Pros and Cons of IVUS Imaging in SFA and Popliteal Interventions

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• Abbott Vascular
• Medtronic
• Covidien
• Avinger
• Bard
• Volcano

Grant/Research Support:
• Avinger
• Bard
• Volcano
Intravascular Ultrasound (IVUS)

- Alternative Imaging technique
- Ultrasound Waves
- Computerized Real time images
- No Radiation
- Intraluminal Imaging over a guidewire
Pros of IVUS

- Measure Vessel Size— specifically when CT/MR not available
- Determine Plaque composition— Calcium
- Locate anatomical landmarks— Lesion length
- Contrast reduction
- Assist with placement of devices
- Completeness of therapy
- Look for unseen issues— Dissection
- ChromoFlo— Colorized blood flow— True/False Lumen
Cons of IVUS

- Additional Procedure time
- Cost
- Reimbursement
- Image quality and user interpretation
Considerations ??

• Does sizing matter?

• Is angiography alone enough?

• Does IVUS aid in Treatment Strategy?
Discussion

• VIPER Trial
  • GORE® VIABAHN® Endoprostheses With Heparin Bioactive Surface in the Treatment of SFA Obstructive Disease.

• SUPERB Trial
  • Comparison of the Supera® PERipheral System to a Performance Goal Derived From Balloon Angioplasty Clinical Trials in the Superficial Femoral Artery.

• Iida O, et. al. Study
  • Efficacy of Intravascular Ultrasound in Femoropopliteal Stenting for Peripheral Artery Disease With TASC II Class A to C Lesions.
Discussion-Continued

• UTOPIA Study
  • Single Center study evaluating the affects of adventitial cuts post atherectomy to restenosis rates

• DEFINITIVE AR Study
  • DEFINITIVE AR, a Multinational Pilot Study Evaluating the Effectiveness of Directional Atherectomy + Anti-Restenotic Therapy versus Drug Coated Balloon alone

• Conclusion
VIPER Trial – Why size matters

<table>
<thead>
<tr>
<th>Objective</th>
<th>Evaluate the performance of VIABAHN Endoprosthesis with Heparin Bioactive Surface (W.L. Gore, Inc.) in treating long-segment SFA disease (&gt; 5 cm in length)</th>
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</thead>
<tbody>
<tr>
<td>Design</td>
<td>Single-arm, Prospective, 12 U. S. sites, 120 patients</td>
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</table>
| Primary Endpoints | Primary patency at 12 months  
• No evidence of restenosis or occlusion within the originally treated lesion based on CDUS; PSVR < 2.5;  
• No angiographic evidence of stenosis > 50% when the CDUS was uninterpretable or unavailable or TVR performed  
Proportion of subjects experiencing major procedure related adverse events within 30 days of procedure |
| Secondary Endpoints | Primary assisted patency  
Secondary patency  
Device related major adverse events at 12 months |

The overall 1-year primary patency rate for complex lesions with a mean length of 19 cm was 73%.

The 1-year primary patency rate for devices that were not over sized (≤ 20%) relative to the proximal landing zone was 88%, significantly better than the 70% 1-year primary patency rate for devices that were oversized > 20% (P = .047).

Primary patency rate was 88% in the VIPER trial if the stent was sized $\leq 20\%$ relative to the proximal landing zone to the vessel.

In the VIPER Trial if the stent was oversized by more than 20% then the primary patency rate dropped to 70% ($P < 0.05$).

Per the investigators, “Most of the excessive over sizing in this trial resulted from operators’ overestimation of the diameter of the arterial lumen. To avoid this, clinicians may employ quantitative techniques to optimize stent graft treatment.”

"In order to improve the clinical results with endovascular approach in the superficial femoral artery, physicians must follow the instruction for use, Saxon said. If one uses quantitative means to size a vessel such as intravascular ultrasound or quantitative angiography and is careful to not oversize the endoprosthesis too much (<20% according to the instruction for use, I think ideally <10%) then, according to VIPER, one gets results that are over 20% better than if you do not follow these guidelines.”

Presented at Late Breaking Session at VIVA 2011

Richard Saxon, San Diego Cardiac and Vascular Institute, North County Radiology Medical Group in Oceanside, USA, principal investigator of the VIPER study

SUPERB TRIAL

Comparison of the Supera® PERipheral System to a Performance Goal Derived From Balloon Angioplasty Clinical Trials in the Superficial Femoral Artery
## SUPERB Trial

<table>
<thead>
<tr>
<th>Objective</th>
<th>Comparing percutaneous transluminal angioplasty (PTA) and primary stenting with the Supera® Peripheral Stent Systems to performance goals of PTA alone in the treatment of atherosclerotic lesions of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries.</th>
</tr>
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<tbody>
<tr>
<td>Design</td>
<td>Prospective, multicenter, non-randomized, un-blinded single arm clinical study</td>
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</table>
| Primary Endpoints | • The primary safety endpoint for the SUPERB SFA/PPA study was a composite of Major Adverse Events (MAEs) defined as all death, TLR or any amputation of the index limb to 30 days (±7 days).  
• The primary effectiveness endpoint for the SUPERB SFA/PPA study was primary stent patency rate at 12 months. Primary patency was defined as Peak Systolic Velocity (PSV) ratio < 2.0 at the stented target lesion assessed by duplex ultrasound (DUS) with no clinically-driven reintervention within the stented segment. |
SUPERB Trial-Results

12 month primary patency rate was 78.9%

- Due to the mechanical behavior of the woven Supera stent, the stent should not be oversized by more than 1 mm relative to the RVD.
- This ensures optimum deployment of the Supera stent, maximizing radial strength and assisting in accurate stent length deployment.

PMA P120020: FDA Summary of Safety and Effectiveness Data
Primary patency rate was 90.5% in the SUPERB trial if the stent was sized appropriately to the vessel.

If the stent was not sized appropriately in a 1:1 ratio then there was an increased rate of stent elongation and a drop in primary patency – from 74.4% to 57.7% ($P = 0.026$ to $p < 0.001$) depending on the amount of elongation.
Angiography alone is not enough

IVUS GUIDED STENT STUDIES
Efficacy of Intravascular Ultrasound in Femoropopliteal Stenting for Peripheral Artery Disease With TASC II Class A to C Lesions

- A retrospective review from 1198 limbs (965 patients) with TASC II A-C femoropopliteal lesions (28% CLI).
- Compared primary patency rates of IVUS vs. non-IVUS guided procedures in 234 propensity score matched pairs.
- Of the 1198 procedures, IVUS was used in 22% (n=268) and was more likely to be used in cases with more complicated femoropopliteal lesions (e.g., more severe TASC II class, longer lesion length, and narrower reference diameter).
- Analysis of the 234 propensity score-matched pairs (mean follow-up 1.9±1.5 years; 142 events) revealed that IVUS use was associated with:
  - Higher 5-year primary patency with IVUS than without (65%±6% vs. 35%±6%, p<0.001).
  - Significantly better assisted primary patency (p<0.001), secondary patency (p=0.004), freedom from any re-intervention (p<0.001), freedom from any adverse limb event (p<0.001), and event-free survival (p<0.001).

IVUS use was associated with a significantly higher primary patency rate than no IVUS use in TASC II class A-C femoropopliteal lesions (p<0.001 by log-rank test).

Angio Alone is Not Enough

90±2% Primary Patency at 1 year in IVUS Guided group

<table>
<thead>
<tr>
<th></th>
<th>0 yr</th>
<th>1 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVUS Use (-)</td>
<td>No. at risk</td>
<td>234</td>
</tr>
<tr>
<td>Rate ± SE</td>
<td>100±0%</td>
<td>72±3%</td>
</tr>
<tr>
<td>IVUS Use (+)</td>
<td>No. at risk</td>
<td>234</td>
</tr>
<tr>
<td>Rate ± SE</td>
<td>100±0%</td>
<td>90±2%</td>
</tr>
</tbody>
</table>

IVUS use was associated with a significantly higher primary patency rate than no IVUS use in TASC II class A-C femoropopliteal lesions (p<0.001 by log-rank test).

The group with IVUS use had a significantly higher rate of primary patency compared to the group without IVUS use.

These findings suggest a favorable impact of IVUS use on patency regarding femoropopliteal stenting.

IVUS use in femoropopliteal stenting might enable more accurate evaluation of vessel diameter and more appropriate stent selection according to vessel diameter prior to stenting.

IVUS May aid in treatment strategy
• **Background:** Although effective, directional atherectomy of lower extremity peripheral arterial disease (PAD) is limited by frequent restenosis. Histopathologic correlates of restenosis and the impact of deep cuts into the adventitial layer of the vessel wall on risk for restenosis is not known.

• **Methods:** The investigator conducted a prospective study of 102 patients with lower extremity peripheral arterial disease (PAD) undergoing directional atherectomy. The presence of adventitial cuts was determined by histopathologic analysis of atherectomy specimens. Restenosis was defined as greater than 60% stenosis by duplex ultrasound. Clinical follow-up with ultrasound was performed at 3, 9 and 12 months in all patients.

• **Results:** Adventitial cuts were identified in 55 (54%) of patients. Baseline demographic and clinical features were similar between groups. There were no differences in lesion length (59.6 ± 15.0 mm vs. 57.4 ± 16.9 mm, p=0.49) or vessel run-off (1.9 ± 0.65 vs. 1.9 ± 0.62, p=0.81) between patients with and without adventitial cuts, respectively. The overall one-year incidence of restenosis was 62% and was significantly higher in those with vs. without adventitial cuts (96.4% vs. 14.9%, p<0.001, Figure). Final results after independent vascular lab adjudication will also be presented.

• **Conclusions:** Vascular injury as assessed by adventitial cuts seen on at the time of atherectomy for lower extremity PAD was strongly related to risk for restenosis at one year.
UTOPIA Study Results

Cross-classification of adventitial cuts by histopathology and IVUS

<table>
<thead>
<tr>
<th>HISTOPATHOLOGY</th>
<th>IVUS</th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>46</td>
<td>14</td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>Positive</td>
<td>7</td>
<td>41</td>
<td></td>
<td>48</td>
</tr>
</tbody>
</table>

Sensitivity: 75%
Specificity: 87%
Positive Predictive Value: 85%
Negative Predictive Value: 77%

Adventitial cuts demonstrated a strong and significant association with restenosis at 3, 6 and 12 months.

IVUS demonstrated a modest, yet significant correlation with histopathology for detection of adventitial cuts.

Adventitial cuts were identified in 55 (54%) of the 102 patients studied.

Restenosis was common following extremity revascularization.

IVUS May aid in treatment strategy
# DEFINITIVE AR Study
(Multinational Pilot Study Evaluating the Effectiveness of Directional Atherectomy + Anti-Restenotic Therapy versus Drug Coated Balloon alone-DAART Technique)

<table>
<thead>
<tr>
<th>Objective</th>
<th>DEFINITIVE AR is a prospective, multicenter, randomized pilot study conducted in Europe to evaluate DAART (Directional Atherectomy + Paclitaxel-coated balloon) vs. DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>Prospective, randomized (DAART vs. DCB alone) and Registry arm to evaluate DAART in severely calcified lesions. 121 patients enrolled at 10 centers in Europe</td>
</tr>
<tr>
<td>Primary Endpoint</td>
<td>Percent stenosis at 12 months per Angiographic Core Lab assessment</td>
</tr>
</tbody>
</table>


DEFINITIVE AR Study-Results

Percent stenosis at 12 months

<table>
<thead>
<tr>
<th></th>
<th>DAART (n = 48)</th>
<th>DCB (n = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.6%</td>
<td>36.4%</td>
<td></td>
</tr>
</tbody>
</table>

**Long and Severely Calcified Lesions**

DEFINITIVE AR suggests added patency benefit of using DA in long lesions and severely calcified lesions.

**≤ 30% Residual Stenosis**

DEFINITIVE AR suggests improved patency when a higher volume of plaque is removed with DA prior to DCB.

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Lesions > 10 cm

<table>
<thead>
<tr>
<th></th>
<th>DAART</th>
<th>DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS Patency</td>
<td>96.8%</td>
<td>85.9%</td>
</tr>
<tr>
<td>Angiographic Patency</td>
<td>90.9%</td>
<td>68.8%</td>
</tr>
</tbody>
</table>

All Severely Calcified Lesions

<table>
<thead>
<tr>
<th></th>
<th>DAART</th>
<th>DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS Patency</td>
<td>70.4%</td>
<td>62.5%</td>
</tr>
<tr>
<td>Angiographic Patency</td>
<td>58.3%</td>
<td>42.9%</td>
</tr>
</tbody>
</table>

N=20  N=18  N=17  N=16


DEFINITIVE AR Study-Results

**Larger Lumen with DA**

DAART results in significantly larger MLD vs DCB following treatment.

<table>
<thead>
<tr>
<th></th>
<th>DAART Arm</th>
<th>DCB Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD</td>
<td>4.27</td>
<td>3.78</td>
</tr>
<tr>
<td>DCB</td>
<td>0.92</td>
<td>1.61</td>
</tr>
<tr>
<td>DA</td>
<td>2.16</td>
<td>1.39</td>
</tr>
<tr>
<td>Pre-Dilation</td>
<td>0.23</td>
<td>0.78</td>
</tr>
<tr>
<td>Baseline</td>
<td>0.96</td>
<td>0.78</td>
</tr>
</tbody>
</table>

\[ p = 0.045 \]

DEFINITIVE AR vs. CSI TRUTH^ Study

Larger MLD and lower residual stenosis rate with DAART may improve drug uptake.

- **COVIDIEN DEFINITIVE AR | DAART**
  - 4.27 mm MLD
  - Patency: 93%
  - Residual Stenosis: 17%

- **CSI TRUTH Study | OA+ + PTA**
  - 3.4 mm MLD
  - Patency: Not Reported
  - Residual Stenosis: 43%


DEFINITIVE AR Study-Key Takeaways

Significantly lower dissection rate and low bailout stent rate vs DCB alone

Added patency benefit in long and calcified lesions

Higher lumen gain results in improved 12-month patency

Conclusion

PRE-TREATMENT STRATEGY

Confirm Diameter of Treatment Area¹,²

Assess Plaque Morphology³

Assess Length of Stenosis¹,²

References:
## Conclusion

### POST TREATMENT IMAGING

<table>
<thead>
<tr>
<th>Assess Completeness of Treatment</th>
<th>Is the stent fully apposed?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Did I cover the area of interest?</td>
</tr>
<tr>
<td></td>
<td>Did I achieve the necessary luminal gain?</td>
</tr>
<tr>
<td></td>
<td>Did I cut into the adventitia?</td>
</tr>
</tbody>
</table>

Image Courtesy of Volcano Corporation
3 Key Messages

• **Sizing is Important to Clinical Outcomes**
  • VIPER Trial
  • SUPERB Trial

• **Angio Alone is Not Enough**\(^1,2,3\)
  • Are you appreciating the extent of disease?
  • Where is “normal to normal”?

• **Aid in Decision of Treatment Strategy**\(^1,3\)
  • What size and length stent?
  • Is there superficial calcium?
  • Did I cut into the adventitia during atherectomy?

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Closing Remarks / Thank You
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