Brachytherapy For Severe Or Extensive ISR: It Is Still A Viable Treatment Option For A Difficult Problem: Advantages And Limitations

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HISTORICAL BACKGROUND

> Initial clinical benefit of brachytherapy for ISR of coronary stents was shown in several trials
  > Gamma 1, Wrist, Long Wrist, Inhibit

> Further application was studied in de novo lesions in the peripheral circulation
  > Vienna and Paris studies

EFFECTIVENESS OF TREATMENTS FOR ISR IN FEMOROPOPILATEAL ARTERY

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Primary patency 6 months</th>
<th>Primary patency 1 year</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat balloon angioplasty</td>
<td>27%</td>
<td>--</td>
<td>Dick et al. Radiology 2008</td>
</tr>
<tr>
<td>Cutting balloon angioplasty</td>
<td>35%</td>
<td>--</td>
<td>Dick et al. Radiology 2008</td>
</tr>
<tr>
<td>Cryoplasty</td>
<td>50%</td>
<td>28%</td>
<td>Kurfürst et al. EVS 2007</td>
</tr>
<tr>
<td>Directional atherectomy</td>
<td>--</td>
<td>50%</td>
<td>Zeller et al. JACC 2008</td>
</tr>
<tr>
<td>Laser atherectomy and stent-graft</td>
<td>--</td>
<td>48%</td>
<td>Lard et al. Card Cath Int 2011</td>
</tr>
<tr>
<td>PTA, laser, or excisional atherectomy</td>
<td>55%</td>
<td>47.6%</td>
<td>Yeo et al. Card Cath Int 2011</td>
</tr>
<tr>
<td>PTA+EBT</td>
<td>90%</td>
<td>79.8%</td>
<td>Vienna 4 (2007)</td>
</tr>
<tr>
<td></td>
<td>90%</td>
<td>79.8%</td>
<td>Leipzig 2012</td>
</tr>
</tbody>
</table>

BRACHYTHERAPY IN THE LOWER EXTREMITY: VIENNA-2

- 90 patients, symptomatic ISR
- Beta-emitting isotope, 13 gray
- 25 cm average lesion length
- Patency: >50% restenosis by duplex
- 80% 1 year patency
**Failure points of prior EVBT studies**

**EDGE RESTENOSIS**
- Restenosis adjacent to the proximal and distal edges of the implanted stent (“edge effect” or “candy wrapper” phenomenon)

**Key features:**
- Higher radiation dose (20 gray)
- 2 cm “safety margins” of radiation coverage proximal and distal to angioplastied/stented area
- Customized treatment depth: a.gmn + radius of largest PTA balloon

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**Methods**

- Retrospective, single-center review of 43 cases of EVBT for lower extremity ISR at Brigham and Women’s Hospital between 2004-2012
- Stents undergo duplex ultrasound surveillance for recurrent ISR at 1, 3, 6, 9, 12, and 18 months and then yearly
- Primary endpoint: stent patency at 1 and 2 years
  - Stent patency: freedom from ≥ 50% recurrent stenosis by duplex ultrasound

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**Patient cohort**

<table>
<thead>
<tr>
<th>Stent location</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iliac artery</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>Superficial femoral artery</td>
<td>26 (62%)</td>
</tr>
<tr>
<td>Popliteal artery</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Combined SFA/popliteal segments</td>
<td>5 (12%)</td>
</tr>
</tbody>
</table>

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**Brachytherapy Catheter**

**Catheter placement**

- SFA in-stent restenosis before PTA
- Calibrated dummy strand for EVBT planning
- SFA in-stent restenosis after PTA
Indications for Brachytherapy

Claudication
Critical stenosis on duplex
Critical limb ischemia

50%  41%  9%

Technical details

Mean EVBT treated length 24 ±13 cm

Additional stent placement 10 (31%)

Outcomes

- **Recurrent ISR (50-99% stenosis):** 8/42 (19%)
  - Mean time to recurrent ISR: 505 ± 348 days
  - In-stent recurrence: 4/8
  - In-segment recurrence: 4/8

- **Early thrombotic occlusion:** 2/42 (5%)
  - Time to occlusion: 1 day, 26 days

- **Death:** 1 (acute coronary syndrome)

Patency

<table>
<thead>
<tr>
<th>Time after EVBT</th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>88%</td>
<td>77%</td>
<td>64%</td>
</tr>
<tr>
<td>Primary assisted patency</td>
<td>92%</td>
<td>89%</td>
<td>81%</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>92%</td>
<td>89%</td>
<td>80%</td>
</tr>
</tbody>
</table>

2-year Patency

<table>
<thead>
<tr>
<th>Time after EVBT</th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>87%</td>
<td>79%</td>
<td>67%</td>
</tr>
<tr>
<td>Primary assisted patency</td>
<td>90%</td>
<td>85%</td>
<td>77%</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>90%</td>
<td>85%</td>
<td>85%</td>
</tr>
</tbody>
</table>
Methods

- Retrospective review of consecutive patients who underwent brachytherapy for angiographically proven in-stent restenosis, thrombosis, or occlusion
- 2003 to 2010, Brigham and Women’s Hospital
- 42 lower extremities lesions in 32 patients
- Dose 20 gray
- Patient follow-up duration has been 5 years

Index lesion characteristics

<table>
<thead>
<tr>
<th>Index Lesion</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mean, range)</td>
<td>266, 40-480 mm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Index intervention</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iliac</td>
<td>24%</td>
</tr>
<tr>
<td>SFA</td>
<td>76%</td>
</tr>
<tr>
<td>Popliteal</td>
<td>2%</td>
</tr>
</tbody>
</table>

Brachytherapy characteristics

<table>
<thead>
<tr>
<th>Brachytherapy Indication</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claudication</td>
<td>95%</td>
</tr>
<tr>
<td>Critical limb ischemia</td>
<td>2.5%</td>
</tr>
<tr>
<td>Ultrasound (high grade stenosis, no symptoms)</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

Results

- Average improvement in ABIs: 0.35 (.03 to 0.8)

Overall freedom from Target Vessel Re-intervention by Kaplan-Meier estimates:
  - 100% at 1 year
  - 97% at 2 years
  - 74% at 5 years

Target vessel revascularization

<table>
<thead>
<tr>
<th>Event</th>
<th>Occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late stent thrombosis</td>
<td>2/5</td>
</tr>
<tr>
<td>Restenosis</td>
<td>1/5</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
<td>1/5</td>
</tr>
<tr>
<td>Total occlusion</td>
<td>1/5</td>
</tr>
</tbody>
</table>

Note: All cases presented with claudication
5-year Freedom from TVR

Advantages

- It works!
- Can be used in all vessels
  - renal, iliac, femoral, tibial
- Minimal additional time (30 minutes)
- Safe

Limitations

- Small, single-center, retrospective cohort study
- Logistic challenges to general applicability
- Need close collaboration between endotherapist and dedicated radiation therapist
- Procedural planning
- Trained staff

Conclusion

Endovascular brachytherapy is an effective and safe adjunctive option in patients with symptomatic lower extremity in-stent restenosis.