

Update on the OPTIMIZE BTK Trial

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Disclosure

Speaker name: Marianne Brodmann, MD

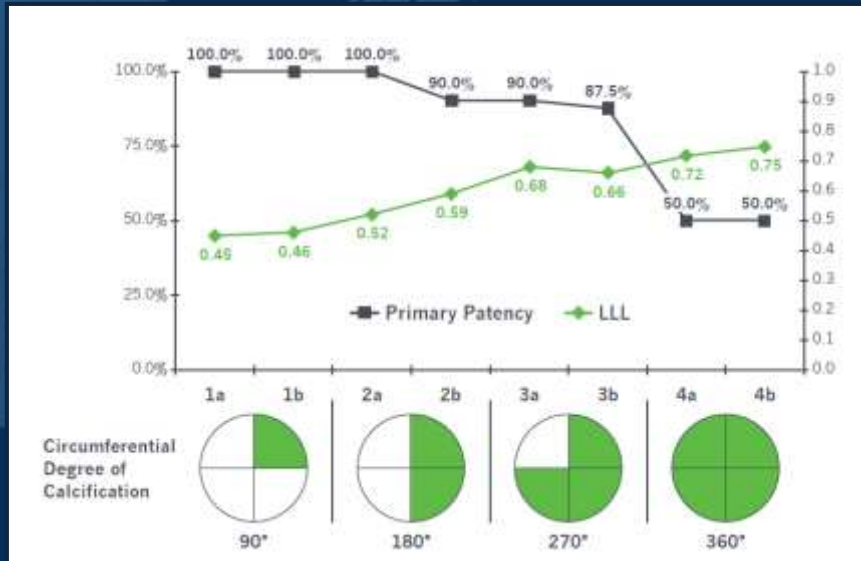
I have the following potential conflicts of interest to report:

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

- I do not have any potential conflict of interest

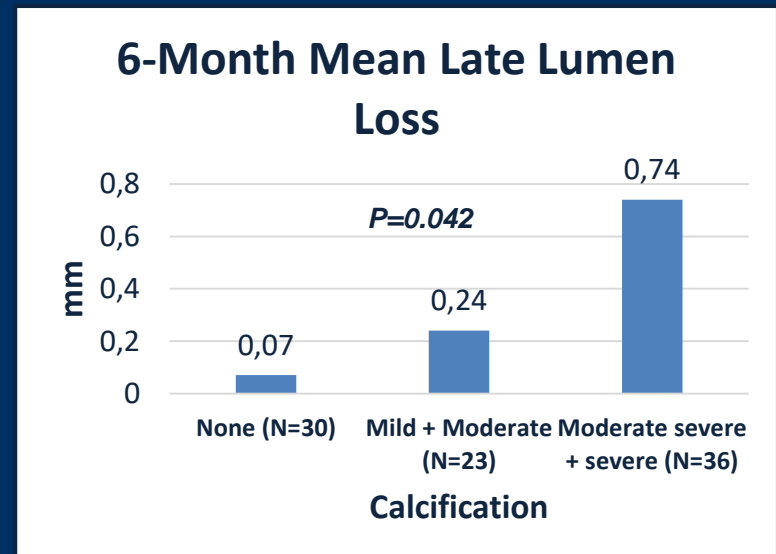
Limitation of Drug Coated Balloons in Calcified Lesions

- As circumferential calcium increases, the effectiveness of DCBs decreases
- Late lumen loss increased & primary patency decreased with calcium severity



Dr. Fanelli's Calcium Impact on DCB Study (Prospective, 60 patients, SFA lesions treated with DCBs, 12 month follow-up)

- As calcium severity increases, late lumen loss at 6 months increases
- Severity of lesion calcification was a single independent predictor of late lumen loss outcome after DCB treatment

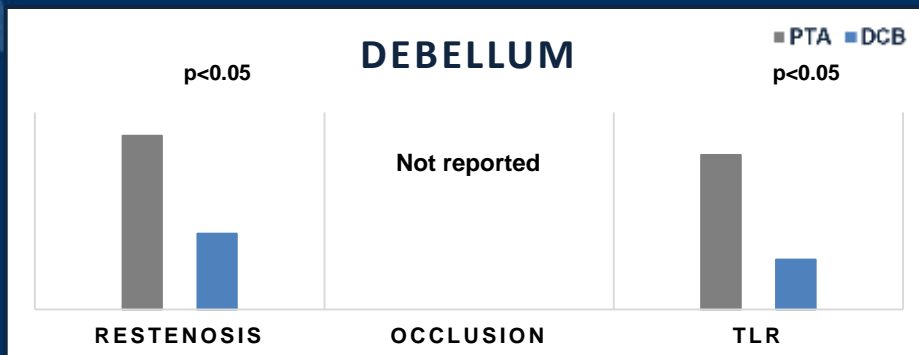
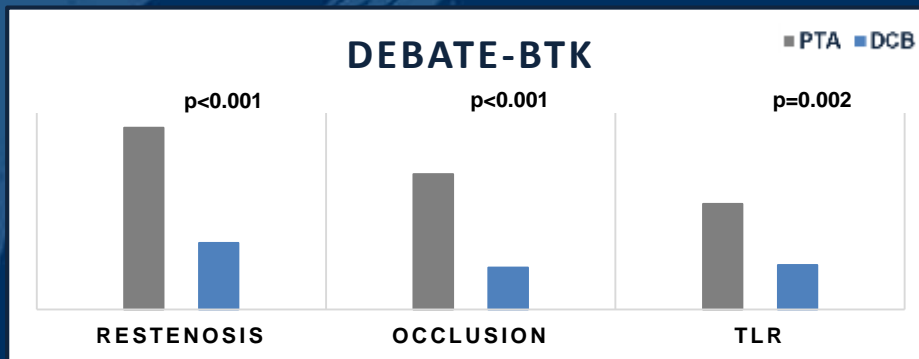


Dr. Tepe's Peripheral DCB Study (Retrospective, 91 patients, Fempop lesions treated with DCBs, 6 month follow-up)

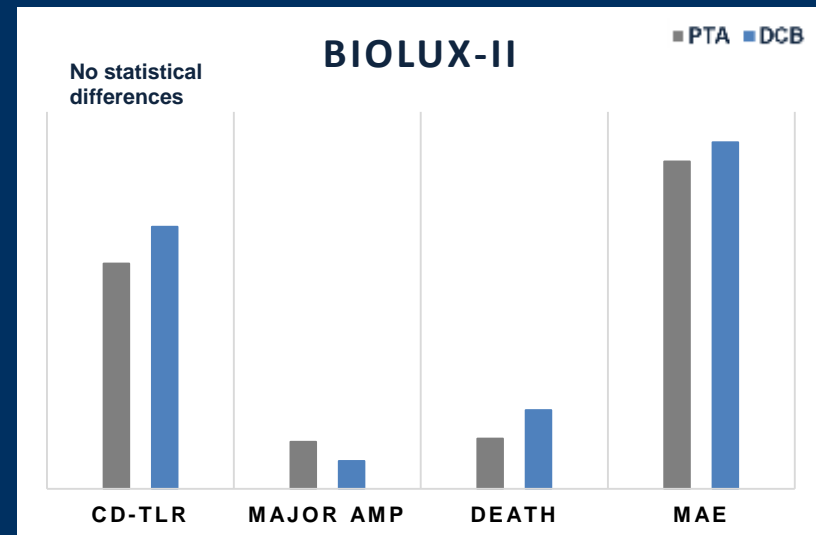
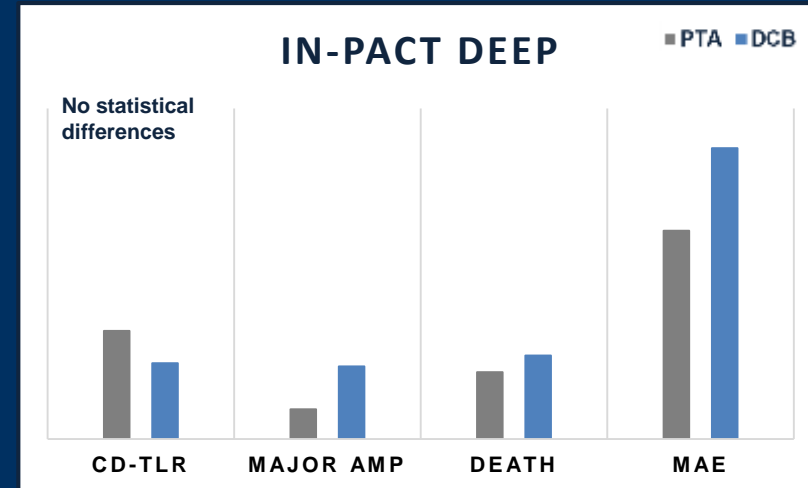
Below the Knee DCB Studies

Single center studies suggest DCBs may lower reintervention rates; however, RCTs have failed to show superiority of DCBs for BTK treatment

Single-center studies – 1-year results



RCTs – 1-year results



STEALTH 360[®] Peripheral Orbital Atherectomy System

Streamlined Setup and Treatment

Sleek Electric-Powered Handle

- Simple device set-up
- Optimum torque transfer to the shaft and crown
- Short overall treatment times

Crowns

- Micro Crown
- Classic Crown
- Solid Crown

Prime Control

- Flush saline device

Simple Speed Settings

Instant Response On/Off Switch

Brake

OAS Pump

- Mounts directly to an I.V. pole
- Bathes shaft and crown with ViperSlide Lubricant to facilitate smooth device operation



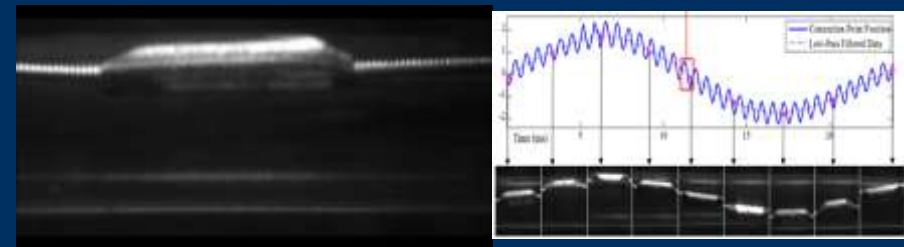
CSI's Unique MOA:

Changing Compliance using Centrifugal Force

- 360° crown contact designed to create a smooth, concentric lumen
- Allows constant blood flow and particulate flushing during orbit



- Average particulate size¹ = 2 μm
- Bi-directional sanding of superficial calcium
- Healthy elastic tissue flexes away from the crown, minimizing damage to the vessel



- Low frequency (18-40 Hz) represents crown orbit inside vessel*
- High frequency (1000-1900 Hz) represents rotation of eccentric crown over the wire, producing pulsatile mechanical forces*
- These pulsatile forces may affect deeper plaque and contribute to compliance change**

* In a phantom non-diseased popliteal artery

** Results vary based upon plaque morphology, calcification, and anatomy

1. Based on cadaver atherosclerotic lesions, porcine coronary lesions, and graphite blocks

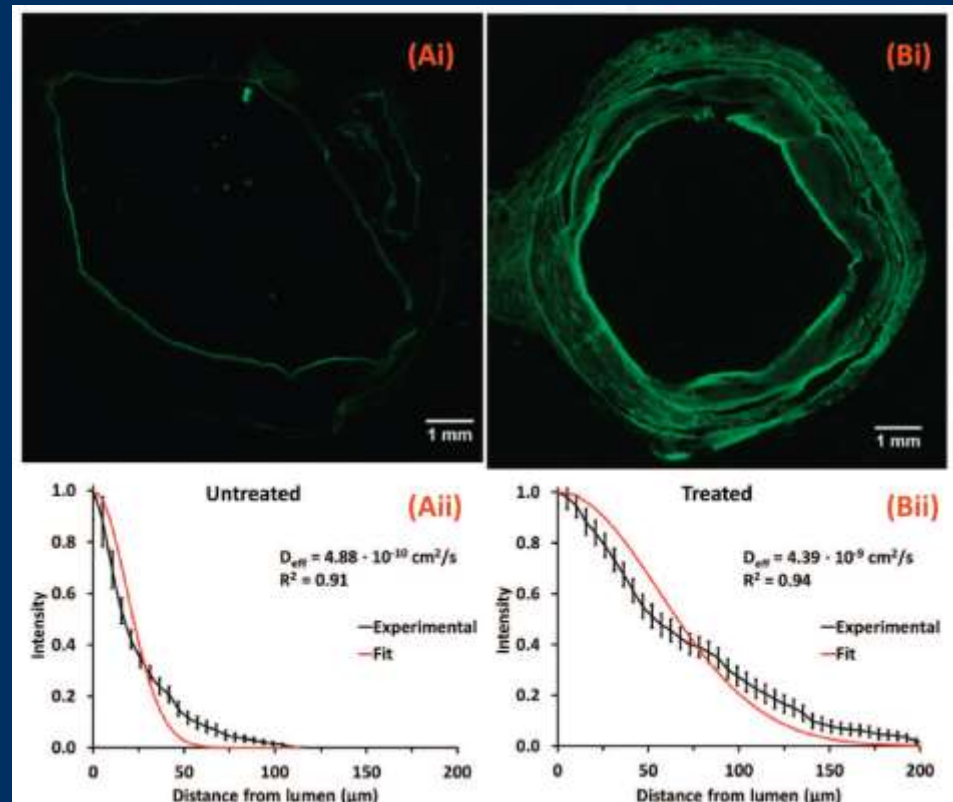
2. Test models: Zheng Y, et al. *Med Eng Phys.* 2016;38(7):639-47.

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

These data illustrate that calcified plaque limited intravascular drug delivery, and controlled OAS treatment of calcific plaques trended in greater drug permeability and improved adjunct drug delivery to diseased arteries.

Untreated

OAS Treated



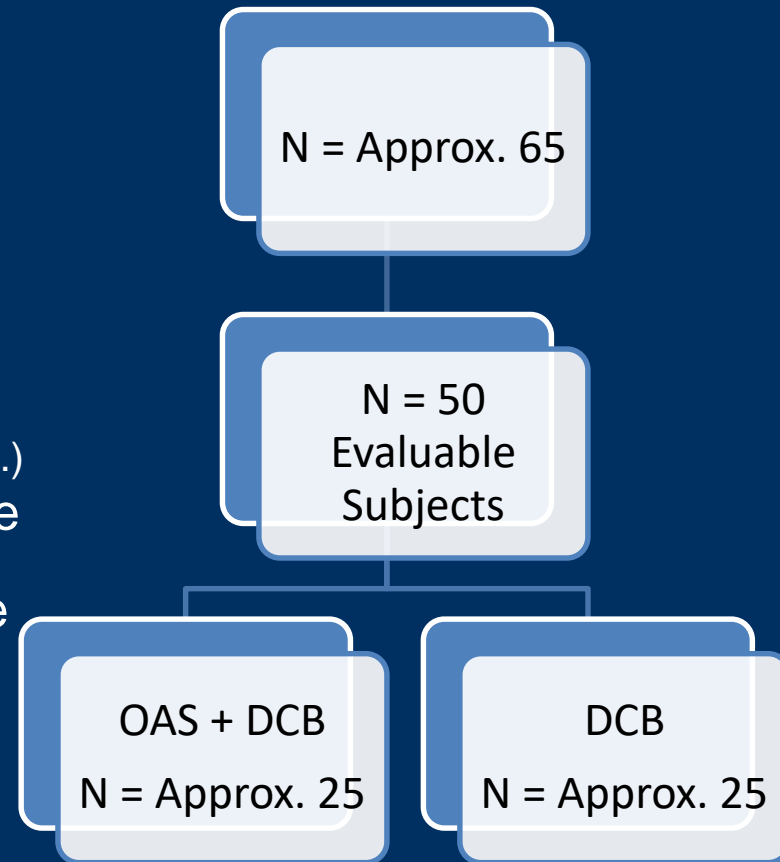
Study performed in 5 cadaveric lower limbs with calcified arteries. Freshly excised arterial segments were lumenally infused with a buffered solution (PBS/4% BSA) of radiolabeled (^{14}C , 10 μM) or fluorescent (Oregon Green 488, 10 μM) paclitaxel.

OPTIMIZE-BTK

OAS+DCB vs. DCB Alone in BTK Lesions

Study Details:

- Pilot study
- Prospective, 1:1 Randomization
- Calcified below the knee lesions
- Study devices:
 - Peripheral Orbital Atherectomy System (Cardiovascular Systems, Inc.)
 - Lutonix® 014 Drug Coated Balloon (C.R. Bard, Inc.)
- Evaluable subject: subject who met all of the inclusion and none of the exclusion criteria (angiographic criteria confirmed by the Core Lab) and alternative (non-study devices) or post-adjunctive treatment(s) were not required during the index procedure
- 2-year follow-up



Purpose: Demonstrate the ability of the OAS to prepare calcified, BTK lesions for optimal DCB deployment

OPTIMIZE-BTK: Inclusion/Exclusion Criteria

Notable Inclusion Criteria:

- Rutherford Clinical Category 3 – 5
- Lesions [except in-stent restenosis (ISR)] of the distal POP (POP segment below the anatomical knee *joint*), AT, PT, TPT, and PR arteries with ≥ 70 % DS by angiography
- Presence of clearly visible calcification in two views (both sides of vessel at the same location) evaluated angiographically
 - CT angio images may substitute to confirm distribution of calcium
- Length of calcium ≥ 25 % of total lesion length or ≥ 2 cm total length
- Target lesion length up to 20 cm

Notable Exclusion Criteria:

- Presence of inflow lesion (≥ 50 % DS) or inflow not successfully treated (≥ 50 % DS and/or unresolved significant angiographic complication)
- Compromised outflow distal to the target lesion (≥ 70 % DS) or presence of lesion(s) or occlusion(s) located from 5 cm above the ankle to below the ankle joint space
- Subject has more than 2 target vessels requiring treatment
- Presence of significant (≥ 70 % DS) lesion(s) or occlusion(s) not meeting the study criteria which were not successfully treated during the index procedure (≥ 50 % DS and/or significant angiographic complication)
- Subject has planned amputation (including minor) of the index limb or previous major amputation of the contralateral limb

OPTIMIZE-BTK: Primary Outcome Measures

- LLL of the target lesion by QVA at 6 months post-procedure or at the time of TLR
- Patency of the target lesion by DUS at 6 mo and 12 mo post-procedure
- Freedom from Major Adverse Events at 30 days, 3, 6, 12, and 24 months post-procedure
 - MAEs include: clinically-driven TLR; unplanned, unavoidable major amputation of the index limb; and death within 30 days of the index procedure
- Freedom from clinically driven TLR at follow up (core lab adjudicated)
- Freedom from unplanned, unavoidable major amputation of the index limb follow up

OPTIMIZE-BTK: Study Update

53 subjects enrolled as of 16Jan2018

Active Sites:

- Austria (Prof. Brodmann/Deutschmann & Dr. Werner)
- Germany (Prof. Zeller, Prof. Tepe, Prof. Andrassy, Prof. Blessing, Prof. Scheinert)
- Switzerland (Dr. Banyai)



Conclusions

- Calcified lesions may reduce the efficacy of DCBs by blocking uptake of drug into vessel wall
- Preclinical data suggest OAS treatment of calcific plaques trended in greater drug permeability and improved adjunct drug delivery to diseased arteries
- OPTIMIZE-BTK trial is designed to test the hypothesis that pre-treatment with OAS for calcified BTK arteries followed with DCB will provide incremental benefits versus DCB angioplasty alone
 - 53 subjects enrolled as of 16Jan2018