%
Prior Peripheral Endovascular Intervention	54.9%

Key Angiographic Characteristics	
Lesion Length (mm)	179 ± 81
Lesion Length ≥ 150 mm	55.6%
Chronic total occlusion	39.0%
Chronic total occlusion length (mm)	226.0 ± 86.0
Diameter Stenosis	
Baseline (%)	88.8 ± 11.7
Post DA+DCB (%)	28.1 ± 12.0
Procedural Success (defined as ≤30% post DA+DCB) *	57.6%

*As assessed by the angiographic core lab

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REALITY STUDY

Calcium Severity Assessment

Key Baseline Clinical Characteristics	N = 102
PACSS Score	
Grade 0	1.0%
Grade 1	2.9%
Grade 2	0.0%
Grade 3	18.6%
Grade 4 Bilateral wall Ca++ ≥5cm	67.6%
Not assessable	9.8%
Type of Calcification	
Type A: Intimal	0.0%
Type B: Medial	1.0%
Type C: Mixed Intimal + Medial Ca++	86.3%
Not assessable	12.7%

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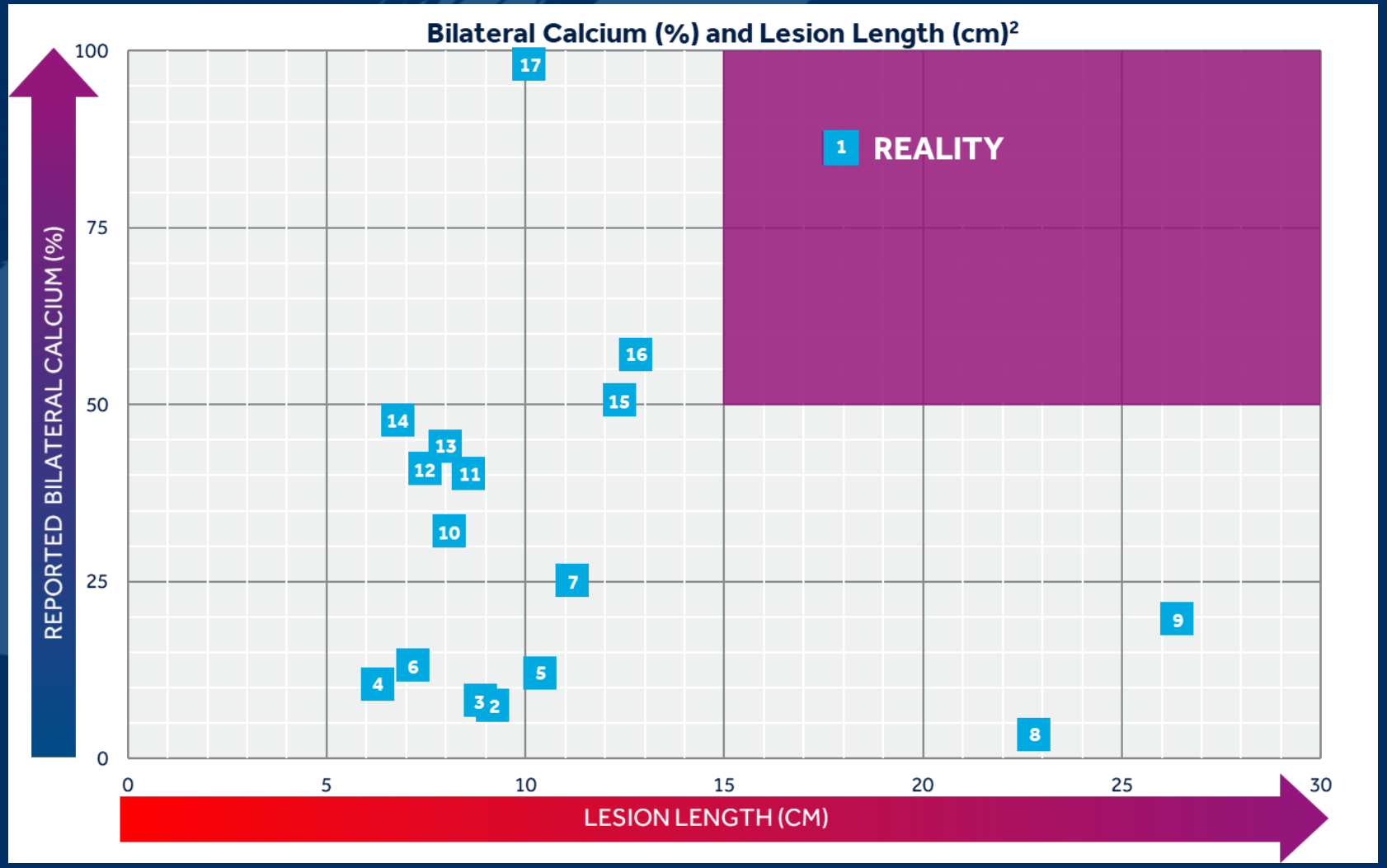
Key Calcium Metrics

PACSS Index:

$$\frac{Total\ bilateral\ calcification}{lesion\ length} x100 = 55.7 \pm 26.2$$

REALITY STUDY[1]

Long and Complex Lesions



With a focus on long and calcified lesions, the REALITY study was designed to explore the boundaries of endovascular therapy.

1 Sponsored and conducted by VIVA Physicians; funded by Medtronic.
2 Calcium definitions differ across studies. These are angiographic, core lab adjudicated reported calcium results. This graph is for illustration purposes only. References are at the end of this presentation.

REALITY STUDY

Procedure-Related Complications

Procedural Characteristics	
Perforations	3.1% (3/98)
Dissection ≥ Grade C	14.3% (14/98)
Distal Embolization	12.8% (11/86)
Provisional Stenting	8.8% (9/102)
Stenting for Perforations (cases)	3
Stenting for Dissection (cases)	5
Stenting for Embolization (cases)	1

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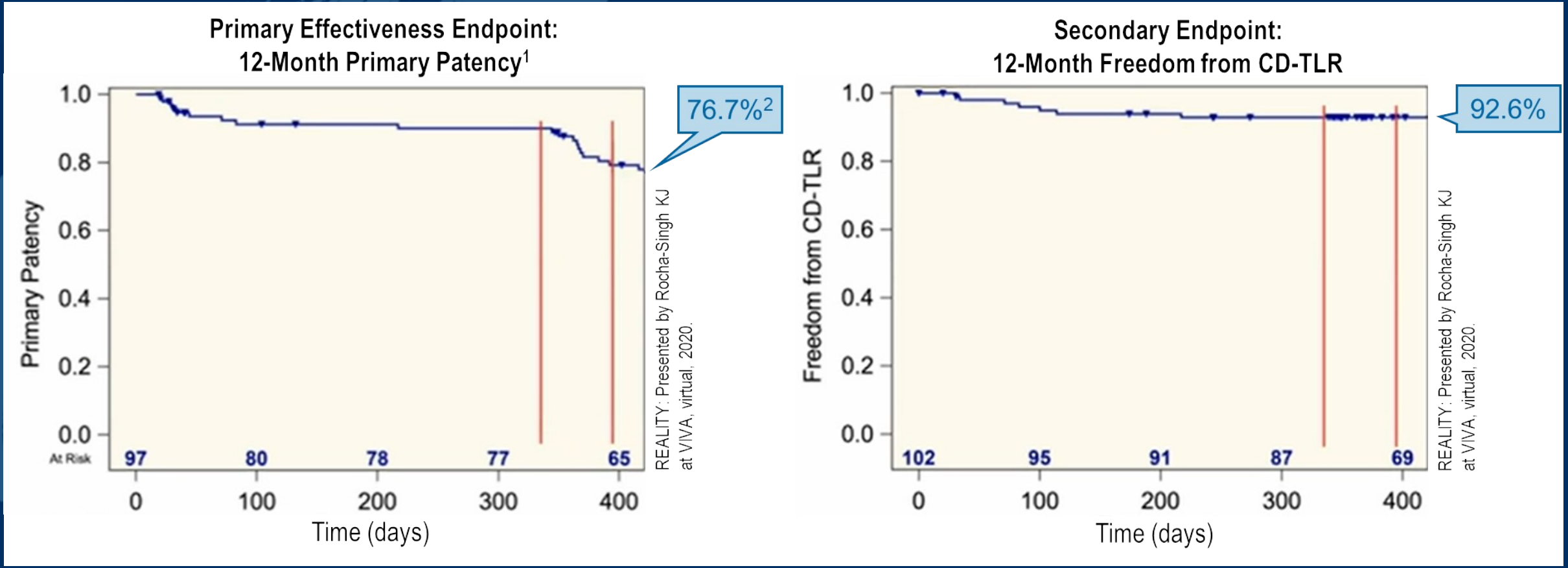
REALITY STUDY

Primary Effectiveness Outcomes



1. Primary patency defined as freedom from restenosis (DUS peak systolic velocity ratio >2.4) and CD-TLR, defined as any reintervention to the target lesion due to a return of symptoms and/or ankle-brachial index (ABI) decrease of 20% or > 0.15 when compared with the post index procedure baseline ABI.
2. 12-month data include patients beyond the follow-up window. Red lines indicate the 12-month follow-up window.

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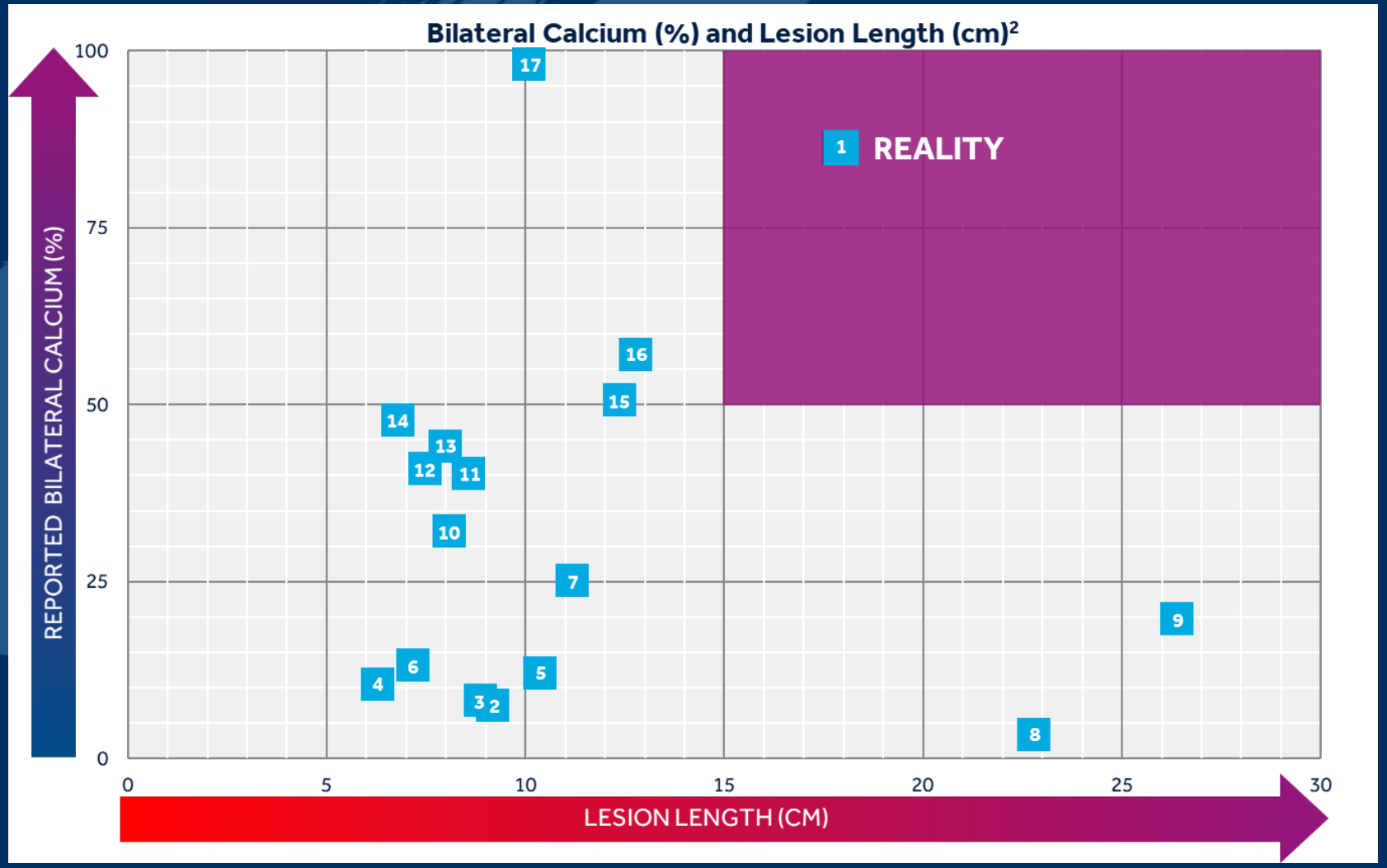
REALITY STUDY[1]

Showcasing the Synergy of DA and DCB in Highly Calcified Lesions



LESION CHARACTERSTICS

86.2%	17.9cm	39.0%
Bilateral Calcium	Average Lesion Length	Chronic Total Occlusion

OUTCOMES

92.6%	76.7%
FF-CD TLR	Patency

12-month data include patients beyond the follow-up window.

PRESERVED TREATMENT OPTIONS

8.8%

Bailout stent rate

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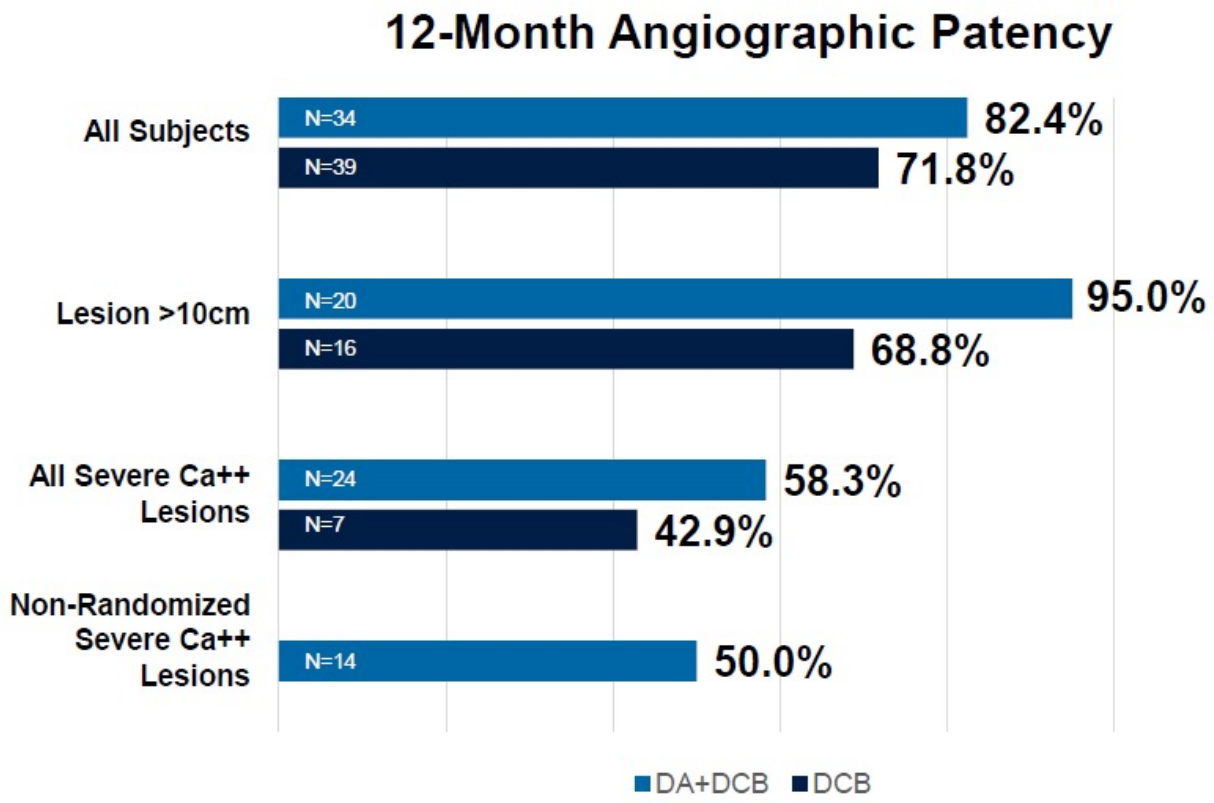
DEFINITIVE AR:
The Data Behind Directional Atherectomy



Peripheral Vascular Disease

OPEN

Directional Atherectomy Followed by a Paclitaxel-Coated Balloon to Inhibit Restenosis and Maintain Vessel Patency

Twelve-Month Results of the DEFINITIVE AR Study

Thomas Zeller, MD; Ralf Langhoff, MD; Krishna J. Rocha-Singh, MD; Michael R. Jaff, DO; Erwin Blessing, MD; Beatrice Amann-Vesti, MD; Marek Krzanowski, MD; Patrick Peeters, MD; Dierk Scheinert, MD; Giovanni Torsello, MD; Sebastian Sixt, MD; Gunnar Tepe, MD; on behalf of the DEFINITIVE AR Investigators

Background—Studies assessing drug-coated balloons (DCB) for the treatment of femoropopliteal artery disease are encouraging. However, challenging lesions, such as severely calcified, remain difficult to treat with DCB alone. Vessel preparation with directional atherectomy (DA) potentially improves outcomes of DCB.

Methods and Results—DEFINITIVE AR study (Directional Atherectomy Followed by a Paclitaxel-Coated Balloon to Inhibit Restenosis and Maintain Vessel Patency—A Pilot Study of Anti-Restenosis Treatment) was a multicenter randomized trial designed to estimate the effect of DA before DCB to facilitate the development of future end point-driven randomized studies. One hundred two patients with claudication or rest pain were randomly assigned 1:1 to DA+DCB (n=48) or DCB alone (n=54), and 19 additional patients with severely calcified lesions were treated with DA+DCB. Mean lesion length was 11.2±4.0 cm for DA+DCB and 9.7±4.1 cm for DCB (*P*=0.05). Predilation rate was 16.7% for DA+DCB versus 74.1% for DCB; postdilation rate was 6.3% for DA+DCB versus 33.3% for DCB. Technical success was superior for DA+DCB (89.6% versus 64.2%; *P*=0.004). Overall bail-out stenting rate was 3.7%, and rate of flow-limiting dissections was 19% for DCB and 2% for DA+DCB (*P*=0.01). One-year primary outcome of angiographic percent diameter stenosis was 33.6±17.7% for DA+DCB versus 36.4±17.6% for DCB (*P*=0.48), and clinically driven target lesion revascularization was 7.3% for DA+DCB and 8.0% for DCB (*P*=0.90). Duplex ultrasound patency was 84.6% for DA+DCB, 81.3% for DCB (*P*=0.78), and 68.8% for calcified lesions. Freedom from major adverse events at 1 year was 89.3% for DA+DCB and 90.0% for DCB (*P*=0.86).

Conclusions—DA+DCB treatment was effective and safe, but the study was not powered to show significant differences between the 2 methods of revascularization in 1-year follow-up. An adequately powered randomized trial is warranted.

Clinical Trial Registration—http://www.clinicaltrials.gov. Unique Identifier: NCT01366482.

(*Circ Cardiovasc Interv*. 2017;10:e004848. DOI: 10.1161/CIRCINTERVENTIONS.116.004848.)

Zeller T, Langhoff R, Rocha-Singh KJ, Jaff MR, Blessing R, Amann-Vesti B, Krzanowski M, Peeters P, Scheinert D, Torsello G, Sixt S, Tepe G. Directional atherectomy followed by paclitaxel-coated balloon to inhibit restenosis and maintain vessel patency – twelve-month results of the DEFINITIVE AR study. Circ Cardiovasc Interv. 2017;10Sep;10(9).

DiRectional AthErectomy + Drug CoAted BaLIoons to Treat Long CalcIfied FemoropopliTeal ArterY Lesions - REALITY

Summary:

- The REALITY Study investigated the use of directional atherectomy using the HawkOne system followed by IN.PACT Admiral DCB in **long and calcified lesions**[1]
- The REALITY Study demonstrated that this vessel preparation treatment strategy is **effective up to 12-months** with an acceptable safety profile[1]
- The directional atherectomy vessel preparation strategy used in the REALITY Study is associated with a **low provisional stent rate**[1]

1. Rocha-Singh KJ, et al. Catheter Cardiovasc Interv 2021 Jun 3. doi: 10.1002/ccd.29777.

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