Hello again – Re-intervention strategies for sub-optimal results of current technologies

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Adjunct Clinical Associate Professor,
University of Iowa Hospitals
Interventional Cardiologist,
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• IMPORTANT INFORMATION: These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician’s professional judgment in light of all available information for the case at hand.

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• Results from case studies are not predictive of results in other cases. Results in other cases may vary.
Disclosure

Speaker name: Nicolas W Shammas, MD, MS, FACC, FSCAI

I have the following potential conflicts of interest to report:

- Consulting: Boston Scientific, Gilead
- Trainer: Boston Scientific (Jetstream), Covidien (RF)
- Speaker Bureau: Boston Scientific, The Medicines Co, Novartis, Merck, Boehringer Ingelheim, BMS/pfizer, AZ,
- Other(s): Research and educational grants from Boston Scientific, CSI, Bard. Steering Committee: JET, Endomax
- National/Co-National PI: Jet-ISR, Safe-DCB
“Hostile” Peripheral Artery

Reduce chance of procedural success
Increase chance of bailout stenting
Increase rate of complications
Reduce effectiveness of anti-proliferative drugs
Negatively impact stent expansion
Increases rate of distal embolization
Adversely affect long term outcomes
Characteristics of a “Hostile” Artery

Severe Calcification
Thrombus
In-stent restenosis
Total Occlusions
TASC C and D lesions
Long irregular disease
“hostile” milieu:
CLI, Diabetes, CAD, Renal insufficiency, smoking, old age, poor runoff, prior intervention
CALCIUM
Peripheral Arterial Calcium

Found in:
1. Atherosclerotic/fibrotic plaques
2. Medial layers (Monckeberg’s medial calcification)

Atherosclerotic Calcium more common above the knee (Also Medial calcium present in diabetic & renal failure). In 35% of vessels

Medial calcification more common below the knee in both symptomatic and asymptomatic vessels. Circumferential. In 75% of vessels

Angiography underestimates calcification in the arteries

Bone Formation in peripheral arteries: 10-15% of PAD patients

Males more than females & Whites more than African Americans

There is no validated method to quantify Ca in peripheral arteries

Peripheral Arterial Calcium Alters Procedural Success

• Presence of calcium requires greater balloon pressures for arterial dilation

• Plaques associated with dissections and perforations commonly have significant calcium deposits

• Calcium is predictor of the need for bail out stenting

• Calcium lead to stent under-expansion

• Calcium prevents the ability to reach or dilate a lesion

• There is higher risk of stent fracture in calcified vessels

• Ca presents a barrier to anti-proliferative drug absorption

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Atherectomy for calcium modification...

- **JetStream**
  - Rotational Atherectomy
- **Diamondback 360**
  - Rotational Atherectomy
- **Turbohawk**
  - Directional Atherectomy
- **Laser**
  - Directional Atherectomy
# CALCIUM 360° Study
(popliteal/infrapopliteal)

<table>
<thead>
<tr>
<th></th>
<th>Diamondback 360°</th>
<th>Balloon Angioplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average maximum balloon pressures</td>
<td>5.9 atms (p&lt;0.001)</td>
<td>9.4 atms</td>
</tr>
<tr>
<td>Procedural success (≤30% residual stenosis)</td>
<td>93.1%</td>
<td>82.4%</td>
</tr>
<tr>
<td>Dissections</td>
<td>3.3%</td>
<td>11.4%</td>
</tr>
<tr>
<td>Bail-out stenting</td>
<td>2 (6.9%)</td>
<td>5 (14.3%)</td>
</tr>
<tr>
<td>Freedom from revascularization</td>
<td>93.3%</td>
<td>80.0%</td>
</tr>
<tr>
<td>Freedom of major adverse events</td>
<td>93.3% (p=0.006)</td>
<td>57.9%</td>
</tr>
</tbody>
</table>

# COMPLIANCE 360° Study
(Superficial Femoral Artery)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Diamondback 360°</th>
<th>Balloon Angioplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average maximum balloon pressures</td>
<td>4.0 atms (p&lt;0.001)</td>
<td>9.1 atms</td>
</tr>
<tr>
<td>≤30% residual stenosis without stenting</td>
<td>86.8% (p&lt;0.001)</td>
<td>18.5%</td>
</tr>
<tr>
<td>Dissections</td>
<td>15.8% (p=0.02)</td>
<td>48.1%</td>
</tr>
<tr>
<td>Bail-out stenting (for residual over 30%)</td>
<td>5.3% (P&lt;0.001)</td>
<td>77.8%</td>
</tr>
<tr>
<td>Freedom from revascularization (1 yr)</td>
<td>81.2% (P=NS)</td>
<td>78.3%</td>
</tr>
</tbody>
</table>

Jetstream Calcium Study

Objective

• Study the treatment effects of Jetstream in moderately to severely calcified peripheral artery disease

Design

• Prospective, single arm, multicenter study

Key Inclusion Criteria

• Symptomatic lesion with superficial calcium >90° and >5 mm in length by IVUS

Primary Endpoint

• Calcium removal and luminal gain as measured by IVUS from pre to post-Jetstream treatment

IVUS, intravascular ultrasound; MI, myocardial infarction
Jetstream Calcium Study Results

<table>
<thead>
<tr>
<th>Table 1. Lesion and procedural characteristics - 26 lesions.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target lesion location</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>De novo lesion</td>
</tr>
<tr>
<td>Angiographic calcium grade</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Visual total lesion length (mm)</td>
</tr>
<tr>
<td>Visual reference vessel diameter (mm)</td>
</tr>
<tr>
<td>Adjunctive treatment</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Visual diameter stenosis (%)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Atherectomy treatment time (minutes)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Volume of aspirant collected (cc)</td>
</tr>
</tbody>
</table>

Patient characteristics
- Mean age 73 years
- 56% had diabetes mellitus

 Majority of lesions in the SFA
- 63.6% severe calcium by angiography

Adjunctive therapy used for most lesions
- No MAEs (death, MI, TLR, unplanned amputation) reported within 30 days post-procedure


MAE, major adverse event; MI, myocardial infarction; SFA, superior femoral artery; TLR, target lesion revascularization.
Calcium Study: Lesion-Level IVUS Analysis

- Significant increase in the minimum lumen area (from 5.1 to 8.3 mm²)
- Significant decrease in the area stenosis (from 64% to 41%)
- The decrease in calcium area (2.8 mm²) accounted for 86% of the lumen area increase

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Post-atherectomy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal reference lumen area (mm²)</td>
<td>14.6±5.1</td>
<td>14.5±5.2</td>
<td>0.91</td>
</tr>
<tr>
<td>Distal reference lumen area (mm²)</td>
<td>14.8±6.2</td>
<td>14.7±5.9</td>
<td>0.97</td>
</tr>
</tbody>
</table>

**Minimum lumen area site**

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Post-atherectomy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen area (mm²)</td>
<td>5.1±2.8</td>
<td>8.3±2.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Minimum lumen diameter (mm)</td>
<td>2.0±0.4</td>
<td>2.8±0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lumen symmetry index</td>
<td>0.70±0.13</td>
<td>0.76±0.14</td>
<td>0.11</td>
</tr>
<tr>
<td>Area stenosis (%)</td>
<td>64±17</td>
<td>41±18</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Maximum calcium ablation site**

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>Post-atherectomy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen area (mm²)</td>
<td>6.6±3.7</td>
<td>10.0±3.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Minimum lumen diameter (mm)</td>
<td>2.3±0.5</td>
<td>3.0±0.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lumen symmetry index</td>
<td>0.70±0.14</td>
<td>0.74±0.14</td>
<td>0.26</td>
</tr>
<tr>
<td>Area stenosis (%)</td>
<td>53±23</td>
<td>29±22</td>
<td>0.0005</td>
</tr>
<tr>
<td>Maximum superficial calcium (%)</td>
<td>151±70</td>
<td>146±71</td>
<td>0.83</td>
</tr>
<tr>
<td>Decrease of calcium area (mm²)</td>
<td>NA</td>
<td>2.8±1.6</td>
<td>NA</td>
</tr>
<tr>
<td>Calcium reduction (%)</td>
<td>NA</td>
<td>86±22</td>
<td>NA</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation.
PVD Trial

Objective
• Assess performance/safety of the JETSTREAM™ Atherectomy System during percutaneous peripheral vascular interventions

Design
• Prospective, single arm, multi-center study
  • 172 patients at 9 European centers

Primary endpoint
• MAE at 30 days

PVD Study Results

- Jetstream™ device success was 99% (208/210 lesions were cleared)
- 85% of patients TLR-free at 6 months, 74% TLR-free at 12 months
- Stenting performed in 7% of lesions during the index procedure
- Restenosis at one year: 38.2%
- ABI: 0.59 to 0.82
- RB Category 1.5 to 3.0

ATA, anterior tibial artery; MAE, major adverse event; MI, myocardial infarction; PTA, posterior tibial artery; SFA, superficial femoral artery; TLR, target lesion revascularization; TPT, tibioperoneal trunk; TVR, target vessel revascularization.

65 y.o. smoker with severe left leg claudication
IVUS

Pre treatment IVUS

Post treatment IVUS

Case JetStream Atherectomy: Shammas NW
72 y.o. diabetic and smoker patient with right leg rest pain

Case JetStream Atherectomy: Shammas NW
82 y.o. patient with claudication and past history of smoking

Heavily calcified distal SFA CTO

Post JETSTREAM and DCB (Lutonix)

Post stent

Case JetStream Atherectomy: Shammas NW
Lesion preparation with an orbital atherectomy system enhances paclitaxel deposition in calcified peripheral arteries

Abraham R. Tzafriri, 1 Brett Zani, 1 James Stanley, 1 Peter Markham, 1 Alexander Nikanorov, 2 Elazer R. Edelman 3
1CBSET Inc., Lexington, MA; 2Cardiovascular Systems, Inc, Saint Paul, MN; 3Harvard-MIT Biomedical Engineering Center, Cambridge, MA

- Five fresh human lower limbs
- Computed Tomography (CT) was performed on all limbs. FP and tibials included
- Distal segment of each artery treated using the DIAMONDBACK 360
- Arteries were explanted and cut in pairs of 3 cm in length along atherectomy-treated vs. non-treated demarcation lines
- Lumen infused with radiolabeled or fluorescent paclitaxel and incubated 1h at 37°C.

RESULTS:
- All arteries exhibited high levels of calcification in CT angiography.
- Quantification of 14C-labeled paclitaxel revealed a an increase in drug in OAS treated tissue, ranging from 20% more in FP to more than 400% in tibial arteries. The average increase of drug deposit in OAS treated arteries was above 50%.
- Fluorescent microscopy revealed distribution patterns that declined with increasing distance from the lumenal surface and tended to be more diffuse and extended in OAS treated tissue segments
Lesion Calcification May Affect Drug-Coated Balloon Efficacy

- 60 patients with SFA stenosis or occlusion treated with Drug Coated Balloon
- 50% primary patency rates in heavily calcified SFA lesions, regardless of lesion length
- Greater calcification was associated with poorer outcomes at 1 year:
  - Greater TLR rate
  - Lower ankle-brachial index
  - Greater late lumen loss

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DCB, drug-coated balloon; SFA, superficial femoral artery; TLR, target lesion revascularization.

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Calcium burden quantified with computed tomography angiography (CTA), digital subtraction angiography (DSA), and intravascular ultrasound (IVUS).
Calcium Reduces Drug-coated Balloon Efficacy

• Tepe et al analyzed 91 patients retrospectively at 6 months after Drug Coated Balloon treatment.

• Lesions were located in the superficial femoral artery (SFA, n=68) and popliteal artery (n=23)

• Lesion calcification was graded by a core laboratory using 2 published scoring indices: the peripheral artery calcification scoring system (PACCS) and a grading system based on angiographic circumference (arc) and length of calcium.
The median LLL after 6 months was 0.2 mm (interquartile range -0.5, 1.14) and was higher with severity of calcification (p=0.042).

LLL did not differ based on calcium location (intimal, medial, or mixed) or calcium length (p=0.351 and p=0.258, respectively) or the severity of residual stenosis after the intervention.

Diabetes, CAD and prior intervention were also predictors of LLL loss.

**Conclusion:**

- Severity of calcium arc on angiography was an independent predictor of LLL after Drug Coated Balloon treatment (Consistent with Fanelli data)
**Atherectomy and Drug Coated Balloon Efficacy: Clinical Evidence**

- **DEFINITIVE AR**: directional atherectomy + Drug Coated Balloon vs Drug Coated Balloon alone
  - Third non-randomized arm for directional atherectomy + Drug Coated Balloon for severely calcified lesions
- Adjunctive atherectomy may improve procedural and clinical outcomes following Drug Coated Balloon treatment of the SFA and/or popliteal artery, particularly for longer or severely calcified lesions

### Procedural Results

<table>
<thead>
<tr>
<th></th>
<th>Drug Coated Balloon</th>
<th>Atherectomy + Drug Coated Balloon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical Success*</td>
<td>64.2%</td>
<td>89.6%</td>
</tr>
<tr>
<td>Bail-out Stent</td>
<td>3.7%</td>
<td>0%</td>
</tr>
<tr>
<td>Flow-limiting Dissection</td>
<td>19%</td>
<td>2%</td>
</tr>
</tbody>
</table>

### Duplex-Ultrasound Patency @ 12-months

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>DCB</th>
<th>DCB + Ather</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions &gt; 10cm long (N=52)</td>
<td>85.9%</td>
<td>96.8%</td>
</tr>
<tr>
<td>Severely Calcified lesions (N=24)</td>
<td>62.5%</td>
<td>70.4%</td>
</tr>
<tr>
<td>All patients</td>
<td>89.6%</td>
<td>93.4%</td>
</tr>
</tbody>
</table>

*Technical success: Defined as ≤ 30% residual stenosis following the protocol-defined treatment at the target lesion as determined by the Angiographic Core Laboratory. DCB, drug-coated balloon; DUS, duplex ultrasound; SFA, superficial femoral artery

Zeller T. VIVA 2014.
MLA and residual stenosis in Definitive AR

Zeller T. VIVA 14
Directional Atherectomy and Drug Coated Balloon in Heavily Calcified Fempop lesions

- Severe calcified lesions that underwent intravascular ultrasound guided DA and Drug Coated Balloon (In-Pact admiral)
- 30 patients had life limiting claudication (n=18) and critical limb ischemia (n=12).
- Baseline Rutherford class 4.2±1.2
- All procedures performed using a distal protection device.
- Stent implantation was allowed if flow limiting dissections or suboptimal result (residual stenosis>50%) by visual estimation.
- Patients followed up to 12 mo.

RESULTS:
- Procedural and clinical success, was achieved in all cases.
- Bail-out stenting was necessary in only two (6.5%).
- At twelve month follow up median Rutherford class was down to 2.2±1.2, ABI was 0.8±0.1 and Limb salvage rate was 100%, TLR=10%

Calcium...

• Reduces the success of the procedure
  – More residual narrowing, more dissections, more bailout stenting, more recoil, and loss of patency

• Prevents adequate Anti-proliferative drug absorption and reduces the effectiveness of Drug Coated balloons

• Modifying Calcium reduces dissection and bailout stenting, allow better vessel expansion, and increase drug absorption.

• Small studies suggest larger MLA, better long term patency and less LLL with Drug Coated Balloon + atherectomy.

• Larger, well powered trials are needed to show the added value of atherectomy to Drug Coated Balloons or Drug Eluting Stents
Thrombus
Thrombus and Drug Elution

• Thrombus is highly prevalent in the periphery and quite often under-diagnosed by angiography

• Thrombus forms on stents even when not occlusive or angiographically visible

• A fine layer of thrombus can affect drug elution into the arterial wall

• Removing thrombus or modifying its presence may be a promising approach in enhancing Drug Eluting Stent/Drug Coated Balloon effectiveness
Thrombus: Paclitaxel Diffusivity

- Paclitaxel diffusivity is significantly diminished with more RBC cross linked with fibrin in a thrombus
- Clots with 50% RBC retain 50% more Paclitaxel than pure fibrin clot

Hwang et al. Circulation 2005;111:1619-1626
# Atherectomy Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Jetstream™ Atherectomy System (Boston Scientific)</th>
<th>Diamondback 360™, Stealth 360™ Atherectomy System (Cardiovascular Systems, Inc)</th>
<th>SilverHawk™, TurboHawk™ Plaque Excision System (Covidien)</th>
<th>Turbo-Elite™ Laser Atherectomy Catheter (Spectranetics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Front-Cutting</td>
<td>✔</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Differential Cutting</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Active Aspiration</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentric Lumens</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lesion Morphology:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>✔</td>
<td>✔</td>
<td>✔ (large vessel only)</td>
<td>✔</td>
</tr>
<tr>
<td>Soft/Fibrotic Plaque</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Thrombus</td>
<td>✔ Indicated for thrombectomy and atherectomy</td>
<td></td>
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<td>✔</td>
</tr>
</tbody>
</table>

In-stent Restenosis
Jetstream Timeline

First commercially available Jetstream System from Pathway Medical
2008

Bayer Acquires Pathway Medical
2011

Boston Scientific Acquires Bayer Interventional and Jetstream System
2014
# JETSTREAM™ Atherectomy System

## System Evolution

Continuous innovation to support your success

<table>
<thead>
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</thead>
<tbody>
<tr>
<td><strong>JETSTREAM</strong></td>
<td><strong>JETSTREAM G2™</strong></td>
<td><strong>JETSTREAM G2 NXT</strong></td>
<td><strong>JETSTREAM G3™</strong></td>
<td><strong>JETSTREAM G3 GTI</strong></td>
<td><strong>JETSTREAM Navitus™</strong></td>
<td><strong>JETSTREAM Navitus™ L</strong></td>
<td><strong>JETSTREAM™ XC/SC</strong></td>
</tr>
</tbody>
</table>

1. First commercially available Pathway Medical product
2. Expandable blades
3. Aspiration port integrated into distal cutter
4. 8 F introducer sheath
5. Aspiration port moved proximal of cutting blades
6. Macerator added - 10% increase in aspiration efficiency
7. Approved for thrombectomy
8. Pelax outer shaft and stainless steel hypotube (reduced OD, compared to earlier generation designs)
9. 7 F compatibility
10. Increased ease of use/reliability (compared to JETSTREAM G3)
11. Increased torque (power)
12. 54% increase in differential cutting efficiency
13. 11% increase in aspiration efficiency
14. Robust Bushing and Distal Liner (same as GTI)
15. New liner over drive line
16. Improved distal bushing
17. Enhanced GW management
18. Improved User Interface
19. Largest JETSTREAM Catheter - 2.4 mm / 3.4 mm
20. 30% larger lumens
21. Shortened Coupler
22. Improved performance in tortuous anatomy
23. Navitus technology integrated
24. Identical liner and bushing technology
25. Guidewire management enhancements for smoother operation over the wire
26. Entire portfolio redesign
27. New ergonomic POD design
28. 32% smaller than previous
29. Redesigned user interface
30. Improved wire GARD simplifies wire management
31. New package and POD design reduces environmental footprint

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1. Compared to JETSTREAM G2 NXT in blades down during bench testing
2. Compared to JETSTREAM G2 NXT in bench testing
3. Data on file report: EV09-194

JETSTREAM™ Atherectomy System is manufactured and distributed in EU by Bayer Interventional

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Jetstream XC Catheters
Expandable-Blade Technology

2.1 / 3.0mm Catheter
(OTW, 135cm shaft)
- 2.1mm Blades-Down
- 3.0mm Blades-Up

2.4 / 3.4mm Catheter
(OTW, 120cm shaft)
- 2.4mm Blades-Down
- 3.4mm Blades-Up

Expandable-Blade Technology
Allows for sizing flexibility - Treat both the SFA & Popliteal with one catheter
JETSTREAM™ Atherectomy System

NOW WITH CE MARK FOR IN-STENT RESTENOSIS

Proven in Femoropopliteal ISR Lesions
Porcine overstretched injury model of Femoral Artery ISR

Partial overlapping stents, fully overlapping stents, Stent across branches

Stents fully expanded

Baseline MLD 1.6mm

2 Passes with BD MLD 2.1mm

4 Passes with BU MLD 2.9mm

JetStream ISR Feasibility Study

DESIGN: Prospective, feasibility registry at 2 US centers, evaluating JetStream XC atherectomy (JS) in treating Femoropopliteal in-stent restenosis (FP ISR)

OBJECTIVE: To evaluate efficacy and safety of JS with adjunctive PTA (JS+PTA) and assess stent-device interaction using Angiographic Core Lab adjudication

PRINCIPAL INVESTIGATOR
Nicolas W Shammas, MD, MS

SUBINVESTIGATOR
Subhash Banerjee, MD

Angiographic Core Laboratory
Beth Israel Deaconess Med Ctr
Jeffrey Popma, MD

29 patients (32 limbs) enrolled at 2 clinical sites between October 2012 and August 2014 in the United States

32 limbs crossed intraluminally/JS+PTA

Primary Efficacy/Safety endpoints at 1 mo (n=32)

Primary Safety endpoint and TLR at 6 months (n=27 pts; n=29 limbs)

Stent Integrity evaluation per core lab (n=24)

Secondary effectiveness endpoint TLR at 1 year (n=27 pts; n=29 limbs)

1 patient died (2 limbs)
1 patient withdrew (1 limb)
### Clinical and Angiographic Variables

<table>
<thead>
<tr>
<th>Demographic and Clinical</th>
<th>Angiographic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean) yrs</td>
<td>Treated length mm</td>
</tr>
<tr>
<td>Male</td>
<td>Lesion Diam. mm</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Run-off vessels</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>Stenosis Severity %</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Stenosis post JS %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Stenosis post PTA %</td>
</tr>
<tr>
<td>Current smoking</td>
<td><strong>TASC C/D</strong></td>
</tr>
<tr>
<td><strong>Prior index lesion ISR</strong></td>
<td>Blades Up run time min</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>Blades Down run time min</td>
</tr>
<tr>
<td><strong>Rutherford Category</strong></td>
<td>Treatment Interval min</td>
</tr>
<tr>
<td>0</td>
<td>JS XC 2.4</td>
</tr>
<tr>
<td>3</td>
<td>JS XC 2.1</td>
</tr>
<tr>
<td>4</td>
<td>Mean Volume Aspirate ml</td>
</tr>
<tr>
<td>5</td>
<td><strong>Lesions &gt; 30 cm/CTO</strong></td>
</tr>
<tr>
<td>On Aspirin</td>
<td>Stent Fracture 1&amp;2</td>
</tr>
<tr>
<td>On ADP-receptor antagonist</td>
<td></td>
</tr>
<tr>
<td>Age (mean) yrs</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>69.9</td>
</tr>
<tr>
<td>Male</td>
<td>37.9 %</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>82.8 %</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>41.4 %</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>89.7 %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>82.8 %</td>
</tr>
<tr>
<td>Current smoking</td>
<td>41.4 %</td>
</tr>
<tr>
<td><strong>Prior index lesion ISR</strong></td>
<td>66.0 %</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>48.3 %</td>
</tr>
<tr>
<td><strong>Rutherford Category</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6.3 %</td>
</tr>
<tr>
<td>3</td>
<td>65.6 %</td>
</tr>
<tr>
<td>4</td>
<td>12.5 %</td>
</tr>
<tr>
<td>5</td>
<td>15.6%</td>
</tr>
<tr>
<td>On Aspirin</td>
<td>90.6 %</td>
</tr>
<tr>
<td>On ADP-receptor antagonist</td>
<td>75 %</td>
</tr>
</tbody>
</table>
# Safety Endpoints: 30 d, 6 mo, 1 yr

|                                |            
|--------------------------------|------------
| TLR/TVR 30 days                | 0 %        
| Death 30 days                  | 0 %        
| Amputation 30 days             | 0 %        
| Death 6 months (non vascular)  | 3.4 %      
| Freedom from TLR 6 mo (not including intraprocedural bail out stenting as TLR) | 86.2 %      
| Freedom from TLR 6 mo (including intraprocedural bail out stenting as TLR) | 79.3 %      
| Patency 6 mo                   | 72 %       
| New Stent Fracture or Deformities (Core Lab) at 6 mo (n=24) | 0 %        
| Amputation 6 mo                | 0 %        
| Freedom from TLR 1 yr (bailout stent not TLR) | 58.6 %      
| Freedom from TLR 1 yr (bail out stent as TLR) | 48.3 %      

Freedom from TLR (censored) at 1 year (excluding bail out stenting as TLR)
FP ISR treatment: Summary of Data

Bail out stent not included as TLR
**JET-ISR Trial**

**Study Protocol Synopsis**

<table>
<thead>
<tr>
<th><strong>JET-ISR Trial</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective</strong></td>
</tr>
</tbody>
</table>
| **Primary Investigator** | Nicolas W Shammas, MD, MS, FACC, FSCAI  
                          Subhash Banerjee, MD, FACC, FSCAI |
| **Study Design**   | A prospective, multicenter, single arm study  
                          Comparator arm is historic data from plain old balloon angioplasty derived from a Meta-analysis of the 3 published randomized trials |
| **Subjects**       | • 140 subjects treated with JS+PTA |
| **Investigational Centers** | Up to 14 site in the U.S. |
| **Primary Efficacy Endpoint** | Target Lesion Revascularization (TLR) at 6 months  
                          • TLR defined as retreatment of the index lesion (extended 1 cm proximal and distal to the lesion) at 6 months  
                          For the primary endpoint, intra-procedural bail out stenting of the index lesion is considered meeting a TLR endpoint. (ITT analysis) |
| **Primary Safety Endpoint** | Major Adverse Events (MAE) at 30 days:  
                          • Unplanned amputation  
                          • Total mortality  
                          • TLR at 30 days (TLR includes bail out stenting) |
### JET-ISR Trial

#### Study Protocol Synopsis

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject presents with a Rutherford Classification of 2-4 and has symptoms of rest limb pain or claudication.</td>
<td>Diagnosed with chronic renal failure or has a creatinine level &gt; 2.5 mg/dl and is not on chronic dialysis.</td>
</tr>
<tr>
<td>Target lesion(s) must be viewed angiographically and have ≥50% stenosis.</td>
<td>Known allergy to heparin, ASA, Plavix.</td>
</tr>
<tr>
<td>The main target vessel reference diameter must be ≥ 5 mm and ≤ 7 mm</td>
<td>History of bleeding disorders or platelet count &lt; 80,000 cells/ml.</td>
</tr>
<tr>
<td>One patent distal run-off vessel with &lt;70% disease and with brisk flow is required.</td>
<td>Experiences ongoing cardiac problems (e.g., cardiac arrhythmias, congestive heart failure exacerbation, myocardial infarction, etc.) that, per the investigator, would not make the subject an ideal candidate for study procedures.</td>
</tr>
<tr>
<td>Intraluminal crossing of the lesion. If this is not certain, IVUS may be used to verify this per operator’s discretion</td>
<td>CVA or TIA within 4 weeks prior to JetStream procedure.</td>
</tr>
<tr>
<td>Patient has signed approved informed consent.</td>
<td>Anticipated life span of less than 12 months.</td>
</tr>
</tbody>
</table>

*Includes key inclusion and exclusion criteria only.*
JET-ISR Trial
Follow-up

Index Procedure
For all enrolled subjects

Predischarge Follow-up
Prior to discharge or within 5 days after index procedure

30-day Follow-up Visit
30-45 days after index procedure

6-Month Follow-up Visit
150-210 days after index procedure

12-Month Follow-up
320-410 days after index procedure
Summary

Complex lesions are best prepared with debulking prior to treatment with anti-proliferative technology with this strategy:

1. Less recoil, dissection or bail out stenting
2. Better MLA and likely better stent expansion if needed
3. Reduce calcium and thrombus burden. This will improve drug elution and make it more predictable. Early clinical data encouraging
4. Effective and safe for FP ISR based on the feasibility Jetstream ISR study.
Thank you
Hello again – Re-intervention strategies for sub-optimal results of current technologies

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Adjunct Clinical Associate Professor,
University of Iowa Hospitals
Interventional Cardiologist,
Cardiovascular Medicine, PC, Davenport, IA, USA