Atherectomy Prior to Drug-Eluting–Balloon Angioplasty in a Calcified Vessel

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ABSTRACT: Endovascular treatment options for peripheral arterial disease of the lower extremity include percutaneous transluminal angioplasty, stent implantation, and atherectomy. Drug-eluting balloons (DEB) show promise in reducing long-term restenosis and target lesion revascularization rates by limiting postprocedural neointimal hyperplasia. However, dense calcification is thought to act as a barrier to successful deposition of antiproliferative drug. Atherectomy prior to DEB angioplasty is one approach to reduce mural calcification and improve the efficacy of drug delivery.

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Endovascular treatment options for peripheral arterial disease (PAD) of the lower extremity include percutaneous transluminal angioplasty (PTA), stent placement, and atherectomy. However, PTA alone with or without stenting is associated with a significant risk of restenosis. Conventional PTA of femoropopliteal lesions is associated with a restenosis rate of 40% to 60% at 1 year. This is thought to be a result of vessel trauma, as PTA relies of vessel wall stretching and eccentric plaque fracture. Atherectomy may debulk atherosclerotic lesions but still results in late neointimal hyperplasia, possibly related to additional mechanisms of vessel injury during intervention. Drug-eluting technologies, such as drug-eluting balloons (DEB) and drug-eluting stents (DES) reduce neointimal hyperplasia via the deposition of antiproliferative drug into the medial layer of the treated artery. However, dense atherosclerotic calcification limits mural drug deposition and probably reduces the resulting antiproliferative effect. Vessel preparation with atherectomy prior to DEB angioplasty may have a role in debulking calcific plaque and hence improving effective drug deposition. Herein, we describe our preferred method for vessel preparation with rotational atherectomy prior to DEB angioplasty in heavily calcified vessels.

CASE EXAMPLE
A 55-year-old male with coronary artery disease, peripheral vascular disease, and history of left lower
extremity revascularization presented with disabling right lower-extremity claudication (one-half block). Antegrade access was obtained in the right common femoral artery and a long 7 Fr sheath was placed. Right lower-extremity angiography revealed occlusion of the mid right superficial femoral artery (SFA) with distal reconstitution via collaterals at the right popliteal artery and patent 3-vessel runoff to the foot (Figure 1A and 1B). Parallel linear opacities were noted along the expected course of the distal SFA that were compatible with eccentric calcified plaque. Intra-arterial heparin was administered. A 0.014"
wire was used to cross the long segment occlusion, over which a crossing catheter was advanced, and the crossing wire was replaced with a stiff support microwire (Figure 1C). A rotational atherectomy catheter with active aspiration (Jetstream Atherectomy System, Boston Scientific) was advanced to the level of the occlusion. One-pass atherectomy was performed in the blades-down position, followed by an additional pass in the blades-up position (Figure 1D).

Angiography was repeated through the sheath and revealed improved flow through the previously occluded segment. A 4 mm balloon was used to predilate along the length of the SFA and popliteal artery (Figure 1E). A 6 mm x 120 mm IN.PACT Admiral DEB (Medtronic) was advanced over the wire to the popliteal artery, and distal SFA and inflation was maintained for approximately 3 minutes. The process was repeated with 2 additional DEBs more proximally to the level of the mid SFA (Figure 1F). Final digital subtraction angiography revealed a patent treated vessel and the procedure was terminated.

**DISCUSSION**

Given the perceived advantages of drug-eluting technologies in maintaining long-term vessel patency, our preference is to utilize DEB and DES when feasible. Long-segment steno-occlusive disease of the femoropopliteal axis poses challenges to both approaches. Stents are avoided in long segments and at stress points unless persistent significant stenosis or flow-limiting dissection is seen post angioplasty. Our approach with heavily calcified vessels that would otherwise benefit from DEB angioplasty is to pretreat the vessel with a rotational or orbital atherectomy system to debulk eccentric calcium and improve drug delivery. Following atherectomy, the native lesion is treated as with standard DEB angioplasty: predilatation is performed 1 mm to 2 mm undersized to the reference vessel diameter, and the DEB is sized equivalent to the reference vessel diameter and kept inflated for 1-3 minutes. When the treated lesion length exceeds the length of the DEB, 1 cm to 2 cm of overlap is obtained with subsequent balloons.

Paclitaxel selectively inhibits arterial smooth muscle cell proliferation and the ensuing deposition of extracellular matrix, which otherwise contribute to neointimal hyperplasia following endovascular intervention. DeB delivery of paclitaxel is dependent on successful penetration and deposition of antiproliferative drug into the medial layer of the target artery.

### Table 1: Randomized Controlled Trials Evaluating Drug-Eluting Balloons

<table>
<thead>
<tr>
<th>Trial</th>
<th>Enrollment Dates</th>
<th>Number of Patients</th>
<th>Lesion Location</th>
<th>Drug-Eluting Balloon Type</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>THUNDER13</td>
<td>2004-2005</td>
<td>102</td>
<td>Femoropopliteal</td>
<td>Standard balloon, paclitaxel-coated</td>
<td></td>
</tr>
<tr>
<td>Werk et al (Berlin and Greibswald Registry)14</td>
<td>2004-2006</td>
<td>87</td>
<td>Femoropopliteal</td>
<td>Standard balloon, paclitaxel-coated</td>
<td></td>
</tr>
<tr>
<td>LEVANT 15</td>
<td>2009-2009</td>
<td>75</td>
<td>Femoropopliteal</td>
<td>Lutonix (Bard)</td>
<td>Severe calcifications excluded</td>
</tr>
<tr>
<td>DEBATE-SFA16</td>
<td>2010-2011</td>
<td>104</td>
<td>Femoropopliteal</td>
<td>IN.PACT Admiral (Medtronic)</td>
<td></td>
</tr>
<tr>
<td>BIOLUX-PI17</td>
<td>2010-2011</td>
<td>60</td>
<td>Femoropopliteal</td>
<td>Passeo-18 Lux (Biotronik)</td>
<td>Severe calcifications excluded</td>
</tr>
<tr>
<td>PACIFIER18</td>
<td>2010-2012</td>
<td>85</td>
<td>Femoropopliteal</td>
<td>IN.PACT Pacific (Medtronic)</td>
<td></td>
</tr>
<tr>
<td>IN.PACT SFA17</td>
<td>2010-2013</td>
<td>331</td>
<td>Femoropopliteal</td>
<td>IN.PACT Admiral (Medtronic)</td>
<td></td>
</tr>
<tr>
<td>LEVANT 218</td>
<td>2011-2012</td>
<td>476</td>
<td>Femoropopliteal</td>
<td>Lutonix</td>
<td></td>
</tr>
</tbody>
</table>
New technologies aim to minimize loss of drug into the vasculature and enhance deliverability to the vessel wall. At present, 2 DEBs containing paclitaxel have received US Food and Drug Administration approval due to promising long-term restenosis and target lesions revascularization rates in clinical trials (Table 1).

Densely calcified atherosclerosis reduces the efficacy of PTA and increases the risk for flow-limiting dissections. Furthermore, calcium is not reliably detected by standard angiography. Eccentric calcification poses additional problems when DEB angioplasty is planned. Dense calcification is thought to act as a physical barrier to penetration, mitigating the perceived long-term benefits of paclitaxel deposition. This concept was recognized in the planning phases of several clinical trials. The BIOLUX-PI and LEVANT-I trials, which examined the use of DEBs in femoropopliteal lesions, both excluded heavily calcified lesions. The BIOLUX-PII trial examining DEBs in below-the-knee interventions established noninferiority and safety relative to PTA. However, in explaining the lack of a statistically significant benefit of DEB angioplasty, the authors suggested that more baseline calcified lesions in the DCB arm may have played a role in reduced drug delivery, affecting outcomes.

Fanelli et al in 2014 correlated DEB performance with degree of vessel calcification. In this study, the authors classified vessel calcification according to circumferential involvement and length of calcification as seen on preprocedure computed tomography angiography. Sixty patients were treated with DEB angioplasty and followed to 12 months. Restenosis was significantly higher in patients with more complete circumferential calcium (>270 degrees) relative to less calcification (<90 degrees), as indicated by ankle-brachial index, late lumen loss, and primary patency outcomes. Complications associated with large calcium burden included flow-limiting dissections and residual stenosis, both occurring only in patients with >50% circumferential calcifications.

Cioppa et al in 2012 reported the use of DEB with directional atherectomy to overcome problems faced with heavily calcified femoropopliteal lesions. Thirty patients underwent directional atherectomy with TurboHawk (Covidien) followed by DEB with IN.PACT Admiral paclitaxel-coated balloon. Target lesions revascularization rate was 10% at 1 year, with secondary patency of 100%, comparing favorably to DEB, PTA, or atherectomy alone.

CONCLUSION

DEB in the femoropopliteal axis is safe, effective, and demonstrates improved long-term outcomes relative to PTA alone. Early evidence regarding the use DEB in densely calcified lesions suggest that efficacy is decreased with increased circumferential vessel calcification. Debunking with atherectomy is one method of overcoming this limitation. Early experiences with this approach have been favorable, but studies examining its long-term efficacy are lacking.

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