Role of Atherectomy in Treatment of Complex Peripheral Vascular Disease

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INTERVENTIONAL CARDIOLOGIST
Faculty Disclosure

*Raghotham Patlola, MD*

For the 12 months preceding this CME activity, I disclose the following types of financial relationships:

- **Honoraria received from**: Spectranetics, Edwards, Medtronics
- **Consulted for**: None
- **Held common stock in**: Morris Innovative, RDN
- **Research, clinical trial, or drug study funds received from**: Medtronics, Spectranetics, Boston Scientific

I will not be discussing products that are investigational or not labeled for use under discussion.
Advance Age

- 40.3 million Americans (13%) are age 65 and above. This number will be more than double by 2050

Type I & Type II Diabetes

- 10.9 million Americans over the age of 65 (26.9%) have diabetes
- Diabetes is America’s fastest growing health problem

Kidney Disease

- 26 million Americans have kidney disease
- Diabetes is the leading cause of kidney disease

12%-14% of Americans with PAD

Which Patients Are more Likely to Benefit from Endovascular Intervention?

• Clinical guidelines remain vague regarding the absolute indications for and the appropriate use of revascularization strategies in patients with PAD.¹

• With improvements in endovascular techniques and equipment, the use of balloon angioplasty, stenting, and atherectomy has led to the application of endovascular revascularization to a wider range of patients over the past decade, both among those with more severe symptoms and those with less severe symptoms.¹

¹ Jones, WS. et al. Treatment Strategies for Patients With Peripheral Artery Disease Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 May. Report No.: 13-EHC090-EF. AHRQ Comparative Effectiveness Reviews.
In theory atherectomy enlarges the vascular lumen by removing tissue with little vessel stretching whereas balloon angioplasty and stenting have their predominant effect as a direct result of vessel stretching.
There are many atherectomy tools that have been utilized.

These are quite different from each other making an argument broadly supporting atherectomy difficult.

Various devices have different mechanisms of action, different effects on thrombus and plaque, require different skill sets and have different outcomes (particularly complications).
Atherectomy Devices

- Rotational
  - Diamondback (CSI)
  - Jetstream $G_2$ (Pathway Medical)
  - Rotoblator (Boston Scientific)
  - Slow speed rotational device (Bard)
- Excisional
  - Fox Hollow Silverhawk (Ev3)
  - PAC Pullback (Arrow)
- Ablative
  - Excimer Laser (Spectranetics)
Debulk: Removal of the Major Portion Composing a Lesion

**Orbital**
- Diamondback 360

**Directional**
- SilverHawk

**Rotational**
- Jetstream
- Rotablator

**Laser**
- Laser
PAD Plaque Morphology: IVUS

**Homogenous**  **Heterogeneous**  **Calcific**

or a combination such as CTOs
## Reasons for Using Atherectomy “What We Think We Know”

### Homogenous
- Decrease the risk of emboli
- Increase the size of the lumen
- Prevent cheese-grating the stent

### Heterogeneous
- Reduce elastic recoil
- Increase the size of the lumen
- Prevent dissection
- Optimize stent
  - Apposition
  - Expansion

### Calcific
- Reduce elastic recoil
- Increase the size of the lumen
- Prevent dissection
- Reduce stent fracture
- Optimize stent
  - Apposition
  - Expansion

---

2. JACC. 2005;45: 312-315.

*Filter with Thrombus*
Factors considered in determining any type intervention

- Probability of short and long term success
- Risk of short term and long term complications
- Cost (Short and long term)
- Will the intervention limit future therapeutic options
Factors Affecting Therapeutic Choices

- Lesion location
- Lesion length
- Lesion Morphology
- De novo versus restenosis versus graft versus instent restenosis
- Stenosis versus occlusion
- Associated thrombus
- Runoff Status
- Age of patient
Atherectomy: Why and Where

- Non-stentable Locations
- Limiting adjunctive Therapy
SFA and Popliteal Arteries are a Challenge to Intervention

- PTA associated with high restenosis rate.
- Multiple stent trials have shown nitinol tubular stents to be superior to PTA on a relatively short term basis in relatively short lesions. Long term data are lacking and there is little data on the popliteal artery.
- Stent patency falls dramatically during extended follow up. Stent fractures are common.

Martin Schillinger, MD, et al, NEJ May 4, 2006
Sirocco, Stephan H. Duda, MD et al J Endovasc Ther, 2006
RESILIENT Trial
Known SFA Nitinol Tubular Stent Complications Include

- Kinking
- Stent fracture
  - Occlusion
  - Pseudoaneurysm
  - Restenosis
Stent Fracture

- Type I
- Type II
- Type III
- Type IV
Clinical Relevance of Stent-Fractures

Scheinert et al. – TCT 2007
Known SFA Nitinol Tubular Stent Complications Include

- Kinking
- Stent fracture
  - Occlusion
  - Pseudoaneurysm
  - Restenosis
- Insufficient radial force to expand vessel
Insufficient Radial Force
CSI Orbital Atherectomy System (OAS)

Crown

- Diamond grit coated
- Creates lumen 1.75x greater than crossing profile
Mechanism of Action: Differential Sanding

Speed = Lumen Size

- Increased speed and/or increased mass increase the centrifugal force
- Greater centrifugal force creates bigger lumens

\[ \text{CF} = \text{mass} \times \text{rotational speed}^2 \]

radius of the orbit

1.9mm crown at 80k RPM's

1.9mm crown at 200k RPM's
Diamondback 360 Particulate

5 studies, 37 experiments
(Carbon blocks; Porcine coronary artery; Diseased cadaver peripheral arteries)

Diamondback360 Particulate Distribution
Mean particle size: 2.3 um (± .1 um) (99.95% CI)
Rotablator Particulate Distribution  Mean particle size 7.0um
93.14% < Red Blood Cell Diameter (99% CI)
99.3% < Capillary Diameter (99% CI)
99.97% < 30 um (theoretically the smallest protection device)
Orbital Atherectomy System (OAS)

Diamond Coated

Excellent in Calcified Vessels
ESRD CLI
Heavy Calcium
Patent SFA
Severe Infrapopliteal Disease

Calcium
ESRD CLI
Heavy Calcium
Patent SFA
Severe Infrapopliteal Disease
ESRD CLI
Heavy Calcium
Patent SFA
Severe Infrapopliteal Disease

PTA CTO
Peroneal
90 % Stenosis
Excellent Proximal Peroneal Results
CSI Orbital Atherectomy Device (Distal Lesion)

Calcium
Excellent Distal Peroneal Results
AT CLI Case. 4mm AT 95% lesion with single vessel runoff. Spun 2.0 classic l/m/h for 1:46, 4mm postdil at 2 atm, 0% residual
Distal Popliteal Lesion. DB 1.75 for 2:10, 4mm postdilation, 3 vessel runoff
Ostial Calcific PT.
DB 1.75 for 3:35, no adjunct, minimal residual
PRE & POST DIAMONDBACK OF POSTERIOR TIBIAL ARTERY (NO ADJUNCT)
PRE & POST DIAMONDBACK OF POSTERIOR TIBIAL ARTERY
PRE & POST DIAMONDBACK PERONEAL (PROXIMAL) NO ADJUNCT THERAPY
Superficial Femoral Artery Treatment

Homogenous plaque: stent restenosis

Postatherectomy and balloon angioplasty

SFA

No emboli
Superficial Femoral Artery Treatment

Heterogeneous plaque: stenting without atherectomy

Calcific plaque: stenting with atherectomy
“What We Know”
Review of Atherectomy Clinical Data

Directional  Rotational  Laser  Orbital
### Which Patients Benefit from Mechanical Debunking?

#### Clinical Data

<table>
<thead>
<tr>
<th>Atherectomy</th>
<th>Study</th>
<th>Inclusion Criteria</th>
<th>Demographics</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser</td>
<td>CELLO (65 pts) (multicenter, prospective registry)</td>
<td>SFA/popliteal Rutherford 1-3 1 patent tibial</td>
<td>Age (Mean) = 68 60% Male 40% DM Curr smoker 43%</td>
<td>12% laser alone 65% laser + PTA 23% laser+ STENT Patency: 59% (6 months) 54% (12 months) TLR 23.1% (12 months)</td>
</tr>
<tr>
<td></td>
<td>LACI (145 pts;155 limbs) (multicenter, prospective registry)</td>
<td>SFA-tibial Rutherford 4-6 1 patent tibial</td>
<td>Age (Mean) = 72 53% Male 66% DM Curr smoker 14%</td>
<td>4% laser alone 51% laser + PTA 45% laser + stent 92% CTO 92% 6 month limb salvage</td>
</tr>
<tr>
<td></td>
<td>PATENT (90 pts) (multicenter, prospective registry)</td>
<td>In-stent restenosis SFA/popliteal Rutherford 2-5</td>
<td>50% DM</td>
<td>34% CTO 18% TLR (6 month) 48% TLR (12 month)</td>
</tr>
</tbody>
</table>


_Zeller T. Photo Ablation Using the Turbo-Booster and the Excimer Laser for In-Stent Restenosis Treatment (PATENT). LINC 2013._
<table>
<thead>
<tr>
<th>Atherectomy</th>
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<tbody>
<tr>
<td>Directional</td>
<td>Definitive LE (800 pts) (multicenter, prospective registry) **</td>
<td>SFA-tibial stenosis Rutherford 1-6</td>
<td>Age (Mean) = 70</td>
<td>1 year patency:</td>
</tr>
<tr>
<td></td>
<td>Largest independently adjudicated study for peripheral atherectomy</td>
<td>Exclusion: Severe Ca, in-stent restenosis, or aneurysm</td>
<td>55% Male 52% DM 49% Smoker 18% Renal insuff</td>
<td>83% SFA 78% infrapopliteal Embolization rate 1.6% No significant differences in patency at 1 year between DM and non-DM 77% patency DM 78% patency non-DM</td>
</tr>
<tr>
<td>Rotational</td>
<td>True (18 pts) (Single-center prospective registry) Rotational plus aspiration</td>
<td>SFA-tibial stenosis Rutherford 1-6</td>
<td>Age (Mean) = 70</td>
<td>6-month TLR 11% 12-month TLR 11% No emboli reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exclusion: In-stent</td>
<td>67% Male 44% DM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13 SFA stenosis 2 SFA/Pop stenosis 2 Pop stenosis 1 Tibial stenosis</td>
<td></td>
</tr>
<tr>
<td>CRAG (79 pts)</td>
<td>CRAG (79 pts) (multicenter, prospective registry)</td>
<td>Iliac-tibial stenosis Rutherford 1-6</td>
<td>Age (Mean) = 69</td>
<td>77% technical success rate 50% complication rate 50% requiring urgent/ emergent surgical procedure 6 amputations as result of complication 2-year patency 18.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>67% Male</td>
<td></td>
</tr>
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## Which Patients Benefit from Mechanical Debulking? Clinical Data

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<th>Atherectomy</th>
<th>Study</th>
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</table>
| Orbital         | Compliance (50 pts) *(multicenter, prospective randomized)*            | SF Hospital  
Calcified  
Rutherford 2.4                                                                 | 12-month freedom from bail out stent: TLR or restenosis:  
Atherectomy + PTA = 74%  
PTA alone = 76.2%  
Bail out stenting:  
Atherectomy + PTA = 8.0%  
PTA alone = 84.0% |
| Atherectomy + PTA vs PTA alone |                                                                     |                                                                                     |                                                                        |
| Calcium         | (50 pts) *(multicenter, prospective randomized)*                       | Intrapoplital  
Rutherford 4-6  
1 patent tibial                                                                 | 12-month TVR:  
Atherectomy + PTA = 6.7%  
PTA alone = 20%  
12-month bail out stenting:  
Atherectomy + PTA = 6.9%  
PTA alone = 14.3% |
| Confirm         | (3135 pts) *(multicenter, prospective registry)*                       | All-comers                                                                          | Claudiaic arm *(n=1721; 55%)*  
81% with moderate to severe Ca  
Complications included: flow-limiting dissection 1.8%, perforation 0.6%, embolization 1.8%, thrombus 1.1%  
CLI arm *(n=1340; 42.7%)*  
85.7% with moderate to severe Ca  
Complications included: flow-limiting dissection 1.2%, perforation 0.8%, embolization 2.1%, thrombus 1.4% |
When Should Atherectomy Be a Stand-Alone Therapy?

From the data presented to date, atherectomy is rarely utilized as a sole therapy.

The question should be… what other modalities should be added to atherectomy to improve outcomes?

“What We Hope to Know”
"What We Hope to Know"

<table>
<thead>
<tr>
<th>Atherectomy</th>
<th>Study</th>
<th>Inclusion Criteria</th>
<th>Primary Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser</td>
<td>PHOTOPAC (50 pts) (multicenter, prospective registry) – laser followed by a Paclitaxel drug-coated balloon</td>
<td>In-stent restenosis SFA/popliteal</td>
<td>Target lesion % stenosis at 1 year</td>
</tr>
<tr>
<td>Directional</td>
<td>DefinitiveAR (125 pts; 100 patients randomized to DEB vs DEB and atherectomy and 25 patients with severe Ca enrolled in a registry) (multicenter, prospective randomized study)</td>
<td>Rutherford 2-4</td>
<td>Target lesion stenosis at 1 year</td>
</tr>
</tbody>
</table>
In-Stent Restenosis

WHAT IS APPROVED BY FDA!!
GLOBAL PAD/ISR SCOPE OF PROBLEM

>200M People Living with PAD Globally
<2% Treated Surgically or Endovascularly

>400,000 FemPop Stents Implanted WW Every Year

250,000 ISR Cases

U.S. ISR Incidence
• >200,000 Stents / Year implanted
• Stent volume growing 6-7% annually
• 30-40% 1st time ISR Incidence within 2 years of implant
• ~65% of ISR will recur post-PTA treatment within 2 years

115,000 US ISR Cases
EXCITE ISR Trial

Design

• DESIGN: Prospective, randomized, multi-center clinical evaluation of excimer laser atherectomy (ELA)

• OBJECTIVE: To evaluate safety and efficacy of ELA with adjunctive PTA (ELA+PTA) versus PTA alone for treating femoropopliteal in-stent restenosis

• PRINCIPAL INVESTIGATORS
  Eric J Dippel, MD
  Craig Walker, MD

250 patients enrolled between June 2011 and February 2014 in 40 clinical sites in United States

250 lesions crossable by guidewire

- 7 lesions uncrossable

169 ELA + PTA

Primary Safety endpoint at 37 days (n=155)

Primary Efficacy endpoint at 212 days (n=117)

81 PTA

Primary Safety endpoint at 37 days (n=73)

Primary Efficacy endpoint at 212 days (n=56)
Excimer Laser Atherectomy Catheters

- Turbo Elite → Pilot channel creation
- Turbo Tandem → Biased laser catheter for large lumen ablation
“Real World” Patients

Key Inclusion Criteria
- ISR lesion ≥ 4 cm
- Rutherford classification 1-4
- RVD ≥ 5.0 mm and ≤ 7.0 mm
- ≥ 1 patent tibial artery

Key Exclusion Criteria
- Target lesion extends >3 cm beyond stent margin
- Untreated inflow lesion
- Grade 4 or 5 stent fracture

Follow-up
- Discharge, 30 days, 6 months and 1 year post-procedure

- No lesion length limit
- Multiple stents allowed
- Common stent fractures (Grades 1-3)
- Popliteal stents included
Procedural Complications

- Procedural TLR: 5.3% vs 2.4% (P=0.008)
- Any Dissection: 16.0% vs 7.7% (P=0.03)
- > Grade C: 7.4% vs 2.4% (P=0.08)
- Bailout Stenting: 4.1% vs 8.3% (P=0.02)
- Embolization: 4.9% vs 0.6% (P=0.47)
- Thrombosis: 2.5% vs 1.2% (P=0.25)
- Abrupt Closure: 0.0% vs 1.2% (P=0.23)
Primary Safety Endpoint

*Freedom from MAE thru 30 days*

![Bar chart showing primary safety endpoint](chart.png)

- **ITT**: ELA + PTA (94.2%) vs PTA (79.2%) with a *P* value of *<0.001*.
- **ITT w/o Bailout Stenting as TLR**: ELA + PTA (98.7%) vs PTA (91.8%) with a *P* value of *0.01*.
- **Per protocol**: ELA + PTA (95.3%) vs PTA (82.0%) with a *P* value of *0.003*.
Primary Efficacy Endpoint

*Freedom from TLR thru 6 months*

<table>
<thead>
<tr>
<th></th>
<th>ELA + PTA</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT</td>
<td>73.5%</td>
<td>51.8%</td>
</tr>
<tr>
<td>ITT w/o Bailout Stenting as TLR</td>
<td>78.1%</td>
<td>61.7%</td>
</tr>
<tr>
<td>Per protocol</td>
<td>78.8%</td>
<td>46.7%</td>
</tr>
</tbody>
</table>

*P < 0.005* for ITT, *P < 0.05* for ITT w/o Bailout Stenting as TLR, *P < 0.001* for Per protocol
Survival Probability

Product-Limit Survival Estimates
With number of subjects at risk

$p < 0.003$

Internal Field - randomization group:
1: Excimer Laser Atherectomy + PTA
2: PTA Alone

Days from Index Procedure
Primary Patency

Product-Limit Survival Estimates
With number of subjects at risk

$p < 0.005$

Internal Field - randomization group:
1: Excimer Laser Atherectomy + PTA
2: PTA Alone

Days from Index Procedure
Survival Probability

Number of subjects at risk:
0 160 120 53 32 17
1 61 42 16 8 5
2

Survival Probability
Freedom from MAE

Product-Limit Survival Estimates
With number of subjects at risk

$p < 0.001$
Conclusions

- ELA with adjunctive PTA treatment of ISR is superior to PTA alone for the treatment of femoropopliteal ISR:
  - Complicated lesions averaging 19 cm in length
  - Significantly higher procedural success rate (ELA 93.5% vs PTA alone 82.7%, P=0.02)
  - Significantly higher safety rate (freedom from MAE: ELA 94.2% vs. PTA alone 79.2%, P<0.001)
  - Significantly lower rate of TLR for ELA throughout study

- 1st FDA approved IDE randomized control study demonstrating the benefits of atherectomy in the lower extremities

- ELA with PTA should be considered the standard care for femoropopliteal ISR
CONCLUSIONS - Atherectomy

- Atherectomy is an essential therapeutic tool in PAD.
- Present atherectomy devices have their own niche role.
- Select device based on Experience, patient and lesion characteristics.
- Benefits of Atherectomy not proven: Need good, large atherectomy trials (difficult task !!)
- Nothing approved for ISR
- Potential use of Atherectomy and DEB combo needs evaluation !!