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Plan: Aetna Better Health
Policy Number: 0295
Policy Name: Peripheral Atherectomy and Thrombectomy Devices

Type of Submission – Check all that apply:
- ☐ New Policy
- ☒ Revised Policy*
- ☐ Annual Review – No Revisions
- ☐ Statewide PDL

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

CPB 0295 Peripheral Atherectomy and Thrombectomy Devices

Clinical content was last revised on 05/12/2017. Additional non-clinical updates were made by Corporate since the last PARP submission, as documented below.

Update History since the last PARP Submission:
06/13/2019-This CPB has been updated with additional background information and references.

Name of Authorized Individual (Please type or print):
Dr. Bernard Lewin, M.D.

Signature of Authorized Individual:

Revised July 22, 2019
Peripheral Atherectomy and Thrombectomy Devices

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers mechanical or laser peripheral atherectomy (atheroablation) medically necessary in members who meet all of the following criteria:

I. Member has symptomatic infrainguinal atherosclerotic arterial occlusive disease caused by atherosclerosis involving the femoral, popliteal, and/or infrapopliteal arteries (limb-threatening ischemia or functionally limiting claudication); and

II. Member can not be treated by standard angioplasty techniques alone, (i.e., balloon angioplasty, etc.); and

III. Either A or B:

A. Member has an eccentric lesion that does not dilate with conventional balloon angioplasty, or

B. Member has vein bypass graft stenosis.

http://www.aetna.com/cpb/medical/data/200_299/0295.html
Aetna considers mechanical or laser peripheral atherectomy experimental and investigational for all other indications, including peripheral atherectomy of the renal artery, visceral artery, abdominal aorta, brachiocephalic trunk and branches, and iliac artery, because its effectiveness for these indications has not been established.

Aetna considers isolated segmental pharmacomechanical thrombolysis (Trellis Peripheral Infusion System) experimental and investigational for treatment of deep venous thromboses, Paget-Schroetter syndrome (also known as venous thoracic outlet syndrome) and other indications because there is inadequate evidence in the peer-reviewed published clinical literature regarding its effectiveness.

Aetna considers a drug-eluting balloon for mechanical or laser peripheral atherectomy experimental and investigational for the treatment of in-stent restenosis of peripheral arteries because there is inadequate evidence in the peer-reviewed published clinical literature regarding the effectiveness of this approach.

Aetna considers the use of drug-eluting balloons for in vein grafts and dialysis/vascular accesses, and for the treatment of primary lesion/occlusion of peripheral arteries experimental and investigational because its long-term effectiveness has not been established.

Notes:

The preferred technique for mechanical atherectomy involves the use of the Simpson Atherocath (directional atherectomy). Peripheral atherectomy/atheroablation with other mechanical or rotational devices or rotational aspiration atherectomy devices has not been shown to be effective.

Peripheral laser atherectomy is also known as peripheral laser angioplasty.

Background
Atherectomy was introduced in 1985 to improve upon the limitations of balloon angioplasty, primarily, abrupt reclosure and restenosis. Atherectomy devices cut and remove atherosclerotic plaque from a vessel wall or grind the atheroma into small particles, allowing them to embolize distally. Elastic recoil is reduced after atherectomy because the lumen is widened without stretching of the arterial wall.

Several types of atherectomy devices have been cleared by the U.S. Food and Drug Administration for peripheral use and primary success rates have been favorable with various devices; however, the Simpson Peripheral Atherocath has been the most widely used. This device has a circular cutter that spins at 2,000 rpm inside a metal housing with a window. Balloon inflation on the opposite side of the housing forces the plaque through the window where it is cut by advancing the rotating cutter in the housing. This device is best suited for short, discrete, eccentric stenosis. The catheters are bulky and stiff to use in the tibial or tortuous vessels. Primary success rate have been 82 to 100 % with few complications.

Data support the use of atherectomy as effective in the peripheral vessels in patients who meet the following criteria: have symptomatic peripheral vascular disease (limb-threatening ischemia or functionally limiting claudication); and cannot be treated by standard angioplasty techniques alone, i.e., balloon angioplasty would be ineffective or is contraindicated; and have an eccentric lesion that does not dilate with conventional balloon angioplasty, or vein bypass graft stenosis.

Until the problem of restenosis can be solved, atherectomy is a reasonable treatment for symptomatic peripheral vascular disease (limb-threatening ischemia or functionally limiting claudication) only when balloon angioplasty may be ineffective or contraindicated.

Zeller et al (2007) reported a safety and efficacy study of the first rotational aspiration atherectomy system (Pathway PV) for the treatment of arterial lesions below the femoral bifurcation. A total of 15 patients (9 men; mean age of 71 +/- 9 years) with Rutherford stage 2 to 5 lower limb ischemia were enrolled at 3 study sites. Target lesions were in the superficial femoral (n = 7, 47 %), popliteal (n = 7, 47 %), and posterior tibial (n = 1, 6 %) arteries. Mean diameter stenosis was 97 % +/- 10 %; mean lesion length was 61 +/- 62 mm (range of 5 to 250). The primary study endpoint was the 30-day serious adverse event (SAE) rate. Interventional success (residual stenosis less than 30 %) was achieved in all lesions (100 %). Stand alone atherectomy was performed in 6 (40 %) patients, adjunctive balloon...
angioplasty in 7 (47 %), and stenting/endografting in 2 (13 %). The SAE rate at 30
days was 20 % (3/15), including 1 perforation due to an unrecognized displacement
of the guidewire (sealed with an endograft), 1 false aneurysm at the puncture site
(successful duplex-guided compression therapy), and 1 dissection in conjunction
with a distal embolism (stent implantation and aspiration thrombectomy). Primary
patency rates measured by duplex ultrasound at 1 and 6 months were 100 % and
73 %, respectively; the target lesion revascularization (TLR) rate was 0 % after 6
months. The ankle-brachial index increased significantly from 0.54 +/- 0.3 at
baseline to 0.89 +/- 0.16, 0.88 +/- 0.19, and 0.81 +/- 0.20 (p < 0.05) at discharge, 1
month, and 6 months, respectively. Mean Rutherford categories were 2.92 +/- 1.19
(range of 1 to 5), 0.64 +/- 1.12 (range of 0 to 1), and 0.83 +/- 1.33 (range of 0 to 3)
at the same time points (p < 0.05). The authors concluded that the application of
this new atherectomy device was feasible in all cases. The serious adverse event
rate was moderate; however, all events were solved during the index procedure.
The 0 % 6-month TLR rate is promising.

Mahmud et al (2007) noted that over the past decade, percutaneous
revascularization therapies for the treatment of patients with peripheral arterial
disease (PAD) have evolved tremendously, and a great number of patients can
now be offered treatment options that are less invasive than traditional surgical
options. With the surgical approach, there is significant symptomatic improvement,
but the associated morbidity and mortality preclude its routine use. Although newer
percutaneous treatment options are associated with lower procedural
complications, the technical advances have outpaced the evaluation of these
treatments in adequately designed clinical studies, and therapeutic options are
available that may not have been rigorously investigated.

Bunting and Garcia (2007) stated that atherectomy is experiencing increased
interest from endovascular specialists as a therapeutic treatment in the peripheral
arteries. Long studied in the coronary vasculature, atherectomy has several
theoretical advantages that make it uniquely suited for the peripheral circulation. In
particular, infra-inguinal PAD experiences physiological stresses and forces that
have made traditional percutaneous coronary treatments such as angioplasty and
stenting not as successful. Re-stenosis has been a major problem for angioplasty
and stenting alone. The SilverHawk atherectomy device has favorable short-term
data but important longer-term data are limited and need further study. Laser
atherectomy also has favorable applications in niche patients but the number of
studies is limited. Unfortunately, athero-ablative technologies for PAD require more definitive objective data regarding 12-month and longer-term outcomes in order to obtain widespread scientific acceptance.

Biskup et al (2008) noted that a new atherectomy device (SilverHawk) has recently been approved by the Food and Drug Administration, but the results with its use are unclear. These investigators analyzed a series of consecutive patients undergoing atherectomy. They retrospectively reviewed the charts of 35 patients undergoing infra-inguinal (IF) atherectomy in 38 limbs. The Trans-Atlantic Inter-Society Consensus (TASC) classification and Society of Vascular Surgery run-off scores were calculated. Time to event analysis was performed using Kaplan-Meier estimates. Risk factors affecting patency were analyzed with a multi-variate Cox model. Mean patient age was 70 +/- 9.6 years. Indications for intervention were claudication (26 %), rest pain (21 %), and tissue loss (53 %). Femoro-popliteal (FP) atherectomy was performed in 68 % and tibial atherectomy in 32 %. For FP lesions, the TASC distribution was A, 42 %; B, 23 %; C, 4 %; and D, 15 %. The average lesion treatment length was 9.4 +/- 10.6 cm (range of 1 to 40), and the run-off score was 5.1 +/- 3.5. For tibial lesions, the TASC distribution was A, 0 %; B, 17 %; C, 8 %; and D, 75 %. The average lesion treatment length was 9.2 +/- 6.0 cm (range of 2 to 20), with a run-off score of 5.4 +/- 2.4. A total of 39 % of patients had prior IF interventions. Adjunctive angioplasty of the atherectomized lesion was performed in 55 % of cases, stenting in 0 %, and adjunctive therapy for tandem lesions in 39 %. The post-operative ankle-brachial index increased by 0.30 +/- 0.14 and toe pressures increased by 40 +/- 32.4 mm Hg. Mean follow-up was 10 +/- 8 months (range of 0.3 to 23). During the studied period, 7 patients required major limb amputation and 5 open surgical re-vascularization. Total primary and secondary patency rates were 66 % and 70 % at 1 year, respectively. Primary and secondary patency rates for FP atherectomy were 68 % and 73 % at 1 year, respectively. The limb salvage rate was 74 % at 6 months. Patients with prior interventions in the atherectomized segment had an almost 10-fold decrease in primary patency. Atherectomy produces acceptable results, similar to those in reported series of conventional balloon angioplasty/stenting. Patients with prior IF interventions had a nearly 10-fold decrease in primary patency. A greater than 6-fold decrease in patency rates was noted in patients who underwent simultaneous inflow or outflow procedures, but this finding did not reach statistical significance (p = 0.082). The authors stated that future studies should focus on
cost comparisons with other treatments such as angioplasty and stenting, and prospective randomized trials should be performed to compare these treatment alternatives.

Garcia and Lyden (2009) noted that compared to conventional percutaneous transluminal angioplasty (PTA) and stent implantation for arterial occlusive diseases, atherectomy offers the theoretical advantages of eliminating stretch injury on arterial walls and reducing the rate of restenosis. Historically, however, neither rotational nor directional atherectomy, whether used alone or with adjunctive PTA, has shown any significant long-term benefit over PTA alone in the coronary or peripheral arteries. However, the SilverHawk Plaque Excision System has produced positive results in single-center prospective registries of patients with FP and IF lesions, with reduced adjunctive PTA, minimal adjunctive stenting, and competitive 6-month and 12-month patency rates. In the observational non-randomized TALON (Treating Peripherals with SilverHawk: Outcomes Collection) registry, freedom from target lesion re-vascularization was 80 % for 87 patients at 12 months. Questions remaining for further research with this device include more accurate determination of an event rate for distal embolization, the appropriate use of distal protection, the value of and appropriate circumstances for adjunctive angioplasty, and definitive patency and clinical outcomes.

Indes et al (2010) evaluated the outcomes of atherectomy versus subintimal angioplasty (SIA) in patients with lower extremity arterial occlusive disease. From September 2005 through July 2006, 27 patients (17 women; mean age of 65 years, range of 37 to 85) underwent atherectomy of 46 lesions (11 TASC C/D occlusions) with the SilverHawk device. Results were compared to 67 patients (34 men; mean age of 69 years, range of 46 to 92) undergoing SIA for 67 lower extremity arterial occlusions from July 1999 through June 2004. Technical success in the atherectomy cohort was 100 %. In the 11 patients with occlusions, symptoms improved in 10 and worsened in 1, but 9 (82.0 %) of the 11 patients required re-intervention, and 8 (72.7 %) patients with occlusive lesions re-occluded. Endovascular re-intervention was required to maintain primary patency in only 2 (12.5 %) of 16 patients treated for stenotic lesions. At 1 year, the assisted primary patency was 37.7 % in the atherectomy group. In the 11 patients with occlusive lesions, the patency rates were 36.8 % and 12.3 % at 6 and 9 months, respectively, versus 100 % and 83.3 % at the same time intervals in patients with stenotic lesions. Subintimal angioplasty was technically successful in 56 (83.6 %) of 67 occlusions. The assisted primary patency and limb salvage rates of the entire
group (intention-to-treat) at 12 and 24 months were 59.2 \% and 45.0 \%, respectively, while the assisted primary patency of the 56 technically successful SIAs at 12 and 24 months were 70.7 \% and 53.8 \%, respectively. Limb salvage for the entire group (intention-to-treat) was 90.6 \% and 87.9 \% at 12 and 24 months, respectively. The authors concluded that atherectomy may yield acceptable primary patency and limb salvage in patients with stenotic lesions. Many of the patients treated for occlusive lesions require re-intervention. Based on patency and limb salvage, SIA appears superior to atherectomy for the treatment of lower extremity occlusive disease.

Sixt and co-workers (2010) reported the acute and long-term outcome of Silverhawk-assisted atherectomy for femoro-popliteal lesions. In this prospective study, de novo and re-stenotic lesions of the femoro-popliteal segments were treated with the Silverhawk device. A total of 161 consecutive patients (164 lesions) with PAD Rutherford classes 2 to 5 were included from June 2002 to October 2004 and October 2006 to June 2007 (59 \% male, mean age of 67 +/- 11 years, range of 40 to 88) and the outcome analyzed according to the TASC II classification. Directional atherectomy alone was performed successfully in 28 \% (n = 46), adjunctive balloon angioplasty in 65 \% (n = 107) and stenting in 7 \% (n = 11). The overall technical success rate was 76 \% (124/164) and the procedural success rate 95 \% (154/164). At 12 months primary patency rate was 61 \% (85/140) and the secondary patency rate was 75 \% (105/140) in the entire cohort, being less favorable in TASC D compared to TASC A to C lesions (p = 0.034 and p < 0.001, respectively). Furthermore, the re-stenosis rate differed trendwise (p = 0.06) between de novo and re-stenotic lesions. Changes in the ankle-brachial index (ABI) and the Rutherford classes were significantly in favor of TASC A to C lesions compared to TASC D after 12 months (p = 0.004). The event free survival (myocardial infarction, transient ischemic attack, or re-stenosis) was 48 \% at 12 months and 38.5 \% at 24 months. Predictor for re-stenosis in the multi-variable analysis was only male gender (p = 0.04). The authors concluded that the results in TASC D lesions are inferior to those in the lesser stages. Directional atherectomy of femoro-popliteal arteries showed a trend to better long-term technical and clinical outcome in de novo lesions compared to re-stenotic lesions.

Jaff et al (2010) analyzed therapeutic strategies, outcomes, and medical cost of treatment among Medicare patients with PAD. Patients who underwent therapy for PAD were identified from a 5 \% random sample of Medicare beneficiaries from Medicare Standard Analytic Files for the period 1999 to 2005. Clinical outcomes
(death, amputation, new clinical symptoms related to PAD) and direct medical costs were examined by chosen re-vascularization options (endovascular, surgical, and combinations). One-year PAD prevalence increased steadily from 8.2 % in 1999 to 9.5 % in 2005. The risk-adjusted time to first post-treatment clinical outcome was lowest in those treated with PTA or atherectomy and stents (hazard ratio [HR], 0.829; 95 % confidence interval [CI]: 0.793 to 0.865; p < 0.001) and stents only (HR, 0.904; 95 % CI: 0.848 to 0.963; p = 0.002) compared with PTA alone. The lowest per patient risk-adjusted costs during the quarter of the first observed treatment were associated with "PTA and stents" ($15,197), and stents only ($15,867). Risk-adjusted costs for surgical procedures (bypass and endarterectomy) were $27,021 during the same period. Diabetes was present in 61.7 % of the PAD population and was associated with higher risks of clinical events and higher medical costs compared with PAD patients without diabetes. The authors concluded that clinical and economic burden of PAD in the Medicare population is substantial, and the interventions used to treat PAD are associated with differences in clinical and economic outcomes. They stated that prospective cost-effectiveness analyses should be included in future PAD therapy trials to inform payers and providers of the relative value of available treatment options.

Guidance from the National Institute for Health and Clinical Excellence (NICE, 2011) concluded that "current evidence on the efficacy of percutaneous atherectomy of femoropopliteal arterial lesions with plaque excision devices is inadequate in quality. Evidence on safety is inadequate, specifically with regard to the risk of distal embolisation. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research." The NICE guidance stated that further research into percutaneous atherectomy of femoropopliteal arterial lesions with plaque excision devices should take the form of well-conducted trials, which should define patient selection, treatment protocols and location and types of arterial lesions treated, and report long-term patency outcomes.

An interventional procedure consultation document on percutaneous laser atherectomy for peripheral arterial disease from the National Institute for Health and Clinical Excellence (2011) concluded: "The evidence on percutaneous laser atherectomy for peripheral arterial disease raises no major safety concerns. Current evidence on its efficacy is inadequate in quantity and quality (in particular, the technical indications for the procedure are not well described in the published literature). Therefore, this procedure should only be used with special
arrangements for clinical governance, consent and audit or research." The consultation document stated that further research should describe the criteria for selection of patients and report clearly whether percutaneous laser atherectomy was used instead of conventional balloon angioplasty (and the reasons for this) or whether balloon angioplasty was attempted but found not to be feasible. In addition, reports should specify whether the procedure was used alone to recanalize arteries or with adjunctive balloon angioplasty and/or stenting. When percutaneous laser atherectomy is used instead of balloon angioplasty, then studies should compare the outcomes of the two procedures. Reported outcomes should include objective evidence of arterial patency and blood flow in addition to clinical effects. The consultation documents noted that long-term follow-up (2 years and beyond) would be useful.

Guidance from the National Institute for Health and Clinical Excellence (NICE, 2012) on percutaneous laser angioplasty concluded: "Current evidence on the efficacy and safety of percutaneous laser atherectomy as an adjunct to balloon angioplasty (with or without stenting) for peripheral arterial disease is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit." The guidance stated that patient selection should be carried out by a vascular multidisciplinary team including a vascular surgeon and a vascular interventional radiologist. The guidance stated that the multidisciplinary team should consider carefully whether using percutaneous laser atherectomy as an adjunct to balloon angioplasty (with or without stenting) for peripheral arterial disease is likely to have any benefits over conventional recanalization by balloon angioplasty (with or without stenting) alone. The specialist advisers to NICE listed key efficacy outcomes as an increase in arterial diameter and blood flow, tissue healing, symptom relief, improvement in quality of life, amputation-free survival and reintervention rates. The NICE committee noted that much of the evidence on this procedure is not recent, and that a limited amount of the older evidence described using laser alone for atherectomy but more recent evidence focused on its use as an adjunct to balloon angioplasty (with or without stenting). This more recent evidence and the advice of specialists underpinned the decision to evaluate laser recanalization as an adjunctive procedure. The NICE guidance noted, while the committee considered the evidence adequate to recommend normal arrangements for the use of percutaneous laser atherectomy as an adjunct to balloon angioplasty (with or without stenting), it remained uncertain about whether its use confers any advantages over balloon angioplasty alone and, if so, in which patients.
The Trellis® Peripheral Infusion System has been developed as a percutaneous mechanical thrombectomy treatment for deep vein thrombosis (DVT) that does not respond adequately to anticoagulant and/or thrombolytic therapy. This system consists of a specially designed catheter that is connected to a handheld motorized control unit. Guided by ultrasonographic images, the Trellis catheter is inserted into an appropriate vein and advanced to the thrombosis. A guidewire is threaded through the clot; next the catheter is advanced into the clot so that the distal end of the catheter passes completely through the clot but the proximal end of the catheter does not enter the clot. At this point in the procedure, balloons in the proximal and distal ends of the catheter are inflated to seal off the section of the vein containing the clot, a thrombolytic agent is injected through the catheter into the clot, and the motor is activated, which causes rotation of a sinusoidally shaped wire that lies between the inflated balloons. The combined action of the thrombolytic agent and rotating wire disrupt the clot, and the disrupted material can be aspirated through the catheter. After clot removal, the balloons are deflated and the catheter is removed. The procedure using the Trellis system has been referred to as isolated segmental pharmacomechanical thrombolysis.

The Trellis Infusion System received FDA 515(k) clearance (K013635) on December 11, 2002. According to the clearance summary, the Trellis Infusion System is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature.

The Trellis Plus Infusion System received 510(k) clearance (K021958) on July 3, 2002. The system is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature.

The Trellis Reserve Infusion System received 510(k) clearance (K023514) on December 2, 2002. The Trellis™ Reserve Infusion System is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature.

A "Modification to the Trellis Reserve Infusion System" received 510(k) clearance (K032261) on August 22, 2003. According to the clearance summary, the Trellis™ Reserve Infusion System is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. The Trellis Reserve Infusion System is equivalent to the predicate product, the original Trellis Reserve Infusion System. The indications for use, function, methods
of manufacturing, and materials used are substantially equivalent. Bacchus Vascular, Inc. believes the Trellis Reserve Infusion System is substantially equivalent to existing legally marketed devices.

The Trellis-8 Peripheral Infusion System received 510(k) clearance (K050147) on February 3, 2005. According to the clearance summary the Trellis™-8 Peripheral Infusion System is intended for controlled and selective infusion of physician specified fluids, including thrombolytics, into the peripheral vasculature.

The Trellis-6 Peripheral Infusion System received 510(k) clearance (K071664) on July 13, 2007. According to the clearance summary the Trellis™-6 Peripheral Infusion System is intended for controlled and selective infusion of physician specified fluids, including thrombolytics, into the peripheral vasculature. The system enables the physician to isolate a treatment region, infuse a physician-specified fluid, and disperse the fluid by means of oscillation of a Dispersion Wire. The Isolation/Infusion component is a multi-lumen catheter with two compliant balloons at the distal end and infusion holes located between these balloons. The device also has a central through-lumen that is compatible with a 0.035" guidewire. The Dispersion Wire provides oscillation when activated. The Dispersion Wire is connected to an integral Oscillation Drive Unit that oscillates the Dispersion Wire within the isolated region to further disperse the infused fluid. If desired by the physician, post procedure aspiration of the isolated area between the occluding balloons may be accomplished through the catheter by using the guidewire lumen.

Papantoniou et al (2013) stated that Paget-Schroetter syndrome (PSS) is a rare form of thoracic outlet syndrome caused by axillo-subclavian vein thrombosis that typically presents in healthy young adults. Prompt therapy, traditionally by means of catheter-directed thrombolysis (CDT) prior to definitive surgery, can prevent the subsequent onset of post-thrombotic syndrome (PTS) and considerable disability. As CDT is associated with major hemorrhage and high overall treatment cost, pharmaco-mechanical thrombectomy (PMT) seems to be an attractive alternative that combines pharmacological thrombolysis with mechanical clot disruption. The Trellis-8 peripheral infusion catheter is an example of such a treatment, which provides topical thrombolysis in an isolated zone. These investigators described the use of the Trellis-8 PMT system in the successful management of 3 patients with PSS.
Furthermore, an UpToDate review on “Primary (spontaneous) upper extremity deep vein thrombosis” (Goshima, 2014) states that “Mechanical thrombolysis (e.g., Trellis, AngioJet, EKOS catheter) is often used in combination with pharmacologic thrombolysis. There are limited data involving the use of these devices to treat upper extremity thrombosis”. Moreover, mechanical thrombolysis is not mentioned in the “Summary and Recommendations” of this review.

In a Cochrane review, Wasiak and colleagues (2012) examined the effects of percutaneous transluminal coronary rotational atherectomy (PTCRA) for coronary artery disease in patients with non-complex and complex lesions (e.g., ostial, long or diffuse lesions or those arising from in-stent re-stenosis) of the coronary arteries. For the original review, these investigators searched the Heart Group Specialised Register; The Cochrane Library to Issue 2, 2001; and MEDLINE, CINAHL, EMBASE and Current Contents to December 2002 and reviewed reference lists for relevant articles. For the current review, they searched the same registries from 2002 to 2012 and reviewed reference lists for relevant articles. These researchers included randomized and quasi-randomized controlled trials of PTCRA compared with placebo, no treatment or another intervention and excluded cross-over trials. Two review authors independently extracted data and assessed the risk of bias of the studies identified. Data were extracted independently by 2 review authors. They asked authors of trials to provide information when missing data were encountered. Statistical summaries used risk ratios (RR) and weighted mean differences. These researchers included 12 trials enrolling 3,474 patients. The overall risk of bias was unclear for the majority of articles due to a lack of reported data; however, the authors determined that this would be unlikely to impact negatively as most data outcomes were objective (e.g., death versus no death). There was no evidence of the effectiveness in improving patient outcomes of PTCRA in non-complex lesions. In complex lesions, there were no statistically significant differences in re-stenosis rates at 6 months (RR 1.05; 95% confidence interval (CI): 0.83 to 1.33) and at 1 year (RR 1.21; 95% CI: 0.95 to 1.55) in those receiving PTCRA with adjunctive balloon angioplasty (PTCA) (PTCRA/PTCA) compared to those receiving PTCA alone. Morphological characteristics distinguishing complex lesions have not been examined in parallel-arm randomized controlled trials. The evidence for the effectiveness of PTCRA in in-stent re-stenosis was unclear. Compared to angioplasty alone, PTCRA/PTCA did not result in a statistically significant increase in the risk of major adverse cardiac events (myocardial infarction (MI), emergency cardiac surgery or death) during the in-hospital period (RR 1.27; 95% CI: 0.86 to 1.90). Compared to angioplasty, PTCRA
was associated with 9 times the risk of an angiographically detectable vascular spasm (RR 9.23; 95 % CI: 4.61 to 18.47), 4 times the risk of perforation (RR 4.28; 95 % CI: 0.92 to 19.83) and about twice the risk of transient vessel occlusions (RR 2.49; 95 % CI: 1.25 to 4.99) while angiographic dissections (RR 0.48; 95 % CI: 0.34 to 0.68) and stents used as a bailout procedure (RR 0.29; 95 % CI: 0.09 to 0.87) were less common. The authors concluded that when conventional PTCA is feasible, PTCRA appears to confer no additional benefits. There is limited published evidence and no long-term data to support the routine use of PTCRA in in-stent re-stenosis. Compared to angioplasty alone, PTCRA/PTCA did not result in a higher incidence of major adverse cardiac events, but patients were more likely to experience vascular spasm, perforation and transient vessel occlusion. In certain circumstances (e.g. patients ineligible for cardiac surgery, those with architecturally complex lesions, or those with lesions that fail PTCA), PTCRA may achieve satisfactory re-vascularization in subsequent procedures.

An UpToDate review on “Specialized revascularization devices in the management of coronary heart disease” (Cutlip, 2014) states that “Rotational atherectomy summary -- The American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) guideline update for PCI concluded that there is no evidence that rotational atherectomy improves late outcomes in lesions that can be safely treated with stenting or angioplasty alone. When rotational atherectomy is being considered, the weight of evidence or opinion was in favor of the efficacy of IVUS for establishing the presence and distribution and coronary calcium. However, in our practices, IVUS is rarely used for this indication”.

Beschorner and Zeller (2014) stated that mechanical atherectomy for in-stent restenosis (ISR) appeared to be limited by a low patency rate. This might be due to the mechanical trauma that induces an inflammatory response leading to recurrent ISR. Addition of drug-eluting balloon (DEB) angioplasty could overcome these challenges while preserving the advantages of a better acute result. However, the authors concluded that due to lack of clinical data, combination of atherectomy and DEB remains an experimental procedure for ISR treatment.

In a multi-center, randomized non-inferiority trial, Baan and colleagues (2018) evaluated the relative performance of a DEB and a DES in patients with any (bare-metal or drug-eluting stent) ISR. Patients with any ISR were randomly allocated in a 1:1 fashion to treatment with a DEB or a DES. The primary end-point was non-
inferiority in terms of in-segment minimal lumen diameter (MLD) at 6-month angiographic follow-up. Secondary end-points included angiographic parameters at 6 months and clinical follow-up up to 12 months. A total of 278 patients, of whom 56 % had DES-ISR, were randomized at 8 sites to treatment with DEB (n = 141) or DES (n = 137). As compared with DEB, DES was associated with larger MLD and lower % stenosis immediately post-procedure (1.84 ± 0.46 versus 1.72 ± 0.35; p = 0.018; and 26 ± 10 % versus 30 ± 10%; p = 0.03). Angiographic follow-up was completed at 196 ± 53 days in 79 % of patients. With respect to the primary end-point of in-segment MLD at 6 months, DEB was non-inferior to DES (DEB 1.71 ± 0.51 mm versus DES 1.74 ± 0.61 mm; p for non-inferiority < 0.0001); TVR at 12-month follow-up was similar in both groups (DES 7.1 % versus DEB 8.8 %; p = 0.65). The authors concluded that in patients with ISR, treatment with DEB was non-inferior compared with DES in terms of 6-month MLD. There were no differences in clinical end-points, including TVR up to 12 months. Therefore, use of a DEB is an attractive therapeutic option for ISR, withholding the need for additional stent implantation. Longer follow-up data are needed to validate these findings.

Drug-Eluting (Drug-Coated) Balloons for the Treatment of Primary Lesion/Occlusion of Peripheral Arteries

The Australian Safety and Efficacy Registry of New Interventional Procedures’ Technology Brief on “Drug-eluting stents and balloons for the treatment of peripheral vascular disease” (2012) considered DEBs to be investigational.

In a meta-analysis, Yang and colleagues (2014) evaluated the clinical value of primary stenting for treating PADs in below-the-knee arteries by comparing to PTA. PubMed, ScienceDirect, Embase, and CBM databases were searched for relevant articles. Based on the different types of stents, these researchers divided the primary stent group into the bare metal stent (BMS) group and drug-eluting stent (DES) group. The outcome measures were immediate technical success, freedom from target vessel revascularization (TVR-free) rate and limb salvage. A total of 14 studies (published between 2001 and 2012) satisfying the inclusion criteria were identified; 3,278 patients and 3,699 limbs constituted the final study population. The technical success rate of PTA was 90.95 % (95 % CI: 86.25 % to 94.15 %). Only 1 study reported a technical failure of 4 % (5/118) in the primary stent group. There were no significant differences in the 1-year primary patency and TVR-free rates between the PTA group and BMS groups (p > 0.05 and p > 0.05), respectively. The pooled estimates of 1-year primary patency and TVR-free rate in
DES group were 85.05 % (95 % CI: 79.95 % to 89.02 %) and 90.52 % (95 % CI: 83.68 % to 94.67 %), respectively, which were better than those of the BMS (p < 0.001) and PTA groups (p < 0.001). The pooled estimate of 1-year limb salvage in the PTA, BMS, and DES groups was 88.41 % (95 % CI: 84.53 % to 91.43 %), 94.41 % (95 % CI: 89.52 % to 97.1 %), and 96.81 % (95 % CI: 94.04 % to 98.32 %), respectively. The BMS and DES groups had higher limb salvage rates than the PTA group (p < 0.001 for both comparisons). The rates of severe complications were low both in the PTA and primary stent groups. Although the influence analysis showed rather robust results, the heterogeneity was quite high and they were not adjusted for confounding variables. The authors concluded that primary BMS implantation had no advantage over PTA in reducing restenosis or revascularization for infra-popliteal disease; primary DES implantation appeared to be a promising treatment for focal infra-popliteal lesions. (The MeSH terms of this article included balloon).

In a Cochrane review, Chowdhury et al (2014) determined the effect of percutaneous transluminal angioplasty (PTA) compared with PTA with bare metal stenting (BMS) for superficial femoral artery (SFA) stenoses on vessel patency in people with symptomatic (Rutherford categories 1 to 6; Fontaine stages II to IV) lower limb peripheral vascular disease. In addition, these researchers assessed the efficacy of PTA and stenting in improving quality of life, ankle brachial index (ABI) and treadmill walking distance. For this update the Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator searched the Specialised Register (last searched August 2013) and the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 6, 2013). Randomized trials of angioplasty alone versus angioplasty with BMS for the treatment of superficial femoral artery stenosis were selected for analysis. Two review authors independently selected suitable trials, assessed trial quality and extracted data. Furthermore, these 2 review authors performed assessments of methodological quality and wrote the final manuscript. The third review author (ADM) cross-checked all stages of the review process. These investigators included 3 new studies in this update, making a total of 11 included trials with 1,387 participants. The average age was 69 years and all trials included men and women. Participants were followed for up to 2 years. There was an improvement in primary duplex patency at 6 and 12 months in participants treated with PTA plus stent over lesions treated with PTA alone (6 months: odds ratio (OR) 2.90, 95 % confidence interval (CI): 1.17 to 7.18, p = 0.02, 6 studies, 578 participants; 12 months: OR 1.78, 95 % CI: 1.02 to 3.10, p = 0.04, 9 studies, 858 participants). This was lost by 24 months (p = 0.06). There was a
significant angiographic patency benefit at 6 months (OR 2.49, 95 % CI: 1.49 to 4.17, p = 0.0005, 4 studies, 329 participants) which was lost by 12 months (OR 1.30, 95 % CI: 0.84 to 2.00, p = 0.24, 5 studies, 384 participants); ABI and treadmill walking distance showed no improvement at 12 months (p = 0.49 and p = 0.57, respectively) between participants treated with PTA alone or PTA with stent insertion. Three trials (660 participants) reported quality of life, which showed no significant difference between participants treated with PTA alone or PTA with stent insertion at any time interval. Anti-platelet therapy protocols and inclusion criteria regarding affected arteries between trials showed marked heterogeneity. The authors concluded that although there was a short-term gain in primary patency there was no sustained benefit from primary stenting (PS) of lesions of the superficial femoral artery in addition to angioplasty. Moreover, they stated that future trials should focus on quality of life for claudication and limb salvage for critical ischemia.

Antoniou et al (2014) examined if treatment of infra-inguinal arterial occlusive disease with drug-eluting stents (DESs) provided improved outcomes compared with BMSs or PTA alone. Altogether, 136 papers were found using the reported searches, of which 5 provided the best evidence to answer the question. All papers represent either level 1 or 2 evidence. The authors, journal, date, country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. Main outcome measures varied among the studies, and included patency, in-stent restenosis, target lesion revascularization, major adverse events, clinical improvement and limb salvage. Evidence on the comparative efficacy of DESs in femoro-popliteal arterial disease is mainly based on 2 randomized, controlled trials (RCTs). Paclitaxel-eluting stents were evaluated in the Zilver PTX trial and demonstrated superior 2-year results to either BMSs or PTA, as indicated/shown by patency (DES versus PTA, 74.8 versus 26.5 %, p < 0.01), clinical benefit (DES versus PTA, P < 0.01) and event-free survival (DES vs PTA, 86.6 vs 77.9%, P = 0.02). However, the SIROCCO trial found that the sirolimus-eluting stent did not exhibit statistically significant differences in 2-year in-stent re-stenosis (22.9 versus 21.1 %) and target lesion re-vascularization (6 versus 13 %) compared with the BMS. Treatment of infra-politeal arterial disease with DESs was related with superior outcomes to those of BMSs, as indicated/shown by patency, freedom from target lesion revascularization and freedom from major adverse events. Furthermore, the ACHILLES trial, the only published trial comparing the infra-politeal DES with PTA, revealed lower angiographic restenosis (22.4 versus 41.9 %, p = 0.019) and greater vessel patency (75 versus
57.1 %, p = 0.025) in the DES group at 1 year. However, data related to clinical parameters in patients with critical limb ischemia secondary to infra-geniculate arterial disease, such as limb salvage and ulcer healing, are insufficient. The authors concluded that treatment of infra-inguinal arterial disease with DES was safe and appeared to be superior to treatment with PTA alone or BMS. They stated that the role of DES in sustained improvement in clinical outcome end-points, such as limb salvage, remains to be elucidated.

There is Cochrane “protocol” to evaluate the effectiveness of DEBs compared with non-stenting balloon angioplasty in patients with symptomatic lower-limb PAD (Kayssi et al, 2014).

Limpijankit (2015) stated that “Over the past decade, drug-coated balloons (DCBs) have emerged as an exciting new therapeutic option to prevent restenosis in the treatment of peripheral vascular disease …. In this year, 3 major pivotal trials have confirmed the safety and efficacy of paclitaxel-coated balloons in the endovascular treatment of femoropopliteal artery disease. These are the Drug-Coated Balloon Versus Standard Percutaneous Transluminal Angioplasty for the Treatment of Superficial Femoral and/or Popliteal Peripheral Artery Disease (IN.PACT SFA) trial, the Lutonix Paclitaxel-Coated Balloon for the Prevention of Femoropopliteal Restenosis 2 (LEVANT 2) trial, and 5-year follow-up of the Local Taxan With Short Time Contact for Reduction of Restenosis in Distal Arteries (THUNDER) trial …. Although the initial findings are encouraging, long-term follow-up will be useful in determining whether the benefit of these new devices is sustained, increased, or attenuated over time. In the LEVANT 2 trial, the primary patency endpoint from the Kaplan-Meier curves seem to drop distinctly in the Lutonix arm after 12 months, while the control arm remained unchanged …. although DCBs are generally safe and superior to standard balloon angioplasty, there are many unanswered questions about DCB technology. The results of these trials cannot be generalized to patients not included in these trials. Future studies should be performed in longer lesions, densely calcified lesions, or in-stent restenosis, and consider comparison with bare metal stents and drug-eluting stents. Trials combining DCBs with atherectomy (Atherectomy Followed by a Drug Coated Balloon to Treat Peripheral Arterial Disease [DEFINITIVE AR] trial) are being conducted to clarify if there is an additive effect. Another inconclusive issue is the appropriateness use of these devices. Which patient should be a good candidate for using these DCBs as the first-line therapy instead of standard balloon? In order to justify their broad use, the DCBs must show reduction in repeat revascularization, cost benefit, and
improving quality of life. Another concern is the learning curve of how to use the DCBs to ensure proper uptake of the drug and minimize downstream drug loss. This is important to maximize the results of treatment. Post-approval study is also suitable for longer-term follow-up, which is certainly needed to confirm the durability of the benefit”.

In a Cochrane review, Bekken et al (2015) examined the effects of PTA versus PS for stenotic and occlusive lesions of the iliac artery. The Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator searched the Specialised Register (last searched April 2015) and Cochrane Register of Studies (CRS) (Issue 3, 2015). The TSC searched trial databases for details of ongoing and unpublished studies. These researchers included all RCTs comparing PTA and primary stenting for iliac artery occlusive disease. They excluded quasi-randomized trials, case reports, case-control or cohort studies. They excluded no studies based on the language of publication. Two authors independently selected suitable trials. JB and HJ independently performed data extraction and trial quality assessment. When there was disagreement, consensus would be reached first by discussion among both authors and, if still no consensus could be reached, through consultation with BF. These investigators identified 2 RCTs with a combined total of 397 participants as meeting the selection criteria. One study included mostly stenotic lesions (95 %), whereas the second study included only iliac artery occlusions. Both studies were of moderate methodological quality with some risk of bias relating to selective reporting and non-blinding of participants and personnel. The overall quality of evidence was low due to the small number of included studies, the differences in study populations and definitions of the outcome variables. Due to the heterogeneity among these 2 studies it was not possible to pool the data. Percutaneous transluminal angioplasty with selective stenting and primary stenting (PS) resulted in similar improvement in the stage of peripheral arterial occlusive disease according to Rutherford’s criteria, resolution of symptoms and signs, improvement of quality of life, technical success of the procedure and patency of the treated vessel. Improvement in walking distance as reported by the patient, measured claudication distance, ulcer healing, major amputation-free survival and delayed complications (greater than 72 hours) were not reported in either of the studies. In 1 trial, PTA of iliac artery occlusions resulted in a significantly higher rate of major complications, especially distal embolization. The other trial showed a significantly higher mean ABI at 2 years in the PTA group (1.0) compared to the mean ABI in the PS group (0.91); mean difference (MD) 0.09 (95 % CI: 0.04 to 0.14; p value = 0.001, analysis performed by review authors). However, at other
time-points there was no difference. These researchers considered it unlikely that this difference was attributable to the study procedure, and also believed this difference may not be clinically relevant. The authors concluded that there is insufficient evidence to assess the effects of PTA versus PS for stenotic and occlusive lesions of the iliac artery. From 1 study it appeared that PS in iliac artery occlusions may result in lower distal embolization rates. They stated that more studies are needed to come to a firm conclusion.

Furthermore, an UpToDate review on “Percutaneous interventional procedures in the patient with lower extremity claudication” (Zaetta et al, 2016) states that “Drug-eluting balloons -- A number of medical therapies aimed at preventing restenosis after femoral PTA have been tried, but only local delivery of paclitaxel has been shown to improve outcomes. Local delivery of paclitaxel was initially studied in the coronary circulation, but subsequently drug-eluting balloons (e.g., Lutonix, IN.PACT Admiral) have been approved for use in the United States as a means to deliver paclitaxel and have been used in the femoropopliteal segment. Whether the reduced number of interventions that results offsets the additional expense of the drug-coated balloon remains to be determined”.

Herten et al (2016) stated that PAD, particularly critical limb ischemia, is an area with urgent need for optimized therapies because; to-date, vascular interventions often have limited life spans. In spite of initial encouraging technical success after femoro-popliteal percutaneous transluminal angioplasty or stenting, post-procedural re-stenosis remains the major problem. The challenging idea behind the DCB concept is the biological modification of the injury response after balloon dilatation. Anti-proliferative drugs administered via DCBs or drug-eluting stents are able to suppress neointimal hyperplasia, the main cause of re-stenosis. These investigators reviewed the results of DCB treatments of femoro-popliteal and infra-popliteal lesions in comparison to standard angioplasty with uncoated balloons. A systematic literature search was performed in (i) medical journals (i.e., Medline), (ii) international registers for clinical studies (i.e., www.clinicaltrials.gov), and (iii) abstracts of scientific sessions. Several RCTs with follow-up periods of up to 5 years demonstrated the effectiveness of paclitaxel-DCB technology. However, calcified lesions appeared to affect the effectiveness of DCB. Combinations of pre-conditioning methods with DCBs showed promising results. Although the mechanical abrasion of calcium via atherectomy or laser ablation showed favorable peri-procedural results, the long-term impact on re-stenosis and clinical outcome has to be demonstrated. Major advantages of the DCBs are the rapid delivery of
drug at uniform concentrations with a single dose, their effectiveness in areas wherein stents have been contraindicated until now (i.e., bifurcation, ostial lesions), and in leaving no stent scaffold behind. Re-interventions are easier to perform because DCBs leave no metal behind. The authors concluded that various combinations of DCBs with other treatment modalities may prove to be viable options in future; there is still a lack of respectable prospective long-term data to state the long-term superiority of one DCB technology.

Steiner et al (2016) examined patient outcomes following the use of the Lutonix DCB in patients undergoing endovascular intervention in below-the-knee (BTK) arteries. A retrospective chart review identified 248 patients who were treated for symptomatic PAD with the Lutonix DCB between May 2013 and October 2014. A total of 40 patients were lost to follow-up, leaving 208 patients (mean age of 74.1±9.7 years; 138 men) with evaluable data for outcome analysis. The patient cohort suffered from either severe claudication (38.6 %) or critical limb ischemia (CLI; 61.4 %) in 220 limbs. Almost 2/3 (140, 63.6 %) of the 220 target lesions were total occlusions, and 37 (17.8 %) of all patients had occlusion of all 3 BTK vessels before intervention. Over a median 9-month follow-up, TLR occurred in 15.9 % of patients with an average time to first re-intervention of 8 months. In total, 39 amputations were performed in 31 limbs. However, 17 of these amputations were pre-planned minor amputations below the ankle; only 9 (4.1 %) major amputations occurred corresponding to 6.6 % of the CLI cohort. Freedom from the composite of death or major amputation was estimated as 92 % and 85 % at 6 and 12 months, respectively, by Kaplan-Meier analysis. In the full cohort, improvement of at least 1 Rutherford category was seen in 130 (59.1 %) limbs after 1 year or at the last follow-up, with 104 (80.0 %) of those limbs showing an improvement of greater than or equal to 2 categories. The authors concluded that from this single-center experience, the Lutonix DCB showed therapeutic promise in a disease state where new treatment options are needed.

In a prospective, single-center, non-randomized study, Werner et al (2016) evaluated the safety and effectiveness of the Igaki-Tamai biodegradable scaffold after DEB angioplasty in patients with occlusive SFA disease. A total of 20 patients (mean age 66.7 ± 11.6 years; 14 men) with symptomatic de-novo SFA lesions undergoing angioplasty with the In.Pact Admiral paclitaxel-coated balloon and subsequent implantation of the Igaki-Tamai bioresorbable scaffold were included in this study. All patients were claudicants. The average diameter stenosis was 89.7 %, and the mean length was 43.6 mm. Clinical examinations with duplex sonography were performed after 1, 6, 9, and 12 months. The main study
outcomes were technical success, re-stenosis, TLR, ABI improvement, and changes in quality of life (QOL) evaluated with the walking impairment questionnaire. Safety was assessed by monitoring the occurrence of AEs. Angioplasty with a paclitaxel-coated balloon was performed in all patients, resulting in an average diameter stenosis of 24%. Subsequent implantation of the Igaki-Tamai scaffold reduced the average diameter stenosis to 3.5%. In the first 6 months, 2 cases of re-stenosis were reported, with no TLRs within that period. However, by the 12-month follow-up in 19 patients, 11 patients had lost in-stent patency. Among these patients, 8 had TLRs, which were the only AEs recorded that were referable to the procedure; QOL assessments showed improvement in the majority of patients. The authors concluded that the findings of the GAIA-DEB study showed that DEB treatment of the femoral artery prior to the implantation of the biodegradable Igaki-Tamai scaffold was safe; however, the anti-proliferative actions of paclitaxel in the vessel wall were not effective in preventing re-stenosis, which occurred predominantly after 6 months.

Grotti et al (2016) reported the 3-year safety and effectiveness outcomes from the prospective all-comers DEBATE-ISR study of symptomatic diabetic patients with femoro-popliteal ISR undergoing treatment with paclitaxel-eluting balloons compared with historical diabetic controls. From January 2010 to December 2011, a total of 44 consecutive diabetic patients (mean age of 74 ± 11 years; 32 men) were treated with DEBs and enrolled in the study. The control group comprised 42 consecutive diabetic patients (mean age 76 ± 7 years; 23 men) treated with conventional balloon angioplasty (BA) from 2008 to 2009. No significant differences in terms of clinical, angiographic, or procedural characteristics were observed between the study groups; CLI was present in the majority of patients. Tosaka class III ISR was observed in more than 50% of the patients. Mean lesion length was 132 ± 86 and 137 ± 82 mm in the DEB and BA groups, respectively (p = 0.7). At 3-year follow-up, the rate of TLR was 40% in the DEB group versus 43% in the BA group (p = 0.8); Kaplan-Meier analysis showed no significant differences in terms of freedom from TLR. The presence of a Tosaka class III occlusion was associated with a worse outcome in both study groups (OR 3.96, 95% CI: 1.55 to 10.1, p = 0.004). The authors concluded that using DEBs for femoro-popliteal ISR yielded similar results to BA in terms of TLR at 3-year follow-up. The treatment of more complex ISR lesions was associated with an increased rate of TLR, irrespective of the technology used.
In a Cochrane review, Kayssi et al (2016) evaluated the effectiveness of DEBs compared with uncoated, non-stenting balloon angioplasty in people with symptomatic lower-limb PAD. The authors concluded that based on a meta-analysis of 11 trials with 1,838 participants, there is evidence of an advantage for DEBs compared with uncoated balloon angioplasty in several anatomic end-points (e.g., primary vessel patency [high-quality evidence], binary restenosis rate [moderate-quality evidence], and target lesion revascularization [low-quality evidence] for up to 12 months). On the other hand, there is no evidence of an advantage for DEBs in clinical end-points (e.g., amputation, death, or change in ABI, or change in Rutherford category during 12 months' follow-up). They stated that well-designed randomized trials with long-term follow-up are needed to compare DEBs with uncoated balloon angioplasties adequately for both anatomic and clinical study end-points before the widespread use of this expensive technology can be justified. An editorial (Richards, 2017) noted: "Advances in technology continue relentlessly, but not necessarily for patient benefit? This meta-analysis highlights this problem; 11 trials compared drug eluting angioplasty technology compared to simple angioplasty. Radiological results were better in the short to mid-term but there with no effect on any patient outcomes. Therefore, should the NHS use these devices? On-going NIHR HTA BASIL 2 & BASIL 3 trials are running to compare angioplasty (with or without drug coated balloons to surgical bypass."

In a prospective, single-arm, multi-center study, Schroeder et al (2015) evaluated the safety and effectiveness of the Stellarex DCB to inhibit re-stenosis in the superficial femoral and/or popliteal artery. This trial enrolled 50 patients with 58 lesions in the first cohort that needed pre-dilatation with an uncoated angioplasty balloon prior to inflation of the DCB. The primary effectiveness end-point was 6-month late lumen loss (LLL). The major secondary end-point was major AE (MAE) rate at 6 months, defined as cardiovascular death, amputation, and/or ischemia-driven TLR. The mean lesion length was 7.2 cm and baseline stenosis was 75.1 %. Calcification was present in 62.1 % of lesions and 12.1 % were occluded. Both end-points met their pre-specified performance goals; at 6 months, the MAE rate was 4 % and the mean LLL was 0.54 mm. The primary patency rate was 89.5 % at 12 months and 80.3 % at 24 months. The freedom from clinically-driven TLR rate, per Kaplan-Meier estimate, was 90.0 % at 12 months and 85.8 % at 24 months. Additionally, there were no amputations or cardiovascular deaths.
reported through 24 months. The authors concluded that the Stellarex DCB provided safe and durable clinical outcomes for treatment of femoropopliteal artery disease through 24 months.

The drawbacks of this study included the lack of randomization and small proportion of chronic total occlusions (CTOs; 12.1%). However, all occluded lesions were patent through 24 months, which suggested adequate effectiveness of this DCB in CTOs. These researchers stated that further assessment in complex disease is needed. The study also lacked objective criteria for the exclusion criterion “prohibitive” calcification, which may have left room for investigator bias. They stated that larger studies with robust designs are currently enrolling patients, including 2 RCTs and 1 global registry.

In a prospective, randomized, multi-center, single-blinded trial, Schroeder et al (2017a) evaluated the safety and effectiveness of a next-generation low-dose (2-µg/mm² surface dose of paclitaxel) DCB. Patients were randomized (3:1) to treatment with a low-dose DCB or an uncoated PTA balloon. The primary safety end-point was a composite of freedom from device- and procedure-related death through 30 days after the procedure and freedom from target limb major amputation and clinically driven TLR through 12 months after the procedure. The primary effectiveness end-point was primary patency at 12 months. Patients were randomized to treatment with a DCB (222 patients, 254 lesions) or uncoated PTA balloon (72 patients, 79 lesions) after successful pre-dilatation. Mean lesion length was 7.2 and 7.1 cm, and 19.2% and 19.0% of lesions represented total occlusions, respectively. The primary safety end-point was met, and superiority was demonstrated; freedom from a primary safety event was 94.1% (193 of 205) with DCB and 83.3% (50 of 60) with PTA, for a difference of 10.8% (95% CI: 0.9% to 23.0%). The primary effectiveness end-point was met, and superiority of DCB over PTA was achieved (83.9% [188 of 224] versus 60.6% [40 of 66]; p < 0.001). Outcomes with DCB were also superior to PTA per the Kaplan-Meier estimate for primary patency (89.0% versus 65.0% at 365 days; log-rank p < 0.001) and for rates of clinically driven TLR (5.9% versus 16.7%; p = 0.014). The authors concluded that superiority with a low-dose DCB for femoropopliteal interventions was demonstrated over PTA for both the safety and effectiveness end-points.
This study had several drawbacks. First, although the Clinical Events Committee, Data Safety and Monitoring Board, and core laboratory personnel were blinded to treatment, physicians were not blinded because of the visible coating on the DCB catheter. Secondly, these data cannot be generalized to other DCBs because head-to-head comparative trials have not been completed, and lastly, patients were selected with the use of strict inclusion and exclusion criteria; therefore, generalizability of these data to real-world cases may be limited.

In a prospective, multi-center, pilot study, Schroeder and colleagues (2017b) compared 2-year outcomes in patients treated with or without pre-dilatation prior to DCB angioplasty for symptomatic femoropopliteal lesions. This pilot study was conducted at 3 sites in Germany. It compared claudicants undergoing pre-dilatation with a bare PTA balloon before DCB (pre-dilatation group) with patients undergoing direct DCB (direct DCB group). Patients were followed for 2 years. Outcomes included late lumen loss at 6 months, and ABI, MAE, and primary patency at 2 years. A Clinical Events Committee and core laboratories analyzed AEs and angiographic/duplex images, respectively. Between December 2011 and November 2012, a total of 50 patients were enrolled to the pre-dilatation group (12 % total occlusions) and 28 to the direct DCB group (5 % total occlusions). Follow-up compliance at the 2 year visit was 88 % (n = 44) and 86 % (n = 24), respectively. Late lumen loss at 6 months was lower in the direct DCB group (0.03 ± 0.68 mm versus 0.54 ± 0.97 mm; p = .01); MAE over 2 years occurred in 7 (15 %) patients who underwent pre-dilatation and in 5 (19 %) after direct DCB. Mean ABI at 2 years was 0.94 ± 0.15 after pre-dilatation and 1.0 ± 0.12 after direct DCB. Over 2 years, primary patency (80.3 % versus 78.2 %; p = 0.55) was not statistically different between the groups. After propensity score adjustments, 2 year findings remained unchanged. The authors concluded that paclitaxel-coated PTA, with or without bare pre-dilatation, was effective over 2 years in symptomatic patients with femoropopliteal stenotic lesions; these findings should be considered preliminary and hypothesis-generating. Moreover, they stated that adequately powered RCTs of direct DCB use with or without pre-dilatation are needed to confirm these preliminary findings.

A major drawback of this study was its non-randomized sequential treatment allocation. Despite the use of propensity score co-variate adjustment, potentially confounding unmeasured variables (e.g., balloon inflation time) may introduce bias. These results may not be generalizable to total occlusions, which
represented less than 10% of lesions. Another main drawback of this pilot study was a small sample size (n = 28 in the DCB group) that was not specifically powered to detect clinically important differences between groups.

Krishnan and associates (2017) noted that DCB are a predominant revascularization therapy for symptomatic femoropopliteal artery disease. Due to differences in excipients, paclitaxel dose and coating morphologies, varying clinical outcomes have been observed with different DCBs. These investigators reported the findings of 2 studies investigating the pharmacokinetic (PK) and clinical outcomes of a new DCB in the treatment of femoropopliteal disease. In the ILLUMENATE Pivotal Study, a total of 300 symptomatic patients (Rutherford class 2 to 4), were randomized to DCB (n = 200) or PTA (n = 100). The primary safety end-point was freedom from device- and procedure-related death through 30 days, and freedom from target limb major amputation and clinically-driven TLR (CD-TLR) through 12-months. The primary effectiveness end-point was primary patency through 12-months. In the ILLUMENATE PK study, paclitaxel plasma concentrations were measured after last DCB deployment and at pre-specified times (1, 4, 24 hours and at 7 and 14 days post-procedure) until no longer detectable. In the Pivotal study, baseline characteristics were similar between groups; 50% had diabetes, 41% were women, mean lesion length was 8.3 cm and 44% were severely calcified. The primary safety end-point was met (92.1% for DCB versus 83.2% for PTA, p = 0.025 for superiority) and the primary patency rate was significantly higher with DCB (76.3% for DCB versus 57.6% for PTA, p = 0.003). Primary patency per Kaplan Meier estimates at day 365 was 82.3% for DCB versus 70.9% for PTA (p = 0.002). The rate of CD-TLR was significantly lower in the DCB cohort (7.9% versus 16.8%, p = 0.023). Improvements in ABI, Rutherford class, and QOL were comparable, but the PTA cohort needed twice as many revascularizations; PK outcomes showed all patients had detectable paclitaxel levels after DCB deployment that declined within the first hour (54.4 ± 116.9 ng/ml to 1.4 ± 1.0 ng/ml). The authors concluded that the Stellarex DCB demonstrated superior safety and effectiveness as compared to PTA, and plasma levels of paclitaxel fell to low levels within 1 hour.

These investigators noted that although occurring despite randomization, the higher prevalence of re-stenotic lesions in the PTA cohort may impact the study results. They stated that long-term follow-up is needed in determining the extended durability of the intervention. Moreover, they stated that outcomes from this trial
cannot be generalized to patients not included in this trial or to other DCBs; future studies should encompass adjunctive therapeutic options as well as optimal medical therapy and exercise.

Wu et al (2017) noted that several prospective controlled studies have evaluated the safety and effectiveness of drug-coated balloon angioplasty (DCBA) versus standard balloon angioplasty (POBA) for femoropopliteal ISR. These researchers performed a meta-analysis of prospective controlled trials to pool the results of these trials and obtain more reliable conclusions. Prospective controlled trials comparing DCBA versus POBA were searched through PubMed, Embase, the Cochrane Central Register of Controlled Trials, ISI Web of Knowledge, and relevant websites without language or publication date restrictions. The keywords were "drug-eluting balloon", "angioplasty", "femoropopliteal" and "in-stent restenosis". They selected recurrent ISR, freedom from CD-TLR, clinical improvement, ABI, and MAEs as the outcomes of this meta-analysis. Based on the inclusion criteria, these investigators identified 3 prospective clinical trials. The 1-year outcomes of DCBA and POBA were as follows: recurrent ISR (34.8 % versus 73.1 %, respectively; OR, 0.18; 95 % CI: 0.10 to 0.32, Z = 5.56, p < 0.00001), freedom from CD-TLR (82.2 % versus 54.1 %, respectively; OR, 4.20; 95 % CI: 2.05 to 8.61, Z = 3.92, p < 0.0001), clinical improvement (76.2 % versus 55.7 %, respectively; OR, 2.58; 95 % CI: 1.41 to 4.72, Z = 3.07, p = 0.002), ABI (MD, -0.04; 95 % CI: -0.13 to 0.04, Z = 1.01, p = 0.31), and MAEs (11.0 % versus 18.3 %, respectively; OR, 0.54; 95 % CI: 0.25 to 1.15, Z = 1.60, p = 0.002). The authors concluded that for femoropopliteal ISR, DCBA was associated with superior efficacy outcomes compared with POBA, with the same safety outcome after a 1-year follow-up. Moreover, they stated that multi-center and large-scale prospective controlled trials comparing DCBA with other endovascular strategies are needed to further evaluate the safety and effectiveness profiles of DCBA in the treatment of femoropopliteal ISR.

Andrassy et al (2017) stated that despite a constantly expanding spectrum of therapeutic options for lower limb artery disease, there is not yet a well-defined consensus on the specific type of endovascular treatment that is best suited. Clinical data on patients with femoropopliteal disease treated with DCBs have not been elaborated sufficiently, especially in the case of ISR. These researchers performed a systematic search of the medical databases (PubMed). Keywords such as "drug-coated balloons" (DCB), "drug-eluting balloons", "in-stent restenosis", "de novo stenosis", "angioplasty", "superficial femoral artery", "popliteal artery", "above the knee", "below the knee", "peripheral artery disease" (PAD) have
been used. Furthermore, data from reviews, original contributions regarding RCTs, observational studies, registries and single-center experiences have been included. Many trials have shown superiority for DCB over PTA-treatment alone in TASC IIA and TASC IIB femoropopliteal lesions. However, the currently available DCB systems are different in terms of efficacy and long-term outcomes depending on their mechanical and pharmacological features. Moreover, angiographic characteristics of femoropopliteal lesions classified by Tosaka seem to influence subsequent outcomes of DCB treatment. The authors concluded that there is still lack of reliable prospective long-term data regarding DCB technology.

In a meta-analysis, Candy et al (2017) reviewed all available literature to evaluate outcome of patients treated with DEBs compared with PTA through measuring the rate of TLR. These researchers performed an electronic search of the Medline, Scopus, Embase, Web of Science, and Cochrane Library databases. Articles reporting RCTs that compared treatment with DEBs versus PTA were selected for inclusion. A meta-analysis was performed by pooling data on rates of TLR, binary restenosis (BR), and LLL. The 10 included articles comprised a sample size of 1,292 patients. Meta-analysis demonstrated the rate of TLR in DEB-treated patients was significantly lower compared with patients treated with PTA at 6 months (OR, 0.24; 95 % CI: 0.11 to 0.53; p = 0.0004), 12 months (OR, 0.28; 95 % CI: 0.13 to 0.62; p = 0.002), and 24 months (OR, 0.25; 95 % CI: 0.10 to 0.61; p = 0.002). Decreased LLL and BR was demonstrated at 6 months in patients treated with DEBs compared with patients treated with PTA (MD, -0.74; 95 % CI: -0.97 to -0.51; p = 0.00001; OR, 0.34; 95 % CI: 0.23 to 0.49; p = 0.00001). The authors concluded that the findings of this meta-analysis demonstrated that treatment with DEBs compared with PTA resulted in reduced rates of re-intervention in patients with PAD. Moreover, they stated that comparison of DEBs to other emerging treatments to determine which method results in the lowest re-intervention rates and in the greatest improvement in QOL should be the focus of future trials.

In a systematic review and meta-analysis, Zhang et al (2017) evaluated the current available studies investigating outcomes of DEB and DES in the treatment of infrapopliteal artery disease. Multiple databases were systematically searched to identify studies investigating the outcomes of DEB and DES in the treatment of patients with infrapopliteal artery disease. The quality of studies was assessed by Cochrane Collaboration method. The demographic data, risk factors, outcomes, and anti-platelet strategy were extracted. A total of 9 studies were identified with 707 and 606 patients in DEB/DES and standard PTA/BMS group, respectively.
The risk of TLR (OR = 0.38, 95 % CI: 0.23 to 0.63, p < 0.01), re-stenosis rate (OR = 0.30, 95 % CI: 0.18 to 0.50, p < 0.01), and amputation rate (OR = 0.49, 95 % CI: 0.29 to 0.83, p < 0.01) significantly decreased in the DES group. The overall survival (OR = 0.86, 95 % CI: 0.56-1.32, P = .50) was similar in DES and standard PTA/BMS group; TLR (OR = 0.59, 95% CI: 0.32-1.09, P = .09), restenosis rate (OR = 0.49, 95% CI: 0.11-2.14, P = .35), amputation rate (OR = 1.32, 95 % CI: 0.51 to 3.40, p = 0.57), and overall survival (OR = 1.40, 95 % CI: 0.72 to 2.71, p = 0.32) were similar in DEB and standard PTA group. The authors concluded that the findings of this meta-analysis suggested that compared with standard PTA/BMS, DES may decrease the risk of CD-TLR, re-stenosis rate, and amputation rate without any impact on mortality. However, DEB has no obvious advantage in the treatment of infrapopliteal disease. Moreover, they stated that due to the limitations of this study, more RCTs, especially those for DEB, are needed.

Jongsma et al (2017) evaluated the effects of DEB angioplasty versus uncoated balloon (UCB) angioplasty to rescue infrainguinal autologous bypass grafts at risk (BAR). The study included all consecutive patients treated endovascularly for BAR from December 1, 2012, to July 31, 2015. As of April 1, 2014, the primary treatment of BAR was changed from UCBs to DEBs. Patients treated with DEBs were prospectively recorded in a database and retrospectively analyzed. Patients treated with UCBs were retrospectively collected from a historical cohort with a similar inclusion period length as the DEB cohort. The follow-up scheme did not differ between the 2 groups. The primary end-point was the combined end-point of freedom from recurrent stenosis or bypass occlusion; secondary end-points were primary assisted patency, secondary patency, technical success, major amputation, and mortality. A total of 21 patients were treated in the DEB group and 18 were treated in the UCB group. The 2 groups were evenly distributed in demographics, bypass, treatment, and lesion characteristics. No statistically significant differences were found in the combined end-point of freedom from recurrent stenosis and the occlusion rate after 1 year between the UCB group (77.8 %) and the DEB group (80.0 %; p = 0.76). After 1 year, the primary assisted patency rate was 88.2 % in the UCB group versus 95.2 % in the DEB group (p = 0.47), and the secondary patency rate was 94.1 % in the UCB group versus 95.2 % in the DEB group (p = 0.91). During follow-up, re-stenosis developed in 4 patients (22.2 %) in the UCB group and in 4 patients (19.0 %) in the DEB group (p = 9.80); 1 bypass (5.6 %) in the UCB group and 1 bypass (4.8 %) in the DEB group occluded during follow-up (p = 0.884). The authors concluded that DEBs and UCBs performed equally in the treatment of significant stenosis in infrainguinal autologous bypasses with regard to
freedom from re-stenosis or bypass occlusion, primary assisted patency, and secondary patency at 1 year. These investigators suggested using a less expensive UCB in the treatment of BAR.

The National Institute for Health and Care Excellence (NICE, 2016) evaluated the Lutonix drug-coated balloon for peripheral arterial disease. The Lutonix DCB is a paclitaxel-coated percutaneous transluminal angioplasty (PTA) catheter that is indicated for treating peripheral arterial disease (PAD). The briefing found that the key points from the evidence are from 2 randomized trials (citing LEVANT studies I and II; n=101 and 476) comparing the Lutonix DCB with standard angioplasty using non-coated balloons in patients with symptomatic femoropopliteal PAD. The Lutonix DCB showed significantly lower late lumen loss rates at 6 months post-procedure with a similar complication rate to standard balloon angioplasty. Two non-comparative, retrospective case series (citing Steiner et al. 2016 and Micari et al. 2016) indicate that the Lutonix DCB is a potentially viable treatment for below-the-knee PAD, with acceptable outcomes and safety rates. The briefing noted, however, that key uncertainties around the evidence are that the primary outcome of the 2 randomized studies is late lumen loss. This is considered to be a technical outcome so its clinical impact is unclear. The additional clinical evidence comprises retrospective non-comparative case series (n=246 and n=55).

An earlier assessment of drug-eluting balloons and stents for peripheral arterial disease by the Swedish Regional Health Technology Assessment Centre (HTA-centrum) (Falkenberg, et al., 2015) reached the following conclusions: "Despite almost 3,000 studied patients, no positive effects on patient-related outcomes have consistently been observed with drug eluting stents or balloons in the treatment of atherosclerotic disease of the lower extremities, compared with uncoated stents or balloons. Mortality rate within 12 months was reported to be between zero and 18 %, probably mainly related to the underlying general atherosclerotic disease. Commonly encountered SAEs are mortality, amputations, pseudo aneurysms and thrombosis. For patients with intermittent claudication (P1) due to below the knee lesions, it is uncertain whether there is little or no difference regarding mortality, restenosis or symptom severity with DES (sirolimus) compared with BMS. Very low certainty of evidence (GRADE +000). In patients with critical ischemia (P2) and lesions below the knee, DES (everolimus) may reduce restenosis compared with BMS. In the same patient group, DEB with paclitaxel compared with UCB may slightly reduce symptom severity (Rutherford score). Low certainty of evidence (GRADE ++00). Importantly, for patients with critical ischemia below the knee, in
Bajraktari and co-workers (2016) performed a meta-analysis to evaluate the clinical efficiency and safety of DEB compared with DES in patients with drug-eluting stent restenosis (DES-ISR). A systematic search was conducted and all RCTs and observational studies that compared DEB with DES in patients with DES-ISR were included. The primary outcome measure -- major adverse cardiovascular events (MACE) -- as well as individual events such as TLR, stent thrombosis (ST), MI, cardiac death (CD) and all-cause mortality, were analyzed. A total of 3 RCTs and 4 observational studies were included with a total of 2,052 patients. MACE (RR = 1.00, 95 % CI: 0.68 to 1.46, p = 0.99), TLR (RR = 1.15 [CI: 0.79 to 1.68], p = 0.44), ST (RR = 0.37[0.10 to 1.34], p = 0.13), MI (RR = 0.97 [0.49 to 1.91], p = 0.93) and CD (RR = 0.73 [0.22 to 2.45], p = 0.61) were not different between patients treated with DEB and with DES. However, all-cause mortality was lower in patients treated with DEB (RR = 0.45 [0.23 to 0.87, p = 0.019) and in particular when compared to only 1st generation DES (RR 0.33 [0.15 to 0.74], p = 0.007). There was no statistical evidence for publication bias. The authors concluded that the results of this meta-analysis showed that DEB and DES had similar efficacy and safety for the treatment of DES-ISR.

Basavarajaiah and colleagues (2016) compared DEBs versus 2nd-generation DES in the treatment of DES-ISR. These researchers evaluated all procedures between 2009 and 2011, involving DES-ISR that were treated either with DEB or 2nd-generation DES. The measured end-points during the follow-up period were CD, target-vessel MI, TLR, TVR, and MACE defined as composite of cardiac-death, TV-
MI, and TVR. A total of 247 patients (302 lesions) with DES-ISR were treated with either DEB (81 patients; 104 lesions) or 2nd-generation DES (166 patients; 198 lesions). The mean age of patients was 66.1 ± 9.4 years. There were higher numbers of patients with diabetes in the DEB group (DEB 47 % versus DES 33 %; p = 0.03). The mean length of DEB was significantly longer than the DES (35.4 versus 19.8 mm; p < 0.001). During the 12-month follow-up, there were no significant differences in the MACE rates (12.3 % versus 8.4 %; p = 0.3) and TLR rates (9.9 % versus 7.8 %; p = 0.6) between DEB and DES, respectively. On the multivariate analysis, use of DEB or DES was not the predictor of MACE (HR: 0.84, 95 % CI: 0.46 to 1.85; p = 0.6). There were no cases of definite or probable stent thrombosis in either group. The authors concluded that there were no significant differences in the clinical outcomes between DEB and 2nd-generation DES in the treatment of DES-ISR. They stated that these results should encourage operators to consider DEB in the treatment of DES-ISR, which offers certain advantages over DES.

Wang and associates (2017) evaluated the efficacy of DEB with DES in patients with ISR. Electronic databases were searched for RCTs and observational cohort studies which reported the clinical outcomes of using DEB comparing with DES implantation in patients with ISR. Clinical endpoints such as MACE, death, and MI were assessed. A total of 5 RCTs and 5 observational cohort studies with 962 patients in the DEB group and 908 patients in the DES group met inclusion criteria. There was no significant difference between DEB and DES in major clinical outcomes, such as MACE (OR 1.01; 95 % CI: 0.64 to 1.58; p = 0.97; I² = 0 %), all-cause death (OR 1.04; 95 % CI: 0.54 to 1.98; p = 0.91; I² = 0 %), cardiovascular death (OR 1.44; 95 % CI: 0.57 to 3.65; p = 0.44; I² = 0 %), stent thrombosis (OR 0.61; 95 % CI: 0.16 to 2.33; p = 0.47; I² = 0 %), and MI (OR 1.02; 95 % CI: 0.53 to 1.94; p = 0.96; I² = 0 %). DEB was associated with a significant increase in TLR (OR 1.54; 95 % CI: 1.10 to 2.15; p = 0.01; I² = 57 %). The authors concluded that treatment of ISR using DEB led to comparable clinical outcomes with DES implantation.

Drug-Eluting Balloon for Vein Grafts and Dialysis/Vascular Accesses

Bjorkman and colleagues (2017) analyzed outcomes of the first experiences with DEBs in native arteries, vein grafts, and vascular accesses. The study was also a pilot for the authors’ future prospective, randomized, and controlled studies regarding the use of DEBs in the treatment of the stenosis in bypass vein graft and
dialysis access. A total of 93 consecutive patients were retrospectively analyzed and 81 were included in the study. Inclusion criteria included at least 1 previous percutaneous angioplasty to the same lesion. Patients were divided into 3 groups according to the anatomical site of the lesion: (i) native lower limb artery, (ii) vein bypass graft, or (iii) vascular access. Time from the previous percutaneous angioplasty to the DEB was compared to the time from the DEB to end-point in the same patient. End-points included any new re-vascularization of the target lesion, major amputation, or new vascular access. The median time from the DEB to end-point was significantly longer than the median time from the preceding percutaneous angioplasty to DEB in all 3 groups. This difference was clearest in native arteries and vein grafts, whereas the difference was smaller from the beginning and disappeared over time in the vascular access group. No significant differences were seen between the groups with regard to smoking, antiplatelet regime, diabetes, Rutherford classification, or sex. The authors concluded that although the setup of this study had several limitations, the results suggested that there could be benefit from DEBs in peripheral lesions. Moreover, they stated that very little data have been published on the use of DEBs in vein grafts and vascular accesses, and randomized and controlled prospective studies are needed to further investigate this field.

Peripheral Atherectomy for Peripheral Arterial Disease

Mohand and colleagues (2018) stated that peripheral atherectomy has been shown to have technical success in single-arm studies, but clinical advantages over angioplasty and stenting have not been demonstrated, leaving its role unclear. These investigators described patterns of atherectomy use in a real-world U.S. cohort to understand how it is currently being applied. The Vascular Quality Initiative was queried to identify all patients who underwent peripheral vascular intervention from January 2010 to September 2016. Descriptive statistics were performed to analyze demographics of the patients, co-morbidities, indication, treatment modalities, and lesion characteristics. The intermittent claudication (IC) and CLI cohorts were analyzed separately. Of 85,605 limbs treated, treatment indication was IC in 51 % (n = 43,506) and CLI in 49 % (n = 42,099). Atherectomy was used in 15 % (n = 13,092) of cases, equivalently for IC (15 %; n = 6,674) and CLI (15 %; n = 6,418). There was regional variation in use of atherectomy, ranging from a low of 0 % in one region to a high of 32 % in another region. During the study period, there was a significant increase in the proportion of cases that used atherectomy (11 % in 2010 versus 18 % in 2016; p < 0.0001). Compared with non-
atherectomy cases, those with atherectomy use had higher incidence of prior peripheral vascular intervention (IC, 55 % versus 43 % \[p < 0.0001\]; CLI, 47 % versus 41 % \[p < 0.0001\]), greater mean number of arteries treated (IC, 1.8 versus 1.6 \[p < 0.0001\]; CLI, 2.1 versus 1.7 \[p < 0.0001\]), and lower proportion of prior leg bypass (IC, 10 % versus 14 % \[p < 0.0001\]; CLI, 11 % versus 17 % \[p < 0.0001\]).

There was lower incidence of failure to cross the lesion (IC, 1 % versus 4 % \[p < 0.0001\]; CLI, 4 % versus 7 % \[p < 0.0001\]); but higher incidence of distal embolization (IC, 1.9 % versus 0.8 % \[p < 0.0001\]; CLI, 3.0 % versus 1.4 % \[p < 0.0001\]) and, in the CLI cohort, arterial perforation (1.4 % versus 1.0 %; \(p = 0.01\)). The authors concluded that despite a lack of evidence for atherectomy over angioplasty and stenting, its use has increased across the U.S. from 2010 to 2016. It was applied equally to IC and CLI populations, with no identifiable pattern of co-morbidities or lesion characteristics, suggesting that indications were not clearly delineated or agreed on. This study placed impetus on further understanding of the optimal role for atherectomy and its long-term clinical benefit in the management of PAD.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>37225</td>
<td>Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with atherectomy, includes angioplasty within the same vessel, when performed</td>
</tr>
<tr>
<td>37227</td>
<td>Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with transluminal stent placement(s) and atherectomy, includes angioplasty within the same vessel, when performed</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0234T</td>
<td>Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; renal artery</td>
</tr>
<tr>
<td>0235T</td>
<td>Visceral artery (except renal), each vessel</td>
</tr>
<tr>
<td>0236T</td>
<td>Abdominal aorta</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>0237T</td>
<td>brachiocephalic trunk and branches, each vessel</td>
</tr>
<tr>
<td>0238T</td>
<td>iliac artery, each vessel</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>32096</td>
<td>Thoracotomy, with diagnostic biopsy(ies) of lung infiltrate(s) (eg, wedge, incisional), unilateral</td>
</tr>
<tr>
<td>35511</td>
<td>Bypass graft, with vein; subclavian-subclavian</td>
</tr>
<tr>
<td>35512</td>
<td>subclavian-brachial</td>
</tr>
<tr>
<td>35516</td>
<td>subclavian-axillary</td>
</tr>
<tr>
<td>35518</td>
<td>axillary- axillary</td>
</tr>
<tr>
<td>35521</td>
<td>axillary-femoral</td>
</tr>
<tr>
<td>35525</td>
<td>brachial- brachial</td>
</tr>
<tr>
<td>35533</td>
<td>axillary-femoral- femoral</td>
</tr>
<tr>
<td>35537</td>
<td>aortoiliac</td>
</tr>
<tr>
<td>35538</td>
<td>aortobi-iliac</td>
</tr>
<tr>
<td>35539</td>
<td>aortofemoral</td>
</tr>
<tr>
<td>35540</td>
<td>aortobifemoral</td>
</tr>
<tr>
<td>35556</td>
<td>femoral-popliteal</td>
</tr>
<tr>
<td>35558</td>
<td>femoral-femoral</td>
</tr>
<tr>
<td>35563</td>
<td>ilioliac</td>
</tr>
<tr>
<td>35565</td>
<td>iliofemoral</td>
</tr>
<tr>
<td>35566</td>
<td>femoral-anterior tibial, posterior tibial, peroneal artery or other distal vessels</td>
</tr>
<tr>
<td>35570</td>
<td>tibial-tibial, peroneal-tibial, or tibial/peroneal trunk-tibial</td>
</tr>
<tr>
<td>35571</td>
<td>popliteal-tibial, -peroneal artery or other distal vessels</td>
</tr>
<tr>
<td>35583</td>
<td>In-situ vein bypass; femoral-popliteal</td>
</tr>
<tr>
<td>35585</td>
<td>femoral-anterior tibial, posterior tibial, or peroneal artery</td>
</tr>
<tr>
<td>35587</td>
<td>popliteal-tibial, peroneal</td>
</tr>
<tr>
<td>35637</td>
<td>Bypass graft, with other than vein; aortoiliac</td>
</tr>
<tr>
<td>35638</td>
<td>aortobi-iliac</td>
</tr>
<tr>
<td>37211</td>
<td>Transcatheter therapy, arterial or venous infusion for thrombolysis</td>
</tr>
<tr>
<td>37214</td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>37220 - 37223</td>
<td>Revascularization, endovascular, open or percutaneous; iliac artery</td>
</tr>
<tr>
<td>37224, 37226</td>
<td>femoral, popliteal artery(s)</td>
</tr>
<tr>
<td>37228 - 37235</td>
<td>tibial, peroneal artery</td>
</tr>
</tbody>
</table>

HCPCS codes not covered for indications listed in the CPB:

- **C2623**: Catheter, transluminal angioplasty, drug-coated, non-laser

ICD-10 codes covered if selection criteria are met:

- **I70.0 - I70.92**: Atherosclerosis

Isolated segmental pharmacomechanical thrombolysis (Trellis Peripheral Infusion System):

- No specific code

ICD-10 codes not covered for indications listed in the CPB (not all inclusive):

- **I74.4**: Embolism and thrombosis of arteries of extremities, unspecified
  
  [Occlusion of peripheral arteries]

- **I82.401 - I82.429**: Acute embolism and thrombosis of deep veins of lower extremity

- **I82.890**: Acute embolism and thrombosis of other specified veins [Paget-Schroetter syndrome]

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The above policy is based on the following references:


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controlled study of excimer laser atherectomy for treatment of femoropopliteal
in-stent restenosis: Initial results from the EXCITE ISR (EXCimer Laser
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Trellis Peripheral Infusion System


**Drug-Eluting (Drug-Coated) Balloons for the Treatment of Primary Lesion/Occlusion of Peripheral Arteries**


Amendment to
Aetna Clinical Policy Bulletin Number: 0295 Peripheral Atherectomy and Thrombectomy Devices

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania