Overview of New Technologies for Lower Extremity Revascularization

Jason H. Rogers, MD; John R. Laird, MD

Abstract—Lower extremity peripheral arterial occlusive disease poses a unique challenge to traditional angioplasty-based endovascular therapies. The diffuse nature of lower extremity atherosclerotic disease, the presence of chronic total occlusions, poor distal runoff, and the presence of critical limb ischemia all have contributed to the disappointing results of balloon angioplasty for complex infrainguinal arterial disease. These challenges have spawned the development of a host of new technologies in an attempt to improve the safety and effectiveness of percutaneous revascularization for lower extremity peripheral arterial occlusive disease. This review summarizes the recent advances in available technologies, including novel angioplasty balloons; nitinol stents, stent grafts, and drug-eluting stents; excisional, laser, and rotational atherectomy devices; devices for crossing total occlusions; true-lumen reentry devices; thrombectomy catheters; and embolic protection devices. (Circulation. 2007;116:2072-2085.)

Key Words: catheter • lower extremity • peripheral vascular diseases • technology

The limitations of percutaneous transluminal angioplasty (PTA) for the treatment of lower extremity peripheral arterial occlusive disease (PAOD) are well established. Although PTA can be an effective modality for focal lesions in the iliac arteries,1,2 the results of balloon angioplasty for complex infrainguinal arterial disease have been disappointing.3–5 Although incompletely studied, numerous factors have been identified that negatively affect the long-term results of PTA. These include the length of the diseased segment, the presence of total occlusion, diabetes mellitus, poor distal runoff, and critical limb ischemia as the clinical presentation.6,7 Chronic total occlusion may be present in up to 20% to 40% of patients undergoing treatment for symptomatic PAOD, and procedural success rates have historically been lower in the setting of chronic total occlusion.7,8 In addition, there is greater potential for complications such as distal embolization and perforation when balloon angioplasty is used for long occlusions and more complex disease. These limitations of PTA have spawned the development of a host of new technologies in an attempt to improve on the safety and efficacy of percutaneous revascularization for lower extremity PAOD (Figure 1). Many of the devices presented here have been shown to improve procedural and clinical outcomes. However, the lack of uniform performance criteria and reporting standards for new devices has resulted in heterogeneous study end points, making comparative efficacy difficult. Future trials should attempt to adhere to performance criteria that have been developed for superficial femoral artery (SFA) intervention and will likely be developed for other vascular beds.9 This review summarizes the available data supporting the use and potential role of these emerging technologies.

Novel Angioplasty Balloons

Despite improvements in balloon catheter materials, lower balloon crossing profiles, and the availability of longer balloons for peripheral arterial use, plain old balloon angioplasty (POBA) continues to be limited by problems of dissection, acute elastic recoil, and restenosis caused by intimal hyperplasia and negative remodeling. These failings have led to the development of alternative balloon modalities, including cutting or scoring balloons and cryoplasty.

Cryoplasty

Cryoplasty is a technique that combines balloon angioplasty and cold therapy. Cooling of the balloon is achieved by the use of liquid nitrous oxide as the balloon inflation media rather than the usual mixture of contrast and saline. This cooling is hypothesized to have several beneficial effects, including plaque modification, reduction of elastic recoil, and induction of apoptosis in the smooth muscle cells in the vessel wall within the treated segment.10 Although no in vivo human data currently exist, it is thought that cryoplasty-induced smooth muscle cell apoptosis may reduce proliferation rates essential to the restenotic process. The PolarCath (Boston Scientific, Natick, Mass) is a commercially available cryoplasty system approved for peripheral arterial use. The system consists of a disposable computerized inflation control unit, nitrous oxide cylinder, and balloon catheter (Figure 2). As the liquid nitrous oxide is shuttled into the balloon, it...
undergoes a phase shift, resulting in inflation of the balloon and cooling to the desired temperature of $-10^\circ$C. Balloon inflation occurs in 2-atm increments up to the nominal inflation pressure of 8 atm. The treatment cycle lasts 20 seconds before deflation and passive warming of the balloon. Repeat inflations can be performed as needed by replacing the nitrous oxide canister. The PolarCath is available in diameters from 2.5 to 8 mm and lengths from 2 to 10 cm. The smaller-diameter balloons have a 0.014-in guidewire lumen and are designed for infrapopliteal use. The larger balloons have a 0.035-in guidewire lumen.

The PolarCath system was evaluated in a prospective, multicenter registry of cryoplasty for the treatment of lesions in the SFA and popliteal artery. Ultimately, 102 patients with stenoses or occlusions up to 10 cm in length were enrolled at 15 centers in the United States. Procedural success was 94%, with a need for bailout stenting resulting from a suboptimal angiographic result in only 9% of cases. Significant dissec-

Figure 1. Overview of new technologies for lower extremity revascularization.
recently, the cutting balloon (Boston Scientific) balloons in the coronary circulation for a variety of different applications. There is considerable experience with cutting and scoring balloons in the coronary circulation for a variety of different procedures. However, cryoplasty offers any real advantage over PTA or stenting. Comparative studies are necessary to determine whether cryoangioplasty compares favorably with historical PTA outcomes, but comparable data are available; however, the acute angiographic outcomes are favorable, with a low incidence of dissection and an infrequent need for bailout stenting. The 9-month and longer patency rates in these shorter lesions compare favorably with historical PTA outcomes, but comparative studies are necessary to determine whether cryoplasty offers any real advantage over PTA or stenting.

**Cutting and Scoring Balloons**

There is considerable experience with cutting and scoring balloons in the coronary circulation for a variety of different applications. Recently, the cutting balloon (Boston Scientific) was made available in larger diameters and was approved for peripheral vascular use. The peripheral cutting balloon comes in 2 lengths (1 and 2 cm) and in 5-, 6-, 7-, and 8-mm diameters. Each device has 4 longitudinal microsurgical blades bonded to the balloon. The proposed mechanism of action is a focusing of the dilation force at the tips of the atherotomes to provide scoring of the lesion and more gentle dilatation of the vessel with less vessel wall disruption. Potential benefits of the cutting balloon include reduced elastic recoil and more effective dilatation of fibrotic, anastomotic, or calcified lesions with less risk of major dissection.

The lack of availability of balloons longer than 2 cm makes this device impractical for the treatment of diffuse disease or long occlusions in the femoropopliteal and infrapopliteal vessels. The cutting balloon has shown promise, however, for the treatment of anastomotic or intragraft lesions within saphenous vein bypass grafts. In a small study, 19 infrapopliteal vein graft stenoses were treated with a procedural success rate of 100%. A good hemodynamic result was documented on follow-up duplex imaging, and at a mean follow-up of 11.4 months, only 1 patient developed a recurrent stenosis. A larger, more recent study compared PBA with the cutting balloon as the primary treatment for failing infrapopliteal bypass grafts in 36 patients. Although initial technical success was higher with the cutting balloon (74% versus 82%), the primary patency at 12 months was 36% (9 of 25) for POBA and 50% (5 of 10) for cutting balloon angioplasty (P=0.47).

Another potential application for the cutting balloon is to treat focal, calcified, or ostial lesions in the infrapopliteal vessels. Ansel and colleagues reported on their experience treating 93 popliteal and tibial lesions in 73 patients with the cutting balloon. Procedural success was 100%, with a need for bailout stenting as a result of dissection or suboptimal angiographic result in 20%. For those patients presenting with critical limb ischemia (Rutherford category 4), the limb salvage rate at 1 year was 89.5%.

The AngioSculpt balloon (AngioScore, Fremont, Calif) is another scoring device approved for peripheral vascular use. It consists of a semicompliant balloon with an external nitinol shape-memory helical scoring edge. A proposed advantage of this nitinol edge is improved device flexibility and deliverability. Further studies are required to better understand the role of the AngioSculpt balloon and the potential advantages of this device over the cutting balloon or standard balloon angioplasty.

**Nitinol Stents**

Nitinol is a unique alloy composed of nearly equal parts of nickel and titanium. Nitinol has 2 unique characteristics: superelasticity (ie, it returns to its original shape when an external force is removed) and thermal shape memory (it returns to a preformed shape on warming, allowing self-expansion). The superelasticity and thermal shape memory of the alloy make nitinol stents resistant to compression at body temperature and help them to resist external deformation. They are therefore more ideally suited for deployment in areas of flexion and torsion such as the superficial femoral and popliteal arteries.
Although a multitude of nitinol stent designs are available from different manufacturers, only 1 nitinol stent (IntraCoil, ev3, Plymouth, Minn) has been approved by the US Food and Drug Administration for femoral use. The other nitinol stents are approved for biliary or iliac artery use and are implanted “off-label” in the femoropopliteal arteries. The IntraCoil stent, which is constructed from a single strand of nitinol wire, is wound into the shape of a simple coil. This design has distinct advantages and disadvantages with regard to use in the SFA and popliteal arteries. For example, although the coil design affords the stent extreme flexibility and resistance to fracture, the low ratio of metal surface to open area provides less complete plaque coverage. Furthermore, the coiled design makes stent deployment less controlled than with other nitinol stent designs, and foreshortening of the stent on release makes positioning less precise than desired. US Food and Drug Administration approval of the IntraCoil stent was based on results of a randomized trial comparing its use with balloon angioplasty for femoropopliteal lesions. Although the complete results of the IntraCoil randomized trial have not been published, outcomes of the roll-in phase of the trial, in which all patients were treated with the IntraCoil stent, were published by Ansel and colleagues.\textsuperscript{18} They treated 93 patients with obstructive femoropopliteal artery disease up to 15 cm in length with the IntraCoil stent. In the patients who had a successful procedural outcome, the 9-month follow-up showed that 77.9% remained free of major adverse clinical events and that 81.8% had not required target lesion revascularization. Over the same follow-up period, the mean ankle-brachial index increased from 0.66 to 0.83, whereas the mean maximum walking time increased from 4.47 to 5.91 minutes.\textsuperscript{19}

Despite the fact that the only US Food and Drug Administration–approved nitinol stent has a coil configuration, the majority of nitinol stents being implanted today have a mesh design, which affords improved scaffolding and plaque coverage. Mewissen\textsuperscript{20} evaluated the SMART stent (Cordis, Miami Lakes, Fla) prospectively in 137 lower limbs in 122 patients with chronic limb ischemia. The anatomic subtypes included TransAtlantic Inter-Society Consensus A lesions in 12 limbs and B or C lesions in 125 limbs. The mean lesion length was 12.2 cm (range, 4 to 28 cm), and 57% of the lesions were >10 cm in length. Technical success was achieved in 98% of cases, and there were no acute (30-day) stent occlusions. At 1 and 2 years, the hemodynamic primary patency rates determined by duplex ultrasonography were 76% and 60%, respectively.\textsuperscript{20}

In a randomized controlled trial, Schillinger and colleagues\textsuperscript{21} assigned 104 patients with severe claudication or chronic limb ischemia caused by stenosis or occlusion of the SFA to undergo primary stent implantation (51 patients) with the Absolute self-expanding stent (Abbott Vascular, Redwood City, Calif) or angioplasty (53 patients). In that study, the mean length of the treated segment was 132±71 mm in the stent group and 127±55 mm in the angioplasty group. Secondary stenting was performed in 17 of 53 patients (32%) in the angioplasty group, in most cases because of a suboptimal result after angioplasty. The angiographic restenosis rate at 6 months was 24% in the stent group and 43% in the angioplasty group (P=0.05); at 1 year, the restenosis rates by duplex ultrasonography were 37% and 63%, respectively (P=0.01). Patients in the stent group were able to walk significantly farther on a treadmill than were those in the angioplasty group at 6 months (average distance, 363 versus 270 m; P=0.04) and 12 months (average distance, 387 versus 267 m; P=0.04). The ankle-brachial index also was significantly better at 12 months in the stent group compared with the angioplasty group (P=0.03).\textsuperscript{21}

Table 1 summarizes the main findings of available studies examining the use of nitinol stents in femoropopliteal arteries. The intermediate-term data for nitinol stents are promising, with 1- and 2-year primary patency rates superior to those for PTA and for first-generation stents. However, clear limitations remain, including the risk of restenosis after the use of nitinol stents and the potential for nitinol stent fracture in particular. Restenosis appears to occur more frequently when stents are used for long-segment disease and in diabetics. This restenosis appears to occur later than restenosis after coronary artery stenting. Late restenosis (after 1 year) has been noted to occur in most studies of SFA stenting.

In the long-segment study conducted by Sabeti and colleagues,\textsuperscript{22} stent fractures were observed in 15% of cases. The incidence of stent fracture was significantly associated with the length of the stented segment, with longer stents more likely to fracture. There was a trend toward increased risk of restenosis in fractured stents, although statistical significance was not achieved.\textsuperscript{22} The surprising finding of a high incidence of nitinol stent fracture has been confirmed by Scheinert and colleagues.\textsuperscript{23} These researchers investigated the incidence of femoral nitinol stent fractures by radiographic screening in 93 patients (121 limbs) at a mean follow-up of 10.7 months after stent implantation. The mean length of the stented segments in their patients was 15.7 cm. Stent fractures were found in 45 of 121 treated legs (37.2%) and in 64 of 261 stents (24.5%). The stent fractures were classified as minor (single strut fracture) in 31 cases (48.4%), moderate (fracture of >1 strut) in 17 cases (26.6%), and severe (complete separation of stent segments) in 16 cases (25.0%). Fractures occurred in 13.2% of cases when the stented length was <8 cm, 42.4% with a stented length of 8 to 16 cm, and 52.0% when the stented length was >16 cm. Furthermore, in 21 cases (32.8%), there was >50% diameter reduction at the site of stent fracture. In 22 cases (34.4%) with stent fracture, there was total stent occlusion. According to Kaplan-Meier estimates, the primary patency rate at 12 months was significantly lower for patients with stent fractures (41.1% versus 84.3%; P<0.0001). This study demonstrates that stent fracture is not merely a benign, incidental finding but may in fact be associated with a higher risk of restenosis and occlusion.\textsuperscript{23}

More flexible and fracture-resistant nitinol stents have been developed in response to these concerns regarding stent fracture and late restenosis. Further data regarding the performance of one such stent will be forthcoming from the RESILIENT trial (Randomized Study Comparing the Edwards Self-Expanding Life Stent vs Angioplasty Alone in Lesions Involving the Superficial Femoral Artery or Proximal Popliteal Artery), a randomized comparison of the Lifesent NT (Edwards Lifesciences, Irvine, Calif) with balloon angioplasty.
plasty for SFA and proximal popliteal artery lesions up to 15 cm in length.

Nitinol Stent Grafts and Covered Stents

Stent grafts have been developed as therapy for femoropopliteal occlusive disease in an effort to duplicate the surgical gold standard of femoropopliteal bypass with either vein or synthetic graft material. One such device, the Viabahn endoprosthesis (W.L. Gore & Associates, Inc, Flagstaff, Calif), is a self-expanding helical nitinol stent mounted to the outside surface of a tube of expanded polytetrafluoroethylene. The device is deployed into a target lesion after predilation, with the expanded polytetrafluoroethylene membrane postulated to act as a barrier to neointimal formation. The Viabahn endoprosthesis is currently approved by the US Food and Drug Administration for use in patients with symptomatic superficial femoral arterial lesions with reference vessel diameters of 4.8 to 7.5 mm. The device comes in 6-, 7-, and 8-mm diameters and is available in 2.5-, 5-, 10-, and 15-cm lengths.

Kedora et al performed a randomized, prospective study comparing the treatment of SFA occlusive disease percutaneously with the Viabahn stent (n=50) and surgical femoral-to-above-knee popliteal artery bypass with synthetic graft material (n=50). Primary patency at 12 months was not statistically different between the stent graft group and the surgical group (73.5% versus 74.2%, respectively). There were 14 reinterventions in the stent graft group and 12 reinterventions in the surgical group, resulting in similar secondary patency rates of 83.9% and 83.7%. The ongoing Viabahn Versus Bare Nitinol Stent (VIBRANT) trial is a randomized, prospective, multicenter trial intended to examine the performance of the Viabahn endoprosthesis compared with bare metal stents. Enrollment is currently underway, with planned 3-year follow-up and duplex ultrasound surveillance at 1-, 6-, 12-, 24-, and 36-month intervals.

Stent grafts also may be useful for aneurysmal disease, given their unique ability to exclude the vessel wall from the lumen. In a small recent study, 16 patients with 23 popliteal artery aneurysms were treated with the Viabahn endoprosthesis. Complete aneurysm exclusion was achieved in all cases, and during the mean follow-up of 7 months, only 1 patient became symptomatic as a result of stent-graft thrombosis that occurred at 6 months and was successfully treated with repeat

### Table 1: Major Trials Reporting Patency for Nitinol Stents in Femoropopliteal Arteries

<table>
<thead>
<tr>
<th>Author/Study (Year)</th>
<th>Patients, n</th>
<th>Type of Stent</th>
<th>Artery/Lesion Type</th>
<th>Stenoses or Occlusion, n (%)</th>
<th>Mean Lesion Length, cm</th>
<th>Primary Patency, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lugmayr et al81 (2002)</td>
<td>44 (54 limbs)</td>
<td>Symphony stent (Boston Scientific, Natick, Mass)</td>
<td>SFA and popliteal artery</td>
<td>Stenoses, 32 (59); occlusions, 22 (41)</td>
<td>3.2; occlusions, 4.0</td>
<td>At 1 y, 87; at 3 y, 76; Stenoses: at 1 y, 94; at 3 y, 78; Occlusions: at 1 and 3 y, 77</td>
</tr>
<tr>
<td>Jahnke et al82 (2002)</td>
<td>37 (40 lesions)</td>
<td>Intracoil (Intratherapeutics, St Paul, Minn)</td>
<td>SFA, 33; popliteal, 4; TASC A and B</td>
<td>Stenoses, 23 (58); occlusions, 17 (42)</td>
<td>3.6</td>
<td>At 1 y, 86.2</td>
</tr>
<tr>
<td>Vogel et al83 (2003)</td>
<td>41</td>
<td>SMART or Precise stents (Cordis, Johnson &amp; Johnson Co, Miami Lakes, Fla)</td>
<td>SFA, 35; popliteal, 6; TASC B and C</td>
<td>Stenoses, 24 (46); occlusions, 28 (54)</td>
<td>6.69</td>
<td>At 1 y, 84; at 2 y, 84</td>
</tr>
<tr>
<td>Sabeti et al22 (2004)</td>
<td>52</td>
<td>SMART stent (Cordis, Johnson &amp; Johnson Co); Dynalink stent (Guidant, Santa Clara, Calif); Expander stent (Bolton Medical, Nancy, France)</td>
<td>SFA and popliteal artery</td>
<td>Stenoses, 24 (46); occlusions, 28 (54)</td>
<td>6.0</td>
<td>At 1 y, 75; at 2 y, 69</td>
</tr>
<tr>
<td>Mewissen et al19 (2004)</td>
<td>122 (137 limbs)</td>
<td>SMART stent (Cordis, Johnson &amp; Johnson Co)</td>
<td>SFA and popliteal artery; TASC A, 12; TASC B and C, 125</td>
<td>Stenoses, 36 (39); occlusions, 57 (61): 31 in sirolimus group and 26 in bare stent group</td>
<td>8.2</td>
<td>At 2 y, 88.1 (sirolimus group, 87.1; bare stent group, 88.9)</td>
</tr>
<tr>
<td>Duda et al56-58/ SIROCCO (2006)</td>
<td>93: 47 Sirolimus-eluting nitinol stents, 46 bare nitinol stents</td>
<td>Sirolimus and bare SMART stent (Cordis, Johnson &amp; Johnson Co)</td>
<td>SFA; all TASC C</td>
<td>Stenoses, 36 (39); occlusions, 57 (61): 31 in sirolimus group and 26 in bare stent group</td>
<td>10.1</td>
<td>At 1 y, 63 on duplex ultrasonography</td>
</tr>
<tr>
<td>Schillinger et al37 (2006)</td>
<td>51</td>
<td>Dynalink or Absolute stent (Guidant, Santa Clara, Calif)</td>
<td>SFA</td>
<td>Stenoses, 32 (63); occlusions, 19 (37)</td>
<td>12.2</td>
<td>At 1 y, 76; at 2 y, 60</td>
</tr>
</tbody>
</table>

TASC indicates TransAtlantic Inter-Society Consensus.
percutaneous intervention. With primary and secondary patency rates at 12 months of 93% and 100%, respectively, this approach appears promising for an initial endovascular approach in these patients.25

For patients with aneurysmal iliac disease, balloon-expandable covered stents may be used. The iCAST covered stent (Atrium Medical Corp, Hudson, NH) is a balloon-expandable stent with 316L stainless steel struts that are completely covered with microporous polytetrafluoroethylene, which may result in improved deliverability and more uniform radial expansion. The stent is available in 5- to 12-mm diameters, which allows treatment of aneurysms and/or iatrogenic perforations/dissections in a variety of vessel sizes. The iCAST stent also will be evaluated in an upcoming multicenter trial for the treatment of iliac artery occlusive disease. The JOSTENT GraftMaster (Abbott Vascular) is another balloon-expandable covered stent available in 3- to 5-mm diameters that can be used to treat perforations in smaller vessels.

Drug-Eluting Stents

There are currently no approved peripheral drug-eluting stents for use within the United States. This reflects the facts that drug elution has yet to be widely applied to the peripheral arterial circulation and that clinical trials to date involving the superficial femoral arteries have not mirrored the initial successes seen with coronary drug-eluting stents.

Nonetheless, there is a need for improved patency rates after stenting because reported restenosis rates are as high as 75% for the superficial femoral, popliteal, and tibial arteries. Specific challenges to stent-based revascularization of the SFA include diffuse disease, which is often occlusive; involvement of the adductor canal; low-flow/high-resistance conditions; and coexistent disease of distal runoff vessels. Indeed, the physiological stresses on stents in the infrapopliteal location appear to be a major factor in limiting long-term device performance. Neointimal hyperplasia is only one of multiple failure modes, which include stent fracture, incomplete stent expansion, malapposition resulting from mechanical forces and calcification, and impaired endothelialization with thrombosis.

The Sirolimus Coated Cordis SMART Nitinol Self-Expandable Stent for the Treatment of SFA Disease (SIROCCO) trials used a thin uniform coating (5 to 10 μm) of sirolimus in a dose concentration equivalent to coronary stents (90 μg/cm² or 1 mg total per 6×80 cm SMART stent). The SIROCCO I trial randomized 36 patients with SFA disease (defined as ≥70% stenoses [≥7 to ≤20 cm] or total occlusion [≥4 to ≤20 cm] with a maximum of 3 stents) to either sirolimus-eluting or bare metal stents. Although this study failed to reach the primary end point of improved in-stent mean percent diameter stenosis by quantitative angiography (22.6% in the sirolimus group versus 30.9% in the control group; P=NS), there appeared to be an advantage in the subgroup of 5 patients who received the slower-eluting sirolimus stent. Other possible confounding factors included excessive calcification in the sirolimus arm and a total of 6 stent fractures, 3 in the sirolimus arm and 3 in the control arm.26

The SIROCCO II trial was designed to expand on the findings of SIROCCO I by randomizing 57 patients to slower-eluting sirolimus stents or control stents. Patients with shorter ≥70% stenoses (≥7 to ≤14.5 cm) or total occlusions (≥4 to ≤14.5 cm) were enrolled and treated with a maximum of 2 stents. This study again failed to meet its primary end point of in-stent mean lumen diameter at 6 months as determined by quantitative angiography (4.94±0.69 and 4.76±0.54 mm for sirolimus-eluting and bare metal groups, respectively; P=NS).27

A pooled analysis and longer-term follow-up of the slower-eluting formulation from SIROCCO I and II resulted in an early statistically significant difference in the primary end point (mean stent diameter); however, this advantage was lost by 18 months as determined by duplex sonography.28

Another drug-eluting stent currently under investigation in the above-the-knee femoropopliteal artery is the Zilver PTX Stent Platform (Cook Medical, Bloomington, Ind), a self-expanding nitinol stent. Drug elution is via polymer-free paclitaxel applied to the abluminal surface only. The paclitaxel is applied in a 3-μg/mm² dose density, with a 220- to 880-μg total dose per stent. The first phase of a nonrandomized trial has been completed outside the United States in 60 patients with SFA lesions ≤7 cm, allowing 1 stent per lesion. Twenty patients (28 lesions) were treated with the Zilver PTX stents, with a primary patency rate of 90% (mean follow-up, 9 months; range, 6 to 12 months). By intravascular ultrasound, no aneurysm or strut malapposition was associated with the Zilver PTX stents, and no stent fractures were seen. The second expanded study phase will add 420 randomized patients (lesions ≤14 cm, up to 2 stents per lesion) with planned 12-month follow-up to further evaluate safety and effectiveness. The planned primary end point is event-free survival defined as freedom from the major adverse events of death, target lesion revascularization, target limb ischemia requiring surgical intervention, surgical repair of the target vessel, and worsening Rutherford classification. The secondary end point will be patency rate at the 6- and 12-month follow-up as assessed by duplex ultrasound.29

Bare balloon-expandable and nitinol self-expanding stents have been used below the knee to treat severe claudication or critical limb ischemia with high immediate procedural success rates. Limb salvage rates at 1 to 12 months have been reported to be 80% to 96%.30–32 Because infrapopliteal vessels are of small caliber with long lesion lengths, drug elution has been proposed to be of particular benefit. There are limited data reporting the off-label use of sirolimus-eluting coronary stents in below-the-knee applications. Boisiers et al30 reported that when sirolimus-eluting balloon-expandable coronary stents were used in the infrapopliteal arteries, a 6-month follow-up demonstrated survival and limb salvage rates of 94.4% and 94%, respectively, with a mean late lumen loss of only 0.38 mm. Siablis et al33 found significantly less in-stent and in-segment binary restenosis and a decreased rate of repeat endovascular procedures at 1 year in sirolimus-eluting versus bare metal stents. Further studies are needed to assess the safety and efficacy of this approach. Finally, a recent randomized trial demonstrated
that a paclitaxel-coated balloon catheter (Paccocath) was effective in reducing the 6-month mean late lumen loss and binary restenosis when used in the SFA.34 Although drug elution, whether stent based or balloon based in the periphery, is an exciting prospect, many issues remain to be resolved, including the ideal pharmacological agent and release kinetics, the elimination of stent fractures, and the cost-to-benefit ratio.

Debulking Devices: Excimer Laser and Excisional Atherectomy
A variety of atherectomy and laser angioplasty systems have been used to treat PAOD in the past with mixed results. In recent years, there has been a resurgence of interest in debulking devices with the development of a new excisional atherectomy system (SilverHawk, Fox Hollow Technologies, Redwood City, Calif) and improvement in excimer laser atherectomy catheters (ClirPath, Spectranetics Corp, Colorado Springs, Colo) and laser technique.

Excimer Laser Atherectomy
Continuous-wave, hot-tipped lasers were evaluated and abandoned for peripheral arterial use in the late 1980s because of high complication rates caused by thermal damage to surrounding tissue.35 In contrast, excimer laser–assisted angioplasty of the leg arteries has been practiced commercially in Europe since 1994. The 308-nm excimer laser uses flexible fiberoptic catheters to deliver intense bursts of ultraviolet energy in short pulse durations. The advantage of ultraviolet light lies in its short penetration depth of 50 μm and in its ability to break molecular bonds directly by a photochemical rather than thermal process. The excimer laser catheter removes a tissue layer of 10 μm with each pulse of energy. Tissue is ablated only on contact, without a consequent rise in temperature to surrounding tissue. An additional benefit of ultraviolet light is its ability to ablate thrombus and to inhibit platelet aggregation.

Potential advantages of laser atherectomy include the ability to treat long occlusions and complex disease effectively, thereby providing a better angiographic result with less distal embolization and less need for stenting. The excimer laser also may be used to facilitate crossing of chronic total occlusions using the “step-by-step” technique in which the guidewire is advanced just proximal to the lesion and the excimer laser catheter is brought into contact with the occlusion. The laser catheter is gently advanced ahead and activated for 5 to 10 seconds in an attempt to penetrate the fibrous cap. The guidewire is then used to probe antegrade to find a channel through the lesion. If a channel cannot be found, the laser is reactivated, and the above technique is repeated (Figure 3). Scheinert and colleagues37 analyzed the results of 411 consecutive excimer laser–assisted recanalization procedures for long SFA occlusions (mean occlusion length, 19.4 cm) in 318 patients. Despite the treatment of long occlusions, the technical success rate was high (90.5%). Bailout stenting was needed in only 7.3% of cases. Other complications were infrequent and included acute reocclusion (1%), perforation (2.2%), and distal embolization (3.9%). The primary patency rate at 1 year was disappointing; however, with careful surveillance and early reintervention, a secondary patency rate of 75.1% at 1 year was achieved after treatment of these long SFA occlusions.37

Excimer laser–assisted intervention also has been evaluated for the treatment of complex occlusive disease in patients presenting with critical limb ischemia. In the Laser Angioplasty for Critical Limb Ischemia (LACI) trial, 145 patients (155 critically ischemic limbs) were treated with excimer laser–assisted intervention at 15 sites in the United States and Germany. All patients were poor candidates for surgical revascularization because of diffuse distal disease, with poor targets for bypass, the absence of venous conduit, or significant medical or cardiac comorbidities placing the patient at high risk for complications from surgery. A total of 423 lesions were treated in the SFA (41%), popliteal (15%), and infrapopliteal (41%) arteries. The majority of patients (70%) had a combination of stenoses and occlusions, and the mean treatment length was >16 cm. Despite these unfavorable lesion and patient characteristics, an excellent limb salvage rate of 93% was achieved at 6 months.38

There have been numerous improvements in laser catheter technology over the years. A limiting factor has always been the inability to create a channel much larger than the diameter of the catheter. This limitation has been addressed with the latest design iteration, the TURBO-Booster catheter (Spectranetics; Figure 4). The TURBO-Booster uses a custom guide catheter that allows the laser to directionally ablate tissue to obtain a larger lumen. The device is currently undergoing evaluation for the treatment of disease in the SFA and popliteal arteries in the multicenter ClirPath Excimer Laser to Enlarge Lumen Openings (CELLO) clinical trial.
Excisional Atherectomy
The SilverHawk Plaque Excision System (Fox Hollow Technologies) is a forward-cutting atherectomy device. When the catheter is activated and manually advanced through a lesion, a high-speed cutting blade excises a ribbon of plaque that is collected into the catheter nose cone. Multiple catheter passes are made through the lesion, during which the blade is redirected sequentially toward all quadrants of the vessel lumen. Significant debulking of the lesion can be achieved without the barotrauma associated with the previous directional atherectomy catheter that uses a balloon opposite the cutting blade to maximize plaque removal.

The SilverHawk catheter now comes in 7 different sizes to allow treatment of femoral, popliteal, tibial, and even pedal vessels. Two of the catheters have extra-large nosecones for greater plaque capacity, whereas the MS catheter has a slightly lower-profile blade that was designed for greater efficacy in calcified lesions. Some of the catheters feature a design modification that allows easier flushing of the nosecone.

There are no prospective, randomized trials comparing excisional atherectomy with the SilverHawk catheter to balloon angioplasty or stenting. Several single-center experiences with the SilverHawk have been published. Zeller and colleagues have published their experience with femoropopliteal excisional atherectomy. They treated 131 lesions in 100 limbs in 84 patients presenting with Rutherford category 2 to 5 ischemia. Forty-five lesions were de novo (group 1; 34%), 43 lesions were native vessel restenoses (group 2; 33%), and 43 lesions were in-stent restenoses (group 3; 33%). The technical success rate was 86% for atherectomy alone and 100% after adjunctive therapies. Several single-center experiences with the SilverHawk have been published. Zeller and colleagues have published their experience with femoropopliteal excisional atherectomy. They treated 131 lesions in 100 limbs in 84 patients presenting with Rutherford category 2 to 5 ischemia. Forty-five lesions were de novo (group 1; 34%), 43 lesions were native vessel restenoses (group 2; 33%), and 43 lesions were in-stent restenoses (group 3; 33%). The technical success rate was 86% for atherectomy alone and 100% after adjunctive therapies. Primary patency, defined as freedom from >50% restenosis by duplex ultrasound at 18 months, was 73%, 42%, and 49% in the 3 groups, respectively. The secondary patency rates at 18 months were 89%, 67%, and 79%, respectively. The authors concluded that long-term technical and clinical results after atherectomy of femoropopliteal lesions are in favor of de novo lesions compared with restenotic lesions.39

Kandzari and colleagues also evaluated SilverHawk atherectomy for patients presenting with critical limb ischemia (Rutherford category 5 to 6). A total of 76 limbs were treated in 69 patients at 7 centers in the United States. Approximately 40% of the lesions treated were in the infrapopliteal vessels. Procedural success was achieved in 99% of cases. Complications were infrequent, and target lesion revascularization occurred in only 4% of cases. Limb salvage (avoidance of major amputation) was achieved in 87% of patients at 6 months.30 The role of excisional atherectomy for the treatment of critical limb ischemia is to be evaluated further in a prospective, randomized clinical trial comparing SilverHawk atherectomy with the gold standard of surgical bypass (PROOF trial: Plaque Removal versus Open Bypass Surgery for Critical Limb Ischemia).

Future developments will be directed at designing a catheter with greater capability to excise calcified plaque and one that incorporates imaging (optical coherence tomography or intravascular ultrasound) to better direct plaque excision. In addition, the opportunity to study excised atherosclerotic plaque more intensively has led to a partnership between Fox Hollow Technologies and Merck Research Laboratories with a goal of developing novel target therapies to treat atherosclerosis.

Rotational Atherectomy
This resurgence in interest in atherectomy devices for peripheral vascular use has led to the development of 2 new rotational atherectomy systems that are currently in clinical trials. The Pathway Medical PV (Pathway Medical Technologies, Redmond, Wash) system has expandable, rotating scraping blades (“flutes”) with ports between the flutes that allow flushing and aspiration of plaque material or thrombus. The Orbital Atherectomy System (Cardiovascular Systems, St Paul, Minn) is a high-speed rotational atherectomy system that incorporates an eccentric, diamond-coated abrasive crown. When rotated at high speeds, the abrasive crown moves in an orbital path within the artery, potentially creating a lumen larger than the diameter of the crown while gener-
ating only small particles that will pass through the capillary circulation (Figure 5).

**Percutaneous Thrombectomy**

The clinical consequences of arterial thrombus formation or thromboembolism in the lower extremity are significant. If peripheral arterial or graft occlusion occurs acutely, thrombus is almost invariably present. This may occur as a result of in situ thrombosis of a ruptured plaque or cardioembolism. If collaterals are minimal or absent, acute limb ischemia may result, and therapy must be delivered urgently. In the presence of chronic stenoses with varying degrees of collateral formation, thrombotic occlusion may result in severe claudication or in a more subacute presentation of limb ischemia. Clinically significant distal thromboembolism during peripheral percutaneous intervention also may occur, necessitating distal aspiration embolectomy. Percutaneous rheolytic and aspiration thrombectomy catheters have been developed to address these clinical scenarios.

**Rheolytic Thrombectomy**

The Angiojet rheolytic thrombectomy system (Possis Medical, Inc, Minneapolis, Minn) consists of a pump set and drive unit that delivers pressurized saline to the tip of the rheolytic catheter to produce a series of retrograde-directed high-velocity saline jets that entrain thrombus through hemodynamic forces (Bernoulli’s principle/Venturi effect). Thrombus is then fragmented by the saline jets and aspirated mechanically through the effluent lumen.41 Six Angiojet catheters currently are available that can accommodate a wide variety of vessel diameters and clinical applications. Potential advantages of the Angiojet system include the ability to rapidly remove a large amount of fresh thrombus burden in an ischemic limb without the need for chemical thrombolysis with the attendant risks of bleeding. Limitations include the potential for distal embolization (the use of an embolic protection during rheolytic thrombectomy should be considered), the inability to remove chronic or insoluble thrombus, and difficulty in treating the microvasculature. Fortunately, hemolysis with localized adenosine release resulting in bradycardia is not a risk in the periphery as it is with intracoronary use.

The Angiojet catheter has been shown to be effective in the treatment of acutely occluded infra-aortic native arteries and bypass grafts, with the majority of acute thrombotic material (>75%) being removed. For more organized residual or mural thrombus and underlying atherosclerotic lesions, adjunctive angioplasty with stent placement may be required.42 The rheolytic catheter has been used successfully in conjunction with catheter-directed thrombolysis in one series of 86 patients with acute and subacute limb-threatening ischemia. After primary rheolytic thrombectomy was performed, secondary catheter-directed thrombolysis was performed in 50 patients, yielding a high acute success rate (>50% luminal clearance in 84% of treated patients) with a reported 6-month patency rate of 79%.43 The rheolytic catheter also can be used in a combined “power-pulse spray” technique. In this method, a chemical thrombolytic is first infused into the thrombus in a stepwise manner through the rheolytic catheter by occluding the outflow port. After the thrombus has been “laced” with thrombolytic, the same catheter is used to aspirate the thrombus. This technique has been reported to be safe and allows rapid sequential chemical and rheolytic thrombectomy, with success rates >90%.44

**Aspiration Thrombectomy**

Thrombus aspiration also can be achieved with an aspiration catheter. Syringe suction is applied manually to a catheter, with thrombus entrained in the catheter by this extraction force. Although the efficiency and volume of thrombus extracted with these catheters are not equivalent to those of rheolytic catheters, the advantages of these catheters include ease of use and deliverability to small-caliber distal vasculature. The most common application in the lower extremity would therefore be the management of distal embolization during peripheral intervention.
Several aspiration catheters are currently available for use in the peripheral vasculature. The Pronto V3 extraction catheter (Vascular Solutions, Minneapolis, Minn) has a dual-lumen, monorail design that is compatible with a 6Fr guiding catheter and a 0.014-in wire. Thrombus is extracted by bringing the catheter to the desired site over a wire, and aspiration is performed using two 30-mL locking vacuum syringes. The unique feature of this catheter is the rounded distal tip (“olive”) that sits in front of the aspiration orifice. This design may improve thrombus aspiration and protect the vessel wall while advancing during aspiration. The Pronto catheter has been shown to be effective in the intracoronary circulation, but there are no published trials examining its efficacy in the lower extremity vasculature.45

Another effective aspiration catheter is the Export XT catheter (Medtronic Vascular, Inc, Minneapolis, Minn). This catheter features a forward-facing aspiration orifice, which engages thrombus at a different angle than the Pronto catheter. Manual aspiration is achieved by two 30-mL locking syringes. The Export XT catheters are monorail, 0.014-in wire compatible, and available in 6Fr guide-compatible (0.041-in aspiration lumen) and 7F guide-compatible (0.050-in lumen) sizes. Other aspiration catheters include the Rio Catheter (Boston Scientific) and the Diver CE (ev3 Inc), which has multiple side holes designed to improve flow and minimize clogging.

**Embolic Protection in Lower Extremity Revascularization**

Embolic protection devices (EPDs), first developed to provide cerebral protection during carotid artery stenting, have led to marked reductions in the combined end points of stroke or death.46,47 It was therefore natural that these devices should be applied to native coronary and aortocoronary saphenous vein graft interventions in an effort to reduce clinically significant atheroembolism and thromboembolism. Many of these devices have been used in the lower extremities, although this translation offers unique challenges. Vessel diameters in the lower extremities often span a wide range not met by all EPDs, and the burden of thrombus and/or atheroembolic material often far exceeds that seen in the carotid or coronary circulation. Delivery of EPDs in the lower extremity vasculature may be more difficult in view of typically longer diseased segments, and retrieving the filters with captured debris also may be challenging. An advantage of EPD use in the lower extremities is that transient vessel occlusion generally will not be a major issue as it can be in the cerebral or coronary circulation.

Despite multiple clinical trials in carotid artery stenting and saphenous vein graft intervention, there are currently few data to support the routine use of an EPD in patients undergoing routine lower extremity peripheral vascular intervention. Nonetheless, the use of EPDs is likely warranted in thrombus-laden lesions or in patients with vessels with poor distal runoff on the basis of reported rates of distal embolization during thrombolytic therapy in limb-threatening ischemia.48–51 In addition, routine EPD use may be warranted during femoropopliteal excisional atherectomy on the basis of data from one series that demonstrated embolic debris retrieved in 10 consecutive cases.52

**Types of EPDs**

There are 3 main types of EPDs available: distal filtration, distal balloon occlusion, and proximal occlusion devices. Proximal occlusion generally is not used during lower extremity revascularization, given the long length of distal runoff and multiple collaterals. The interventionalist’s choice of EPD depends on a variety of factors, including feasibility, device familiarity, ease of use, cost, and perceived efficacy. The number, size, and volume of particulate debris liberated by stenting saphenous vein grafts have been studied in comparisons of distal balloon occlusion with a distal vascular filter having an average distal pore size of 100 μm. The distribution of particle sizes and embolic load captured was equivalent.53 These data and others are important in establishing the principle that despite a nominal pore size of ~100 μm, the functional orifice size of a filter is smaller, likely because of the deposition of aggregate debris, platelets, or fibrin on the filter surface.54 A summary of currently available EPDs that can be adapted for use in the lower extremities is given in Table 2.

**Devices for Chronic Total Occlusions**

Critical limb ischemia and claudication typically arise in the presence of chronic total occlusions. In such cases, collateral flow often is insufficient to alleviate symptoms. Critical limb ischemia develops when those collaterals are jeopardized by more proximal occlusive disease. The ability to successfully traverse and recanalize these chronic total occlusions is therefore imperative. Attempts at recanalization of these often heavily calcified lesions fail in ~20% of cases using traditional guidewire and balloon technology. The reason for failure stems primarily from the inability to cross a lesion or the inability to reenter the distal true lumen from a subintimal location. Because of this clinical need, several devices have recently become available to assist in this important lesion subset.

**Devices for Crossing**

**Controlled Blunt Microdissection**

Controlled blunt microdissection refers to the ability to perform catheter-based microdissection using a pair of miniature hinged jaws that can be actuated from the catheter handle. Controlled blunt microdissection has been reported to be safe and feasible, with a 91% success rate in treating pelvic and lower limb chronic total occlusions in 1 series of 36 patients with 44 symptomatic chronic total occlusions that had failed conventional percutaneous revascularization.55 In this report by Mossop et al, a prototype catheter with hinged jaws was used to create a channel through the lesion using controlled blunt microdissection and, when paired with a true-lumen reentry device, resulted in a very high procedural success rate. This technology, which is now marketed as the FrontRunner XP chronic total occlusion catheter (Cordis), is intended to facilitate the intraluminal placement of conventional guidewires beyond stenotic lesions (including chronic total occlusions) in the peripheral vasculature before further percutaneous intervention. The current-generation device

Rogers and Laird Lower Extremity Revascularization Technologies 2081
CROSSER Catheter

The CROSSER chronic total occlusion recanalization system (FlowCardia Inc, Sunnyvale, Calif) is an innovative device that uses high-frequency mechanical vibrations (20 000 cycles per second to a depth of 20 μm) propagated through a nitinol core wire to a stainless steel tip. The system consists of a generator, transducer, foot switch, and disposable catheter. The generator applies AC current to the piezoelectric crystals in the transducer, which then converts, amplifies, and transmits this energy to the catheter tip. The vibrational mechanical impact and cavitational effects result in penetration of the occluded artery. The catheter is 1.1 mm in diameter, monorail, and hydrophilic; can be mounted on a standard 0.014-in guidewire; and is compatible with a 6F guiding catheter. Although there are no maximum recommendations for vessel size, a minimum diameter of 2.5 mm is recommended. Although the infusion lumen of the CROSSER is too small to aspirate blood, it is possible to inject diluted contrast to confirm true-lumen position. An irrigation line is required for continuous sterile saline flush through the device during activation, which cools the system and helps to facilitate cavitation at the catheter tip.

The CROSSER system has previously been studied in chronic total occlusions in the coronary circulation with high technical success rates (63% to 76%). The ongoing Peripheral Approach to Recanalization in Occluded Totals (PATRIOT) trial is a US multicenter trial currently enrolling patients to assess the safety and efficacy of using the CROSSER catheter in chronic femoropopliteal occlusions resistant to conventional guidewire technique.

True-Lumen Reentry

Multiple technologies are now available to allow passage of a guidewire beyond an occlusion or stenosis, but this is often in a subintimal fashion. Reentering the true lumen with conventional guidewires is often a lengthy and unsuccessful venture. Two devices are currently available that facilitate true-lumen reentry. In addition to ensuring a high success rate in reentering the true lumen, these...
devices may reduce the chance of vessel perforation and procedure times.

**OutBack LTD Reentry Catheter**
The OutBack LTD reentry catheter (Cordis) is 120 cm in length with a single 0.014-in wire lumen and a 5.9F profile (6F sheath compatible). The catheter consists of a deployment handle mounted to a rotating hemostasis valve, which is attached to the proximal catheter shaft. At the distal end of the catheter is a 22-gauge reentry cannula (needle). The device is passed over a 0.014-in wire into the subintimal space adjacent to the desired reentry location. Orienting the catheter under fluoroscopy by means of distal “L” and “T” markers at the end of the catheter shaft aligns the cannula with the true lumen. The wire is then partially withdrawn, and the cannula is advanced into the true lumen by moving the deployment slide forward. The wire can then be advanced into the true lumen, and conventional therapies can be delivered (Figure 6).

The OutBack catheter was first evaluated in an earlier generation in a series of 36 patients with peripheral (primarily iliac and femoral) chronic total occlusions initially approached with percutaneous controlled blunt microdissection. Of all successful cases, 35% (14 of 40) required true-lumen reentry, which was successfully achieved with this first-generation device. In another series by Joyce et al of 100 consecutive endovascular occlusions in which the distal true lumen could not be reentered, there was a reported 95% clinical success rate in reentering the true lumen with available reentry catheters and successfully completing the intervention.

**Pioneer Catheter**
Another device designed to assist true-lumen reentry is the Pioneer catheter (Medtronic). This catheter incorporates a distal 25-gauge nitinol reentry needle with an integrated 64-element phased-array intravascular ultrasound transducer to allow directed ultrasound-guided reentry into the true lumen (Figure 7). This catheter is 120 cm long, accommodates two 0.014-in guidewires (1 to track the device and 1 for the reentry needle), and is compatible with a 7F sheath. The device is brought into the subintimal tract over a wire, and under intravascular ultrasound imaging, color flow is identified in the true lumen. The catheter is rotated to position the true lumen at the “12 o’clock” position, after which the needle is advanced and the true lumen is wired. The Pioneer catheter can then be removed, and the intervention may proceed. Prior studies have
It is evident that the last decade has seen an unprecedented rate of new device development for the treatment of PAOD. These advancements have made it possible to treat a vast array of lesion subsets with focused technologies and high acute procedure success rates. However, significant limitations remain in the currently available technologies. The diffuse nature of vascular occlusive disease continues to complicate endovascular approaches to revascularization. Long-term target vessel patency after mechanical therapies complicate endovascular approaches to revascularization.

Conclusions

Although we have made tremendous advances in the endovascular treatment of lower extremity arterial occlusive disease, vital improvements in the next decade will depend on sustained clinical and basic investigations that carefully meld both existing and emerging technologies.

Disclosures

Dr Rogers is a consultant for Boston Scientific and Medtronic. Dr Laird is a consultant for Cordis, Boston Scientific, Medtronic, Edwards Life Sciences, ev3, and Spectranetics.

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Jason H. Rogers and John R. Laird

Circulation. 2007;116:2072-2085
doi: 10.1161/CIRCULATIONAHA.107.715433

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