New (and Future) Device Update

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Relevant Conflicts of Interest

• Consultant, Speaker for W.L. Gore & Associates
Four interesting new devices

• Percutaneous Fem-pop Bypass – yes, really!

• New Twist to Renal Denervation – ditching RF?

• Percutaneous AV Fistula – not just for dialysis?

• A new Balloon Expandable Covered (Flexible) Stent
PQ Bypass – the DETOUR Procedure

- Treatment options for long SFA total occlusions are innumerable
  - Atherectomy devices: excimer laser, directional atherectomy “plaque excision” devices, rotational atherectomy, atherectomy devices with aspiration
  - Balloon angioplasty catheteres: POBA, Drug coated balloons, Nitinol caged balloons, scoring balloons, cutting balloons, cryoplasty, others
  - Bare metal stents, Drug-eluting stents, woven stents, covered stents

- Why are there so many? Everyone is chasing the gold standard – the surgical fem-pop bypass

- What if you could do a fem-pop bypass... without surgery???
The DETOUR Percutaneous Bypass Procedure
A Durable First-Line Endovascular Approach for Long, Complex, SFA Occlusions

- Designed to achieve the same end-result as open bypass surgery
- Revascularization via modular stent graft bypass using the femoral vein as a conduit
- Addresses the limitations of treating long, complex SFA lesions with a novel endovascular approach
PQ Bypass DETOUR Product Suite
Trio of proprietary devices designed specifically for the DETOUR procedure

- **PQ Stent Graft**: Self-expanding nitinol wire frame encapsulated in ePTFE
- **PQ Snare**: Over-the-wire dual-caged scaffold. Captures and extracts guidewires through the tibial vein
- **PQ Crossing Device**: Spring-loaded guidewire support and delivery system. Creates initial artery-vein-artery communication
Proximal Anastomosis

SFA   Vein

Crossing device creates anastomosis
Entry to cage

0.014” wire passing to vein
Distal Anastomosis

Crossing device creates anastomosis
Re-entry to artery

Popliteal a. Vein

~28cm
Modular Graft Deployments

Anastomosis PTA

Graft deployment
Baseline Venography
Baseline Angiography

RSFA
CTO
Creating Anastomoses

Proximal

Distal
Final Results - Arterial
Final Results - Venous
DETOUR I Trial

- Prospective, multi-center single arm trial (Europe)
- 59 patients treated at 7 centers
- Mean age 64, 83% male, 95% CTO’s, 93% TASC II-D
- Mean lesion length 28.6 cm
- 33% of patients treated previously with percutaneous revascularization or surgery
DETOUR I Trial

- High procedural and technical success rates of 96.7% and 98.3%

- 30 day MAE (death, TVR, and target limb amputation) = 3.4%

- Primary efficacy endpoint: 6-month primary patency rate = 84.7%

- Venous health was maintained at 6 months with no change on venous function scores as measured by Villalta and VCSS scales

- 94.7 percent achieved ≥1 improvement in Rutherford class at 6 months as compared to baseline (P<0.0001)
• DETOUR II Trial coming to U.S.!
Peregrine System for Renal Denervation
Re-Booting Renal Denervation

- Few technologies have excited and disappointed physicians as much as Renal Denervation for treatment of patients with refractory HTN.

- Early European trials demonstrated dramatic decreases in blood pressure in these difficult to treat patients following renal denervation with RF ablation -- procedure became popular and widely used in Europe.

- US Trial (SYMPLICITY-3) shocked the world by failing to show any benefit!

Many explanations considered
Too few “burns”
Not distal enough

Some companies focus on “multi-point” RF ablation while others develop alternative strategies to RF Ablation as means of achieving renal denervation.
Alcohol-mediated Renal Denervation

• Peregrine Device – designed to deploy three micro-needles through the renal arterial wall into the adventitial (peri-vascular) space

• Medical-grade alcohol (0.6 ml) injected through the micro-needles

• Alcohol diffuses circumferentially within the adventitial space resulting in nearly complete renal denervation
Alcohol-Mediated Denervation via Precise Nerve Targeting Offers Unique Efficacy/Safety Profile

Perivascular Sites Where Device Infuses Alcohol

Expanded View of Device Infusing Alcohol
Superiority of Peregrine (Alcohol) vs. Symplicity (RF) (Values Are Mean ± SD)^

Deeper Ablation Depth

*Both doses of alcohol p<0.05 vs. RF

The Most Distant Damaged Tissue (mm from G)

Greater Nerve Injury

Max injury

p<0.05 vs. RF
fp<0.05 vs. 0.30ml

Larger Ablation Area

Ablation Area (Section Containing Damage Within Adventitia), mm^2

*Both doses of alcohol p<0.05 vs. RF

Conclusion

Significant Superiority of Peregrine (Alcohol) vs. Symplicity (RF)

^Bertog et al, in preparation
**Symplicity (RF) vs. Peregrine (Alcohol):**
**Porcine Model Outcome at 3 Months**

**RF:**
- Modest Arc and Depth
- Nerve Injury + Medial Damage

- Ablation CSA - 4.3 mm$^2$
- Media Damage
- Ablation CSA - 11.4 mm$^2$

**Alcohol (0.6 ml):**
- Circumferential Nerve Injury Without Medial Damage
- Ablation CSA - 58.7 mm$^2$
- Media Healthy
- Ablation CSA - 46.3 mm$^2$

*Morphometry performed by Virmani, et al. CV Path*
3-Month EtOH Safety/Efficacy Evaluation: Angiographic and Neurochemical Follow-up (0.3 mL)

<table>
<thead>
<tr>
<th></th>
<th>Pre-Rx</th>
<th>Rx</th>
<th>3-Month Post-Rx</th>
<th>3-Month Post-Rx</th>
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<td>Angiography</td>
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<tr>
<td>Neurochemistry*</td>
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<td>Control (n=10)</td>
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<td>5637L (n=9)</td>
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<td><img src="chart2.png" alt="Bar Chart" /></td>
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- Mean (SD) Renal Tissue Noradrenaline (ng/g)
- *Control= 10 animals
  * Rx= 1 kidney, 6 measurements

↓ = 88%
Late Stenosis With RF: A Cause for Concern?

Persu, et al. Reporting 4/13 (31%) cases with RF with renal artery stenosis
First-In-Man Study

Unilateral procedure (n=5), followed by contralateral treatment 4 weeks later

Screening
N=19

Screen Failure
N=1*

Procedure
N=18

Patient Death
N=1**

30-Day
N=18

Patient Missed Office Visit
N=1***

6-Month
N=16

30-Day
N=18

*Subject (013) was consented but not eligible for treatment based on anatomical reasons (vessel > 8 mm diameter) as determined by the baseline angiogram.

**Subject (016) expired 9 weeks post procedure during hospitalization for small bowel obstruction with corrective surgery followed by septic shock.

***One subject declined to attend the office visit at 6-month.
First-Human-Use: Case Study

Baseline

Male, 51 yrs, 85 kg, 173cm

Medications
Baseline = 3  6 Month = 1

6 Months

SBP and DBP Reduction
From Baseline Through 6 Months (Office BP)

Baseline 6 Months

SDP  DBP
164  88  113  80

6 Months
Sustained OBP Lowering Despite Significant Reduction in Medication

Peregrine Study: FIM Average Meds – 3.4 (baseline) → 2.0 at 6-Months
Conclusions

- Renal denervation using alcohol delivered to the adventitial space using the novel Peregrine device appears both safe and efficacious in First-in-Man Trial

- Basic science studies indicate nearly 100% renal denervation without damage to the arterial wall; unlikely to provoke renal artery stenosis

- Procedure is entirely painless with short procedure times

- Further randomized clinical trials are required
“Transforming Vascular Access”

EverlinQ EndoAVF System for percutaneously creating AV Fistula

Initial application – Dialysis Fistula creation

Future applications…
# Challenges of Surgical AVF

## Clinical Outcomes

<table>
<thead>
<tr>
<th>Metric</th>
<th>Rate</th>
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<tbody>
<tr>
<td>Primary failure rate</td>
<td>1-4%</td>
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<tr>
<td>Mean maturation time</td>
<td>4-9 months</td>
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<tr>
<td>Average re-interventions</td>
<td>2-3</td>
</tr>
<tr>
<td>Occlusions (thrombosis)</td>
<td>17-25%</td>
</tr>
</tbody>
</table>

## Healthcare Delivery

- Surgical technique consistency
- Availability of AVF anatomical sites with adequate vessels
- Patient acceptance - surgical fatigue
- Cost of interventions & complications

## Significant Unmet Need

Peri-anastomotic stenosis is a primary failure mode of AVF¹

• 27% to 68% reported incidence of lesions at site of surgery as cause of failure¹

• Surgical manipulation of the vein is associated with fistula failure¹,²

From Bharat et al. JVS 2012;55(1):274-80

2. Roy-Chaudhury et al. JASN 2006;17:1112-27

Adapted from Proteon Therapeutics
The Endovascular AV Fistula

### Potential Advantages

**Endovascular AVF creation**
- Consistent hemodynamic anastomosis
- Minimal vessel trauma, torque or tension

**Clinical improvements**
- Low failure rates
- Few interventions
- Low complication rate

**Improved delivery of care**
- Additional anatomic option for patients
- Reproducible outcomes

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DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.

1. TVA Medical data on file. GLP Animal Studies.
3. TVA Medical data on file. NEAT Study Results at 12 months.
EndoAVF Procedure

Arterial Catheter Advanced to AVF Site
The endoAVF Provides an Additional Option for Creation of a Working Fistula

Cephalic, basilic and median cubital veins can be used for dialysis

Creation Sites
- Ulnar-ulnar or Radial-radial

No surgical scar or tissue trauma at site of anastomosis

1. TVA Medical data on file. GLP Animal Studies.
Multiple clinical studies support the endoAVF for hemodialysis

**Pilot Study**
**FLEX Study**
Feasibility and safety of using the everlinQ endoAVF system

**Design**
- Single-center, multi-operator, prospective study
- 33 patients, 4 sequential cohorts

**Key Outcomes**
- 97% Technical success
- 96% Maturation
- 96% 6-mo Patency

**Completed in 2014**

**Expanded Population**

**NEAT Study**
Safety and effectiveness of using the everlinQ endoAVF system

**Design**
- Multicenter, prospective in Canada, Australia and New Zealand
- 60 patients (+20 roll-in), single arm
- 1, 3, 6, & 12 month follow-up

**Key Outcomes**
- 98% Technical success
- 91% Maturation
- 84% 12-mo secondary patency
- 0.6 Intervention per patient-year

**Completed in 2016**
J Vasc Surg 2016; 63(6):7S
J Am Soc Nephrol 2016; 27:31A

**Next Generation Device**

**EASE Study**
Safety and efficacy of using the everlinQ 4 (4Fr)

**Design**
- Single center prospective study
- 32 patients
- 3 - 6 month follow-up

**Initiated in 2016**

**Expanded Population**

**endoAVF Study**
EU Post-Market Study
"Real world" multi-center study designed to continue building clinical evidence with everlinQ endoAVF

**Design**
- Multicenter, prospective study
- ~120 patients, single arm
- 1, 3, 6, & 12 month follow-up
- Includes radiocephalic AVF candidates

**Initiated in 2016**

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Future Application: Endovascular in Situ Tibial Bypass

Preclinical cadaveric feasibility study for endovascular tibial in situ bypass completed
Both 6F and new 4F catheter designs successfully studied
Viabahn VBX Stent Graft
Approved 1/27/17
Indication: Iliac Occlusive Disease
“Wish List” for a Covered Iliac Stent

• **DELIVERABILITY** -- Tortuous anatomy and severe disease

• **ACCURATE PLACEMENT, MULTIPLE LENGTHS** -- Ostial lesions require precise stent placement, multiple stent lengths (to avoid covering internal iliac artery) and no stent elongation or foreshortening

• **HIGH RADIAL STRENGTH, IMPERMEABLE GRAFT MATERIAL** -- Highly calcified vessels require stent with both great radial strength and impermeable graft material in the event of rupture

• **ADJUSTABLE DIAMETER, FLEXIBILITY** -- Tapered, tortuous vessel requires stent with both adjustable diameter and flexibility and conformability
Viabahn VBX Stent Graft Technology
Advanced Technology and Performance

Independent Stainless Steel Rings
• Independent rings for flexibility and conformability
• Minimizes foreshortening
• Provides high radial strength

Highly flexible stent and catheter
• Enables contralateral deployment
• Enables implanted conformability

Ultrathin PTFE balloon cover
• Improves stent retention and deliverability

Semi-compliant covered balloon
• Allows diameter customization

CBAS Heparin Surface
• Ensures lasting thromboresistance
### Available Configurations

<table>
<thead>
<tr>
<th>Stent Labeled / Nominal Diameter (mm)</th>
<th>Crimped Stent Length (mm)</th>
<th>Introducer Sheath Size (Fr)</th>
<th>Maximum Post-dilated Stent Diameter (mm)*</th>
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<tbody>
<tr>
<td>5</td>
<td>15, 19, 29, 39, 59, 79</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>15, 19, 29, 39, 59, 79</td>
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<td>7</td>
<td>16**</td>
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<td>59, 79</td>
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<tr>
<td>11</td>
<td>29, 39, 59, 79</td>
<td>8</td>
<td>16**</td>
</tr>
</tbody>
</table>

- 50% more length offerings compared to other BX stent grafts
- Lengths vary from 15 mm to 79 mm
- Stents can be post-dilated to larger diameters (3-4 mm over nominal)
- Maximum diameter with post-dilatation is 16 mm
| **Objective** | To evaluate the safety and efficacy of the VBX Stent Graft for the treatment of arterial occlusive disease in patients with *de novo* or restenotic lesions in the common and/or external iliac arteries |
| **Design** | Prospective, multicenter, single-arm study. Rutherford 2–4, unilateral or bilateral occlusive lesions in the common and/or external iliac arteries |
| **Eligibility Criteria** | Study procedures included:  
• Total occlusions, severe calcification, tortuous iliacs, kissing stent placement, direct stenting without predilatation |
| **Primary Endpoint** | Composite of the following major adverse events (MAE)  
• Device- or procedure-related death within 30 days  
• Myocardial infarction (MI) within 30 days  
• Target lesion revascularization (TLR) within nine months  
• Amputation above the metatarsals in the treated leg within nine months |
| **Key Secondary Endpoints** | • Primary patency  
• Freedom from target lesion revascularization (fTLR) |
| **Procedural Summary** | • 134 patients across 27 sites  
• 234 devices implanted in 213 lesions |
## Baseline Characteristics
### VBX FLEX Study

<table>
<thead>
<tr>
<th>Category</th>
<th>N = 134</th>
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</thead>
<tbody>
<tr>
<td>Category 2 – Moderate Claudication</td>
<td>26 (19.4%)</td>
</tr>
<tr>
<td>Category 3 – Severe Claudication</td>
<td>101 (75.4%)</td>
</tr>
<tr>
<td>Category 4 – Ischemic Rest Pain</td>
<td>7 (5.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>N = 134</th>
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<tbody>
<tr>
<td>Type A</td>
<td>50 (37.3%)</td>
</tr>
<tr>
<td>Type B</td>
<td>41 (30.6%)</td>
</tr>
<tr>
<td>Type C</td>
<td>32 (23.9%)</td>
</tr>
<tr>
<td>Type D</td>
<td>11 (8.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Access Approach</th>
<th>N = 134</th>
</tr>
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<tbody>
<tr>
<td>Ipsilateral</td>
<td>27 (20.1%)</td>
</tr>
<tr>
<td>Contralateral</td>
<td>24 (17.9%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>83 (61.9%)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Treated Limbs</th>
<th></th>
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<tbody>
<tr>
<td>Right</td>
<td>29 (21.6%)</td>
</tr>
<tr>
<td>Left</td>
<td>38 (28.4%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>67 (50.0%)</td>
</tr>
<tr>
<td>Kissing Stents</td>
<td>57 (42.5%)</td>
</tr>
</tbody>
</table>

**Technical Success**: 100%
Procedural Results -- VBX FLEX Study

100% restoration of lumen diameter
• $\leq 30\%$ residual stenosis due to high radial strength, even in highly calcified and non-compliant lesions

100% stent delivery
• All devices successfully delivered to and deployed at target site with no stent dislodgement

100% maintenance of stent length
• Median length change: 0 mm, pre-deployed to final implant

97% acute procedural success
• No device related serious adverse events
## Clinical Endpoints at Nine Months

### Primary Endpoint at Nine Months

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Count</th>
<th>Percentage</th>
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<tr>
<td>Composite MAE (N = 132 subjects) p &lt; .001*</td>
<td>3</td>
<td>2.3%</td>
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<tr>
<td>P-Value</td>
<td>&lt; .001*</td>
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<tr>
<td>Device or procedure related deaths within 30 days</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>MI within 30 days</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>TLRs within nine months</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Major amputations within nine months</td>
<td>3</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

### Kissing stent subgroup MAE (N = 57 subjects) p < .002*

<table>
<thead>
<tr>
<th>Count</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

### Additional Analyses at Nine Months

#### Primary patency**
(N = 157 lesions)
- TASC II C&D 95.3%
- External iliac 97.4%

#### fTLR**
(N = 157 lesions)
- 97.4%

#### Change in Rutherford from pre-procedure
(N = 112 subjects)
- Worsened 0.0%
- Maintained 5.4%
- Improved 94.6%
• The only balloon expandable stent graft:
  – Indicated to treat de novo and restenotic lesions in the iliac arteries, including the aortic bifurcation

• **Flexible strength of the device design:**
  – Variable diameter for tapering vessels
  – Ensures trackability in tortuous anatomies
  – Restores lumen diameter in highly calcified and non-compliant lesions

• Proven to achieve clinical success in complex lesions, including CTO’s, kissing stents, tortuous and highly calcified vessels
Thank you for your attention

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