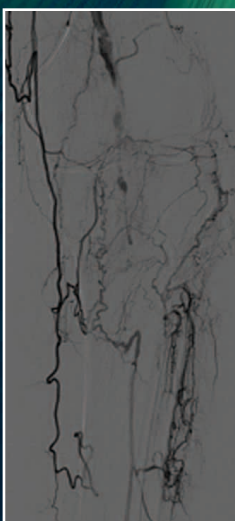
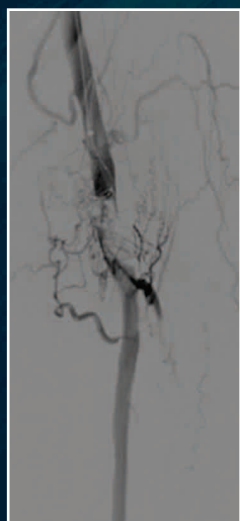


Endovascular TODAY

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CryoPlasty® Therapy in the PVD Toolbox



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Results from case studies are not predictive of results in other cases. Results in other cases may vary.

Cover: Angiographic images courtesy of Colleen J. Moore, MD; Louis A. Lopez, MD; and Baljeet Uppal, MD.

CryoPlasty Therapy for the Infringuinal Arteries

CryoPlasty Therapy offers a unique solution for treating this challenging vascular bed.

BY COLLEEN J. MOORE, MD

The infringuinal vascular bed poses unique challenges to today's interventionist. Although the endovascular specialist's armamentarium has expanded greatly in recent years, the results of these newer modalities leave many of us still looking for durable and predictable results. The trinity of durability, economic viability, and preservation of potential bypass targets has largely remained elusive.

THE PROBLEM

The management of infringuinal arterial occlusive disease has evolved to consist primarily of endoluminal interventions. The superficial femoral artery (SFA) provides unique challenges not seen in other vascular beds. It is an artery of intermediate size (anywhere from 3 to 7 mm) that tends to develop diffuse disease that can span up to 30 cm or more.

There are unique forces at work on the SFA.

Depending on the position of the leg, the SFA can be exposed to flexion forces, torsion, or contraction. The adductor hiatus tethers the artery and can result in arterial compression. These anatomical dynamics are not seen elsewhere and present distinct challenges when planning an intervention that will obtain a durable result.

Angioplasty remains, for the most part, the gold standard to which other endoluminal interventions are compared. Often, angioplasty may not be the ideal modality because results in some instances, however, are not as durable as we may like. Immediate technical success can be challenged by elastic recoil of the artery, creation of significant flow-limiting dissections, or restenosis. In response to these potential sequelae, additional therapeutic modalities have been introduced as adjunctive strategies or used as primary interventional strategies.

CASE 1

A 93-year-old woman seen in the regional wound clinic for a nonhealing wound of her left heel had an arterial duplex ultrasound suggestive of SFA occlusion. Angiography was performed, and the patient was diagnosed with a proximal SFA stenosis of approximately 70% (Figure 1A). The distal SFA occluded with reconstitution of a single posterior tibial artery. The decision was made to dilate the proximal stenosis to improve flow through the collaterals around the occlusion with CryoPlasty Therapy (Boston Scientific Corporation, Natick, MA). Initially, dilation proceeded with a 5-mm PolarCath® Balloon (Boston Scientific Corporation). The balloon was undersized, and there was significant residual stenosis. Therefore, repeat dilation was performed with a 7-mm PolarCath Balloon with < 10% residual stenosis (Figure 1B and C). The patient was amputation-free at 6 weeks after the procedure.

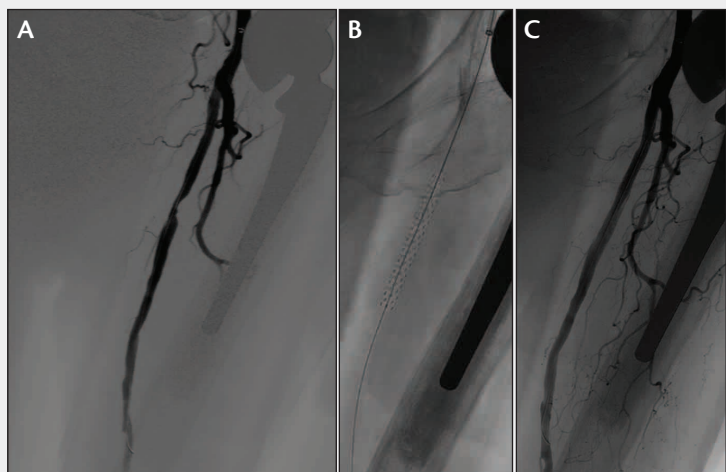
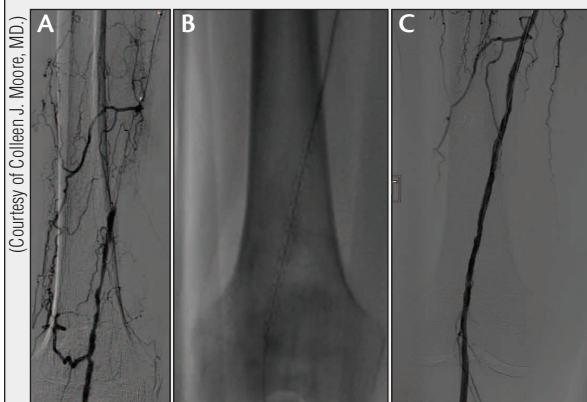


Figure 1. Angiogram showing an approximate 70% stenosis of the proximal SFA in a 93-year-old woman with nonhealing foot ulcers (A). A PolarCath Balloon was used to treat a proximal SFA stenosis (B). Post-CryoPlasty Therapy imaging showing near-total resolution of a proximal SFA stenosis (C).

(Courtesy of Colleen J. Moore, MD.)

CASE 2

A 76-year-old woman presented with worsening right lower extremity rest pain that required admission for pain control. A magnetic resonance angiogram obtained before admission showed occlusion of the mid-to-distal SFA. An attempt at endovascular recanalization was made (Figure 2A). The area of occlusion was traversed, and CryoPlasty Therapy was performed on the lesion (Figure 2B and C). After the procedure, she had a patent SFA and a palpable dorsalis pedis pulse. The patient retained a palpable pulse at follow-up evaluation. A duplex of the treated distal SFA showed no evidence of arterial stenosis.



(Courtesy of Colleen J. Moore, MD.)

Figure 2. Distal SFA occlusion and reconstitution of the above-knee popliteal artery in a 76-year-old woman with rest pain (A). CryoPlasty Therapy to treat a distal SFA occlusion (B). Post-CryoPlasty Therapy imaging showing recanalization of the SFA and restoration of inline flow to the popliteal artery (C).

Stenting in the SFA may be performed to address the complications of angioplasty, namely flow-limiting dissections and elastic recoil, but it has yet to be shown to dramatically reduce the incidence of restenosis or increase patency rates. Flexion forces concentrated at the bifurcation of the common femoral artery and in the popliteal artery at the knee joint also create unique treatment challenges.

Atherectomy has undergone many iterations over the years and continues to be touted as a viable alternative to primary angioplasty. In theory, atherectomy makes sense, but it has not been proven to have long-term benefits over angioplasty alone, and lesions may need postdilatation after the mechanical disruption of the plaque. Atherectomy devices may also potentially result in embolization that can threaten the tenuous tibial outflow seen in many of these patients.

CRYOPLASTY THERAPY: A POTENTIAL SOLUTION

Boston Scientific Corporation's CryoPlasty Therapy has been introduced as an alternative to traditional

angioplasty in treating this unique infrainguinal vascular bed. A single-patient-use inflation unit is used to forcibly inject liquid nitrous oxide into a triple-layer angioplasty balloon. The nitrous oxide undergoes a phase change to a gas and draws in energy. As the balloon inflates to 8 atm, the surface temperature is driven down to -10°C.

In theory, the addition of cold therapy may affect the outcome of simple angioplasty by altering the vessel's response to dilation and by inducement of smooth muscle cell (SMC) apoptosis. Results from in vitro studies have shown that arterial SMCs were found to be susceptible to freeze-induced apoptosis at a temperature range of -5° to -15°C.¹ Theoretically, a reduction in organized SMC apoptosis could alter the intimal hyperplastic response at the area being treated.

“... clinical data have shown an infrequent need for stenting, as well as durable results ...”

Laird et al published the initial safety data on CryoPlasty Therapy in 102 patients. Eighty-four percent (86/102) of the lesions treated were in the SFA. In all limbs treated, a 94.1% (96/102) initial technical success rate was reported. Fewer than 10% (9/102) of treated lesions required stenting.² Follow-up of this initial group was extended and revealed durable results, with freedom from target lesion revascularization of 75% at 1,253 days by Kaplan-Meier estimate.³ The BTK Chill trial studied primary CryoPlasty Therapy treatment of below-the-knee occlusive disease in CLI patients and yielded similar results.⁴

POTENTIAL ADVANTAGES OF CRYOPLASTY THERAPY

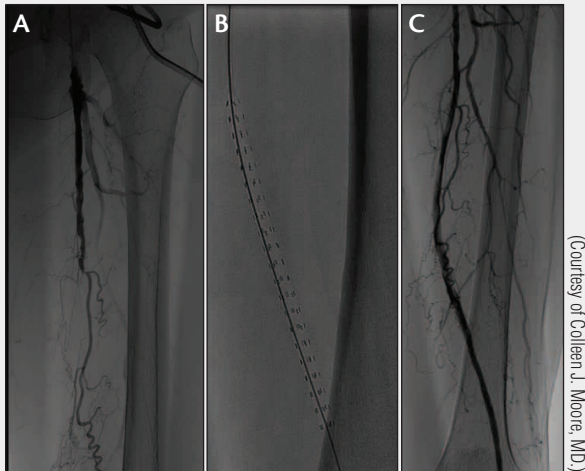
CryoPlasty Therapy was designed to offer a novel approach to the challenges of the peripheral vasculature, including infrainguinal interventions. Clinical data have demonstrated good immediate technical success characterized by a low rate of dissection and an infrequent need for stenting.³ In theory, the addition of cold therapy to standard angioplasty may alter the vessel's response to injury through SMC apoptosis.

Stenting the infrainguinal arteries can, in some instances, limit subsequent bypass options. A stent placed at the adductor hiatus can force any subsequent bypass to be performed below the knee, which can lead to a decrease in primary patency. An infrapopliteal stent can greatly limit potential bypass targets and potentially convert a below-knee popliteal

CASE 3

A 59-year-old diabetic woman was being followed in a wound center for nonhealing ulcerations on her left foot. The preprocedural ankle-brachial index on the affected limb was 0.7, with a toe-brachial index of 0.3. She had a palpable femoral pulse on the affected side but no popliteal pulse. A previous angiogram had been obtained that showed occlusion of the SFA and reconstitution of the above-knee popliteal artery (Figure 3A). An attempt at endovascular recanalization at that time could not be accomplished due to difficulty in traversing the occlusion.

At repeat angiography, wire crossing of the lesion was successful. A channel was dilated along the course of the occlusion to allow for passage of a 5- X 10-mm PolarCath® Balloon. CryoPlasty Therapy was performed in an overlapping fashion of the entire occlusion (Figure 3B). Postprocedural imaging showed a patent SFA. There was a small dissection noted, but this was not flow-limiting and did not require placement of a stent (Figure 3C). At 6 weeks after the procedure, the patient retained a palpable popliteal pulse, with slow but persistent healing of her foot ulcers.



(Courtesy of Colleen J. Moore, MD)

Figure 3. Occlusion of the SFA and a patent popliteal artery with preferential flow through collateral vessels in a 59-year-old diabetic woman with nonhealing foot ulcers (A). CryoPlasty Therapy used to treat an SFA occlusion (B). Postinterventional imaging showing recanalization of the SFA with preferential flow through the native vessel and restoration of a popliteal pulse (C).

artery bypass to a tibial artery bypass. In patients who might have progressed to bypass or those with limited bypass targets, CryoPlasty Therapy may provide an alternative.

In a recent publication by Bakken et al, in which the use of CryoPlasty Therapy as a stand-alone technology was compared to angioplasty in 124 patients with TASC C/D lesions, a 67% cost reduction in the patients treated with CryoPlasty Therapy versus those treated with angioplasty was reported. In their retrospective analysis, the cost reduction was attributed to the decreased use of stents in patients treated with CryoPlasty Therapy (22% [10/39] vs 75% [70/85]).⁵

Bakken et al also reported that the modes of failure between angioplasty and CryoPlasty Therapy were different. The primary mode of failure in the CryoPlasty Therapy group was restenosis rather than occlusion, whereas the angioplasty group primarily failed because of occlusion, making endoluminal revascularization difficult and leading to more bypass procedures in this group. The patients treated with CryoPlasty Therapy in this retrospective review developed restenosis and tended to have endoluminal options for revascularization in addition to potential bypass options. The investigators concluded that CryoPlasty Therapy was a viable stand-alone therapy for these more complex lesions.

CONCLUSION

Because endoluminal interventions have evolved, it is rare that I will use primary angioplasty in a stand-alone fashion. The potential complications of elastic recoil, clinically significant dissections, and restenosis encouraged me to use adjunctive therapeutic modalities and to search for other primary interventional strategies. CryoPlasty Therapy offers a unique variation on primary angioplasty with the addition of cold therapy, and clinical data have shown an infrequent need for stenting, as well as durable results that can be economically viable and may also preserve potential bypass targets.^{2,3,5} ■

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1. Isner JM, Kearney M, Bortman S, et al. Apoptosis in human atherosclerosis and restenosis. *Circulation*. 1995;91:2703-2711.
2. Laird JR, Jaff MR, Biamino G, et al. Cryoplasty for the treatment of femoropopliteal arterial disease: results of a prospective, multicenter registry. *J Vasc Interv Radiol*. 2005;16:1067-1073.
3. Laird JR, Biamino G, McNamara T, et al. Cryoplasty for the treatment of femoropopliteal arterial disease: extended follow-up results. *J Endovasc Ther*. 2006;13:1152-1159.
4. Das TS, McNamara T, Gray B, et al. Primary Cryoplasty Therapy provides durable support for limb salvage in critical limb ischemia patients with infrapopliteal lesions: 12-month follow-up results from the BTK Chill Trial. *J Endovasc Ther*. 2009;16(suppl 2):1119-1130.
5. Bakken AM, Saad WE, Davies MG. Cryoballoon angioplasty broadens the role of primary angioplasty and reduces adjuvant stenting in complex superficial femoral artery lesions. *J Am Coll Surg*. 2008;206:524-532.

Dual-Therapy Approach to Complex Vascular Lesions

One physician's perspective on combining atherectomy with CryoPlasty Therapy.

BY LOUIS A. LOPEZ, MD

There is a greater diversity of treatment modalities for infrainguinal vessels than for any other vascular bed. Most of the treatment options provide good acute results but are still limited in the long-term durability of the procedure. The superficial femoral artery (SFA) is perhaps the most dynamic of the arteries in the human body, because it is subjected to numerous conformational movements and forces of contraction, torsion, compression, and flexion.¹ The SFA is a long vessel that is very susceptible to atherosclerosis and is frequently plagued by diffuse disease and lengthy segments of total occlusion. SFA disease is also very heterogeneous. It can be thrombotic or fibrocalcific and involve softer atherosclerotic plaque or intimal hyperplasia. Therefore, treating this vessel is complicated, and options are diverse.

Trifurcation vessels present similar challenges. The diseased segment is often long and totally occluded. Lesion composition is again heterogeneous and frequently calcific. Vessel diameters are small, and runoff can be very limited. Stent placement in trifurcation vessels may be much less of an option than in the SFA, and perforations may be much more difficult to treat. Very little data exist evaluating durability of the intervention, long-term vessel patency, and reintervention rates. Treatment options are as broad as in the SFA.

BALLOON ANGIOPLASTY AND STENTING

Balloon angioplasty alone can result in undesirable restenosis and dissections and can create challenges in treating certain long total occlusions. Self-expanding stents may provide excellent immediate angiographic results, acceptable resolution of pressure gradients, and can be fast and easy to deploy. Conversely, the long-term results are limited, can be relatively difficult to reopen after restenosis, and in some instances, the options for reintervention and surgical bypass can be limited. Covered stents can provide positive angiographic results within the stented region but can also result in edge restenosis. When restenosis occurs, stents may thrombose and require prolonged infusion of thrombolytics to resolve. The majority of patients in

my practice are elderly with critical limb ischemia, and prolonged infusion of thrombolytics in this elderly population can be risky.

The initial success of infrainguinal stenting can be compromised by restenosis in the SFA and popliteal artery. Stenting in the infrainguinal vessels will often cause a permanent structural alteration of the vessel, which can, in some instances, limit or complicate rein-

CASE 1

A 50-year-old woman with diabetes, hypertension, hyperlipidemia, and peripheral artery disease (PAD) presented 2 years ago with critical limb ischemia. She was revascularized with stand-alone directional atherectomy. She recently developed recurrent claudication both at rest and with exertion, and arterial Doppler and angiography demonstrated left popliteal artery occlusion (Figure 1A). She was treated with atherectomy followed by a 5- X 10-mm PolarCath® Balloon (Boston Scientific Corporation, Natick, MA) in the popliteal artery and a 3- X 40-mm PolarCath Balloon in the anterior tibial and peroneal arteries. This resulted in a positive angiographic result and resolution of her symptoms (Figure 1B and C).

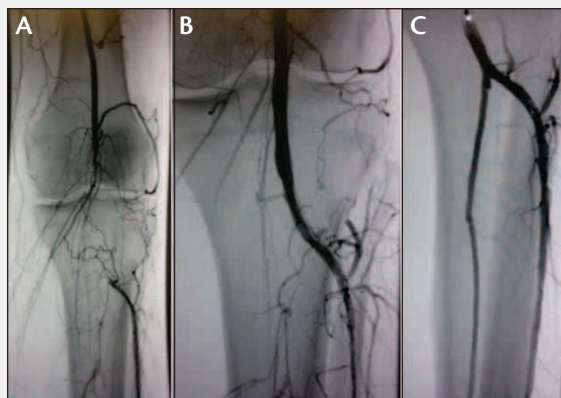


Figure 1. Angiogram showing left popliteal artery occlusion in a 50-year-old patient with claudication (A). Final angiogram of the popliteal artery (B) and tibial arteries (C) after atherectomy and postdilatation with a PolarCath Balloon.

(Courtesy of Louis A. Lopez, MD.)

intervention options.¹ Catheter-based interventions to treat in-stent restenosis are difficult and have been met with limited results. Drug-eluting stent placement in the SFA remains a hopeful strategy for the future.

Choosing a treatment option for the SFA or trifurcation vessels depends on many factors, including lesion morphology, composition, length, location, vessel size, accessibility, etc. It also depends on physician preference, comfort level, experience with particular devices, and what is available in the laboratory. I have tried almost everything on the market for treating infrainguinal vessels and have evolved to a strategy of debulking followed by CryoPlasty Therapy (Boston Scientific Corporation) with the PolarCath® Peripheral Dilatation System. In my experience, this strategy has provided good short-term results and desirable vessel patency rates over time. For de novo lesions, I have also seen examples where this combination strategy has resulted in good luminal diameter, low complication rates, good resolution of pressure gradients, and vessel patency rates of > 80% in my laboratory.

CASE 2

A 76-year-old man with hypertension, hyperlipidemia, and coronary artery disease (CAD) presented with severe left leg rest pain and an ulcer on his foot. Arterial Doppler studies revealed multilevel occlusive disease, and he was referred for angiography and intervention. Angiography demonstrated a heavily calcified complex SFA lesion with collateralization (Figure 2A and B). Due to the calcification, the lesion was treated with directional atherectomy and postdilated with a 5- X 100-mm PolarCath Balloon. End result demonstrated brisk flow, wide patency and no dissection. (Figure 2C). His ulcer healed and claudication subsequently resolved.

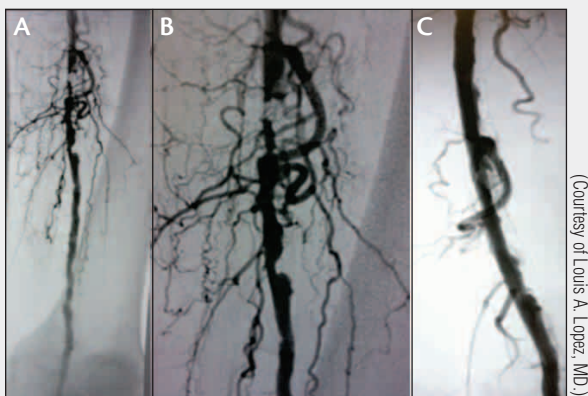


Figure 2. Angiogram showing heavily calcified SFA lesion in 76 year old patient with critical limb ischemia (A). Magnified image of calcified lesion (B). Final angiogram of SFA after atherectomy and CryoPlasty Therapy of the lesion (C).

CRYOPLASTY THERAPY AND ATHERECTOMY

CryoPlasty Therapy demonstrated clinical patency rates of approximately 82.2% (74/90) at 9 months, with a 6.9% (7/102) rate of clinically significant dissections and an 8.8% (9/102) incidence of bailout stenting, in the PVD Chill Registry.² Apoptosis is the theoretical mechanism of action for CryoPlasty Therapy and is a noninflammatory process found in human vascular pathology of proliferative restenotic lesions.³ In vitro studies of human specimen cells have shown application of extreme cold followed by a rewarming can modulate neointimal response in cells through induction of smooth muscle cell apoptosis.⁴⁻⁶ Based on this theory, a large plaque burden within the vessel could prevent the freezing effect from reaching the target cells.

“The combination strategy of atherectomy and CryoPlasty Therapy can potentially create a useful synergy.”

Advantages of atherectomy can include the ability to excise plaque and avoid barotraumas; however, lesions may require postdilatation, and intimal hyperplasia can still occur. Challenges can include the irregular flow pattern that may occur. Luminal gain may improve flow, but the rheology of flow at the end of the procedure may not always be optimal. Overly aggressive attempts to create a cylindrical lumen can result in vessel perforation or aneurysmal segments in the vessel.

In my own practice, stand-alone debulking has produced good short-term results in infrainguinal patients, but I have seen limited long-term patency. Ultimately, debulking followed by drug-coated balloon angioplasty may prove effective, but this is years away from commercial availability in the United States. In the interim, I have employed a strategy of debulking followed by postdilatation with the PolarCath Peripheral Dilatation System as a currently available surrogate, with the hope that the addition of CryoPlasty Therapy may provide some additional impact with respect to restenotic lesions. I try to avoid stenting in the infrainguinal vessels, and debulking followed by CryoPlasty Therapy has been shown to be a useful and attractive alternative for some of my patients.

The combination strategy of atherectomy and CryoPlasty Therapy can potentially create a useful synergy. In theory, postdilating debulked lesions with the PolarCath Peripheral Dilatation System may allow any potential biological effect of stand-alone CryoPlasty

Therapy to bring the freezing surface closer to the target cells. CryoPlasty Therapy may have benefit if “smoothing” the irregular internal lumen that may be left by directional atherectomy can create an improved rheology of flow and/or increase acute luminal gain by stretching the vessel.

In my experience, debulking followed by CryoPlasty Therapy has demonstrated desirable results for long total occlusions as compared to stand-alone CryoPlasty Therapy or atherectomy alone. The dual-therapy approach has allowed me to stop debulking sooner and create a larger lumen.

Treating critical limb ischemia rarely involves simple focal lesions. In my experience, debulking before CryoPlasty Therapy has demonstrated limited dissections, desirable acute luminal gain, infrequent elastic recoil, which in theory may have some relation to the

proximity of the freezing surface to the vessel wall. I have seen excellent end-angiographic results and velocity of flow when using the combined therapy approach. In my experience, the combined technologies have synergy.

Aggressive restenosis is a difficult freight train to stop. In my experience, CryoPlasty Therapy does not stop restenosis once it begins, but restenosis has seemed to occur less often, and I have used this therapy as first-line treatment in the initial intervention. CryoPlasty Therapy has been an excellent postdilatation strategy after debulking in my experience.

CONCLUSION

I have employed the combined method of atherectomy and CryoPlasty Therapy in practical application, and it has been demonstrated to be cost-effective in

CASE 3

The patient was a 93-year-old man with CAD, previous coronary artery bypass graft surgery with history of calcific aortic stenosis and aortic valve replacement, hypertension, hyperlipidemia, and PAD. The patient was followed for his PAD via Doppler over many years, and within the last 6 months, symptoms progressed from exertional claudication to rest pain. Angiography documented heavily calcific disease (Figure 3A through D). Attempts to cross the lesion in an antegrade fashion were unsuccessful. Exercising caution, popliteal artery access was obtained, and the distal popliteal fossa was cannulated. After crossing in a retrograde fashion, the lesion was debulked with directional atherectomy and postdilated with a 5- X 100-mm PolarCath® Balloon. Final angiographic results showed wide patency (Figure 3E through G).

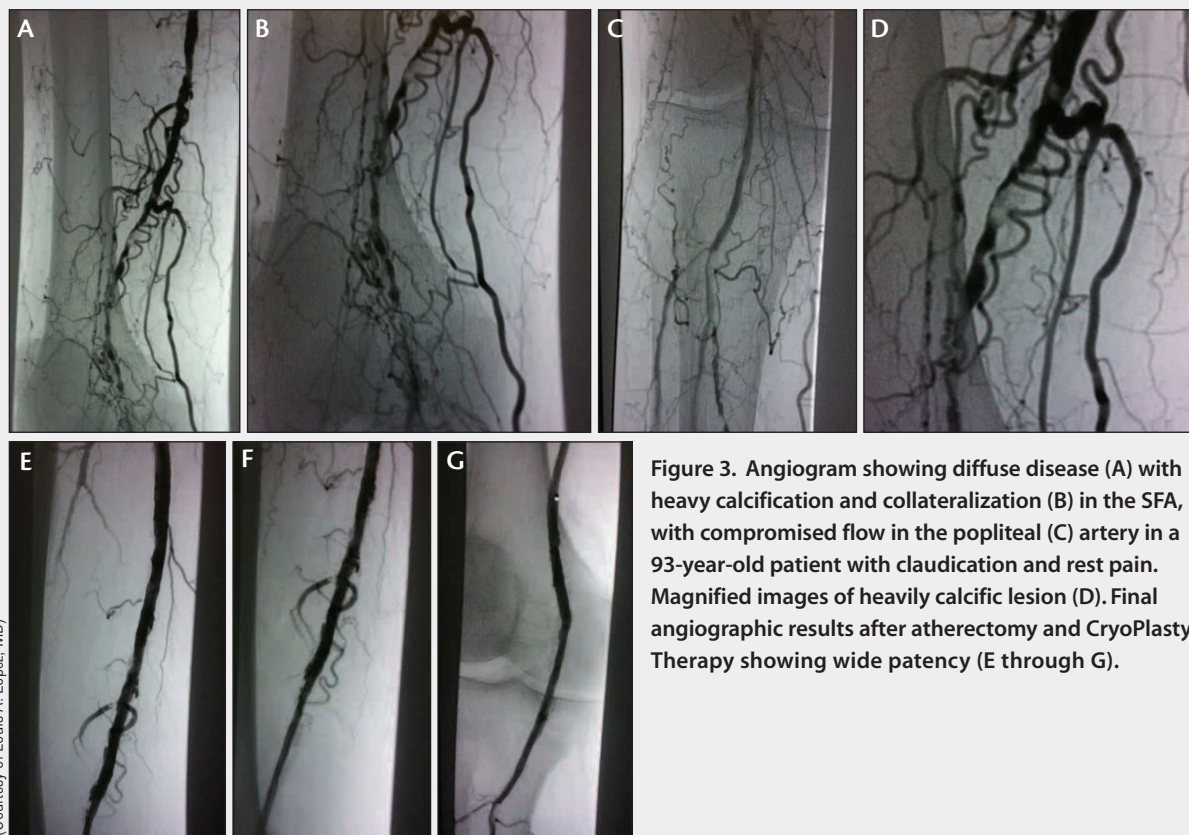
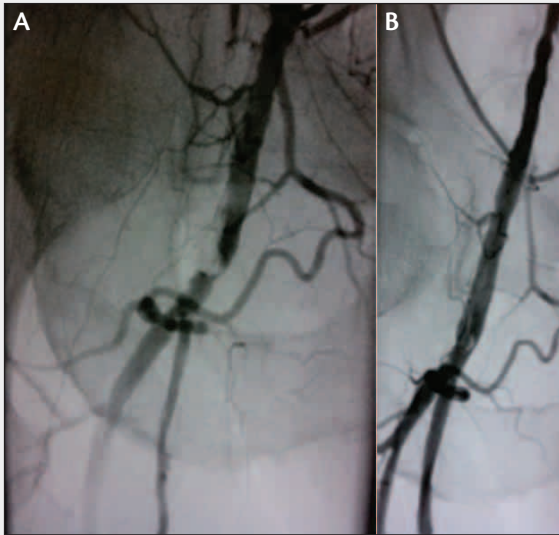


Figure 3. Angiogram showing diffuse disease (A) with heavy calcification and collateralization (B) in the SFA, with compromised flow in the popliteal (C) artery in a 93-year-old patient with claudication and rest pain. Magnified images of heavily calcific lesion (D). Final angiographic results after atherectomy and CryoPlasty Therapy showing wide patency (E through G).

(Courtesy of Louis A. Lopez, MD)

CASE 4

A 72-year-old man with hypertension, hyperlipidemia, and end-stage renal disease presented with severe claudication symptoms in his right leg and severe cramping in his leg during dialysis. Arterial Doppler studies showed a high-grade lesion in the common femoral artery, and angiography confirmed a heavily calcified common femoral artery stenosis (Figure 4A). The lesion was debulked with rotational atherectomy and postdilated with a 6- X 40-mm PolarCath® Balloon. Final angiographic result showed no dissection (Figure 4B), with complete obliteration of the pressure gradient and resolution of his symptoms.



(Courtesy of Louis A. Lopez, MD)

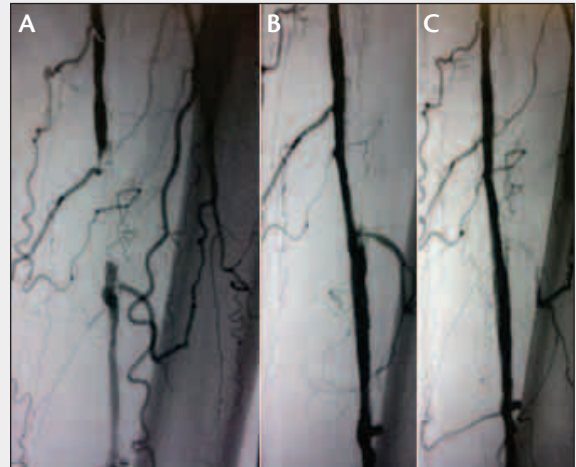
Figure 4. Angiogram showing heavily calcified common femoral artery stenosis in a 72-year-old patient with severe claudication (A). Final angiogram after rotational atherectomy and CryoPlasty Therapy, showing no dissection and elimination of pressure gradients (B).

my experience. To me, debulking before CryoPlasty Therapy makes intuitive sense. It is a technically straightforward alternative that has, in my experience, shown low complication rates and infrequent need to leave an implant.

Although my experience provides initial evidence that may support a dual-therapy approach to complex vascular lesions, further study is warranted, and no data currently exist to measure the true effectiveness of this methodology. We are currently involved in a retrospective evaluation of several hundred cases with several operators to gather outcome data for this strategy both above and below the knee and plan to pursue a prospective multisite evaluation. These types of studies will be required to better define the role of this therapy relative to the other modalities that are currently available for treating femoropopliteal and infrapopliteal disease. ■

CASE 5

The patient was a 78-year-old man with chronic obstructive pulmonary disease, CAD, hypertension, hyperlipidemia, PAD, and a history of carotid endarterectomy. He presented with exertional claudication symptoms in both legs. Arterial Doppler imaging showed bilateral SFA disease, and angiography demonstrated segmental occlusion of the left SFA (Figure 5A). Debulking was then performed with directional atherectomy (Figure 5B). After postdilatation with a 5- X 100-mm PolarCath Balloon, angiography revealed increased luminal diameter (Figure 5C), no dissection, brisk flow, and resolution of pressure gradient. The procedure resolved the patient's claudication symptoms.



(Courtesy of Louis A. Lopez, MD)

Figure 5. Angiogram showing segmental occlusion of the left SFA in a 78-year-old patient with exertional claudication (A). Angiogram after debulking with directional atherectomy (B). Final angiogram after postdilatation with a PolarCath Balloon showing wide patency, no dissection, elimination of pressure gradient, and brisk flow (C).

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1. Rogers JH, Laird JR. Overview of new technologies for lower extremity revascularization. *Circulation*. 2007;116:2072-2085.
2. Laird J, Jaff MR, Biamino G, et al. Cryoplasty for the treatment of femoropopliteal arterial disease: results of a prospective, multicenter registry. *J Vasc Interv Radiol*. 2005;16:1067-1073.
3. Isner JM, Kearney M, Bortman S, et al. Apoptosis in human atherosclerosis and restenosis. *Circulation*. 1995;91:2703-2711.
4. Tatsutani KN, Joye JD, Virmani R, et al. In vitro evaluation of vascular endothelial and smooth muscle cell survival and apoptosis in response to hypothermia and freezing. *Cryo Letters*. 2005;26:55-64.
5. Yiu W, Cheng SWK, Sumpio BE. Direct comparison of endothelial cell and smooth muscle cell response to supercooling and rewarming. *J Vasc Surg* 2007;46:557-64.
6. Yiu W, Cheng SWK, Sumpio BE. Vascular smooth muscle cell apoptosis induced by "supercooling" and rewarming. *J Vasc Interv Radiol*. 2006;17:1971-1977.

CryoPlasty Therapy in Complex Infrageniculate and Dialysis Access Lesions

With the many available treatment options, what makes CryoPlasty Therapy an attractive modality for these lesions?

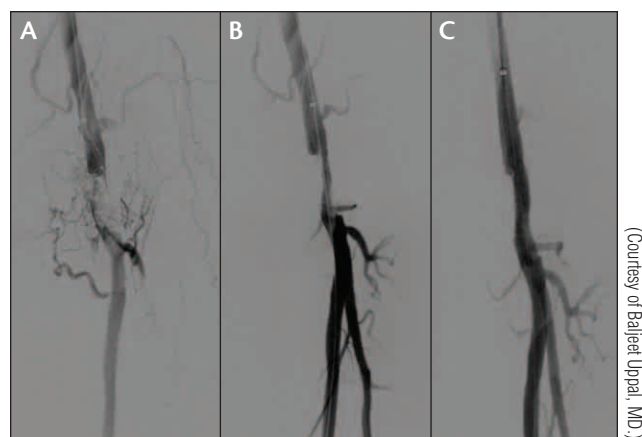
BY BALJEET UPPAL, MD

Traditional treatment for complex lower extremity arterial occlusive disease has often included surgery, but development and improvement of other treatment alternatives has resulted in their application in these procedures as well. The question still remains: which of these alternatives will stand the test of time and replace other treatment options? I present an array of infrageniculate and dialysis access cases in which CryoPlasty Therapy (Boston Scientific Corporation, Natick, MA) was the primary modality for treating the lesions.

CASE REPORTS

Case 1

The patient was a 70-year-old man with debilitating bilateral claudication of the lower extremities (Rutherford category 3) and a history of coronary artery disease and hyperlipidemia. Noninvasive studies showed an ankle-brachial index of 0.6 and duplex findings of mostly calcific occlusive disease of the femoral arteries bilaterally (Figure 2A). Arteriography of the left lower extremity revealed focal calcific plaque with an occlusive lesion of the left common femoral artery (CFA) (Figure 1A). Selective access to the left proximal CFA was obtained via the right CFA using a Pinnacle Destination Sheath (Terumo Interventional Systems, Somerset, NJ). The left CFA occlusion was crossed with a Fathom® Guidewire (Boston Scientific Corporation). The lesion was predilated with a 3-mm Sterling® Balloon (Boston Scientific Corporation) (Figure 1B) and then treated with an 8- X 40-mm PolarCath® Balloon (Boston Scientific Corporation), which provided an excellent arteriographic result (Figure 1C). This was followed 3 weeks later by similar treatment of the right CFA occlusion. The patient had immediate resolution of the symptoms with no evidence of recurrence. Eighteen months later, the patient



(Courtesy of Baljeet Uppal, MD.)

Figure 1. Arteriography of the left lower extremity revealed focal calcific plaque with an occlusive lesion of the left CFA (A). The left CFA occlusion after crossing with a Fathom Guidewire and predilation with a 3-mm Sterling Balloon (B). Final angiography after CryoPlasty Therapy with an 8- X 40-mm PolarCath Balloon (C).

remained symptom free, and noninvasive examination of the CFAs bilaterally showed no evidence of plaque recurrence (Figure 2B).

Case 2

A 98-year-old woman with a history of coronary artery disease, hyperlipidemia, and hypertension presented with gangrene of the left first and fourth toes with noninvasive studies showing ankle-brachial indices of 0.37 and 0.42 on the right and left sides, respectively. With no surgical options available to treat this elderly woman, the decision was made to perform arteriography of the left lower extremity. Access to the left lower extremity was obtained via the right CFA. Arteriography of the left lower extremity revealed generalized calcific plaque of the entire left

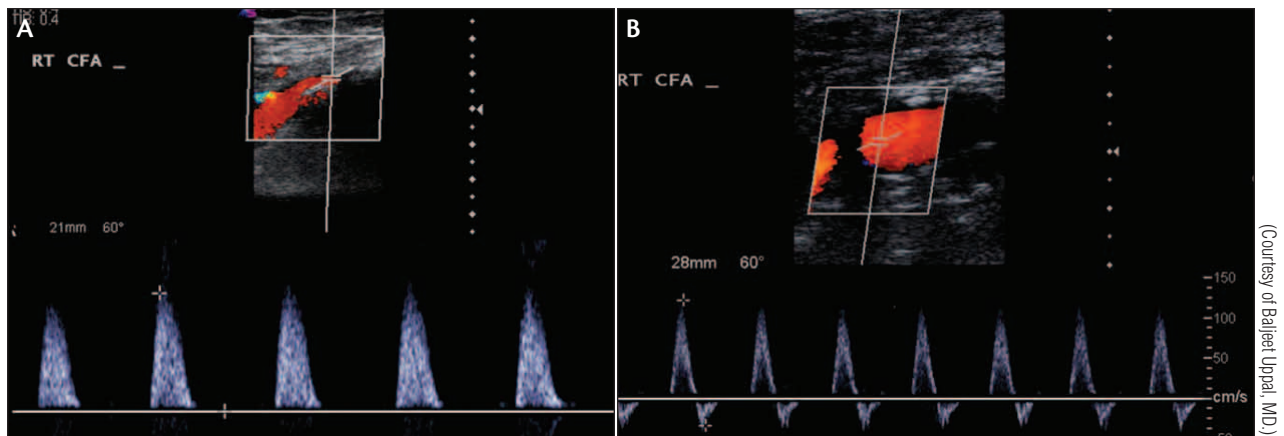


Figure 2. Duplex image of the right CFA at initial presentation showing occluded artery and monophasic waveforms (A). Duplex image of the right CFA at 18 months after CryoPlasty Therapy showing a widely patent artery and triphasic waveforms (B).

lower extremity arterial tree with multisegmental disease of the left superficial femoral artery (SFA) (Figure 3A) followed by complete occlusion of the left popliteal artery (Figure 3B). The only runoff to the leg was with a reconstituted peroneal artery via lateral geniculate collaterals. Selective access to the left SFA was obtained via the right CFA using a Pinnacle Destination Sheath. The left SFA multisegmental disease was treated with a 5- X 100-mm PolarCath® Balloon, which resulted in an excellent arteriographic result (Figure 3C). The left popliteal artery occlusion was crossed with a Fathom® Guidewire and a 3- X 40-mm Sterling® Balloon. The true lumen gain was confirmed with arteriography, and the lesion was predilated with the Sterling Balloon. The vessel was then treated with CryoPlasty Therapy of the popliteal artery with a 5- X 60-mm PolarCath Balloon. Runoff showed brisk flow in the left peroneal artery (Figure 3D) with reconstitution of the left anterior and posterior tibial arteries via collaterals from the left peroneal artery (Figure 3E).

The patient had immediate resolution of rest pain with healing of the ulcers and gangrenous areas. The patient was discharged home later that day. Nine months later, she remained symptom free, and noninvasive examination of the left popliteal artery showed no evidence of plaque recurrence.

Case 3

A 48-year-old man with long-standing type I diabetes mellitus, coronary artery disease, and end-stage renal disease underwent arteriovenous fistula creation at the wrist in the form of radiocephalic fistula. Two years after fistula use, the patient was noticed to have poor dialysis sessions, and noninvasive duplex imaging showed high-grade stenosis of the fistula just distal to the radiocephalic anastomosis. A fistulagram was obtained via a right brachial artery cut-down, and brachial artery access was obtained via a 7-F sheath. A fistulagram obtained via a sheath in the radial artery showed a near occlusive lesion of the proximal seg-

ment of the fistula (Figure 4A). The lesion was crossed using a Fathom Guidewire (Figure 4B) and predilated with a 3- X 40-mm Sterling® ES Balloon. The lesion was definitively treated with an 8- X 40-mm PolarCath Balloon. The follow-up fistulagram showed an excellent arteriographic result (Figure 4C). The patient was able to resume dialysis immediately thereafter, and follow-up surveillance duplex showed no evidence of recurrent lesion. The patient was still dialysis-symptom free and intervention-free at 24 months.

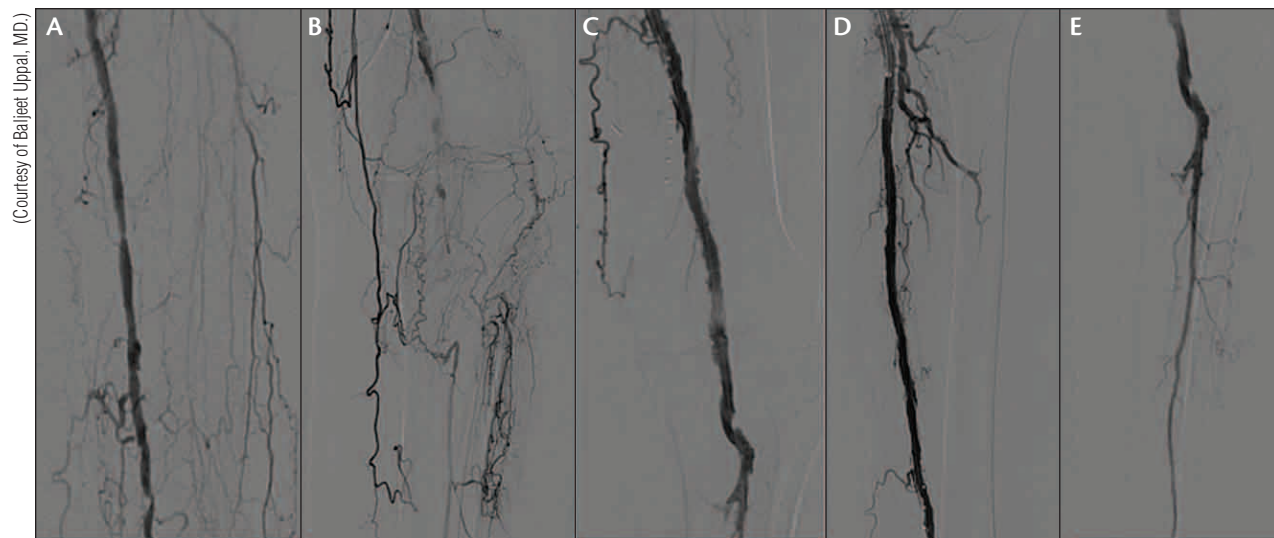
DISCUSSION

In my experience, percutaneous procedures for peripheral artery occlusive disease have generally exhibited inferior patency rates when compared to surgical treatments; however, surgical treatment has demonstrated its own drawbacks. The abundance of available endovascular treatments has led me to one conclusion: none of them are perfect yet. Balloon angioplasty for infrainguinal arterial disease can be successful but can also lead to procedural challenges like arterial wall dissection, recoil, recurrence, and treatment failure.

Traditionally in case 1, I would have suggested surgical treatment in the form of femoral endarterectomy. In case 3, the repair of the fistula with vein patch angioplasty would be certainly considered a premier treatment option. I believe that offering endovascular treatment options to patients without potentially compromising future surgical interventions, should they be needed, has a definitive place in the treatment of vascular disease.

CRYOPLASTY THERAPY

CryoPlasty Therapy combines angioplasty with cold therapy via the PolarCath® Peripheral Dilatation System. The PolarCath Peripheral Dilatation System incorporates nitrous oxide as a dilation medium. Widespread use of nitrous oxide in other medical applications eventually prompted its use in arterial interventions, and it is solu-



(Courtesy of Baljeet Uppal, MD.)

Figure 3. Initial angiography showed multisegmental disease of the left SFA (A) and complete occlusion of the left popliteal artery (B). Left SFA arteriogram after CryoPlasty Therapy with a 5- X 100-mm PolarCath® Balloon (C). Distal left popliteal artery and peroneal artery arteriogram after predilatation with a 3- X 40-mm Sterling® Balloon and CryoPlasty Therapy with a 5- X 60-mm PolarCath Balloon (D). Recanalization of the left peroneal artery (E).

ble in the vascular system. The release of nitrous oxide from liquid form to gaseous form results in volume expansion, exhibiting cooling in accordance with the law of energy conservation. CryoPlasty Therapy is designed to deliver temperatures of -10°C at the interface of balloon and intima. This low temperature theoretically may induce apoptosis in the vessel wall.

The PolarCath® Peripheral Dilatation System consists of several integrated components: a PolarCath Balloon catheter, the PolarCath® Inflation Unit, nitrous oxide canisters, and a power module. The PolarCath Balloon is outwardly similar to a conventional angioplasty balloon but it is composed of three layers. The inner balloon contains the nitrous oxide gas and maintains the pressure, allowing the outermost balloon to expand passively. The middle layer contains a textile fabric that is designed to insulate the reaction for an accurate delivery of the desired outside temperature. A pattern of radiopaque markers is also inscribed on this fabric to allow for visibility under fluoroscopy, because nitrous oxide within the balloon is otherwise radiolucent (Figure 5). This space was engineered to create a vacuum during preparation of the balloon. The device is designed to continuously monitor this vacuum throughout the inflation and treatment cycles. Finally, the balloon also houses a thermocouple that is designed to constantly monitor the temperature and determine whether it is within the ideal working range.

The PolarCath Balloon inflation cycle is automated and regulated by the PolarCath Inflation Unit. This is a micro-processor-controlled device that integrates the PolarCath Balloon and the nitrous oxide cylinder. Once each of the three components is connected, activation of the device runs through a preprogrammed series of methods that

test and monitor the device performance, nitrous oxide delivery, desired balloon dilation and cooling parameters. The balloon undergoes a 20-second controlled inflation up to 8 atm. Once the balloon reaches 8 atm, liquid refrigerant is cycled through the balloon catheter, bringing the outer balloon temperature to -10°C . This treatment cycle lasts 20 seconds, after which the balloon warms, the gas is evacuated, and the balloon may be deflated. Although the PolarCath Inflation Unit may be used for multiple inflations per patient, each PolarCath Balloon inflation requires a new nitrous oxide cylinder, allowing lesions to be treated with multiple inflations if desired.

MECHANISM OF ACTION

The primary theoretical mechanism of action for CryoPlasty Therapy is the induction of apoptosis (programmed cell death) in the intima and media, which may theoretically affect the restenosis process. In *in vitro* cell specimen studies, Tatsutani et al demonstrated conversion to an apoptotic life cycle in human smooth muscle and endothelial cell lines with exposure to temperatures of -10°C .¹

It has been shown in *in vitro* cell specimens that freezing interstitial saline in the medial layer of the vessel wall can create a hypertonic environment. Applying this concept to CryoPlasty Therapy, it is theorized that after deflation and rewarming, free water that was forced out of the cells may re-enter the cells, which should re-establish isotonicity. It is believed that this intracellular dehydration and rehydration may induce apoptosis. If this occurs, isotonicity may maintain cell membrane integrity, which could potentially prevent systemic inflammatory response, theoretically modulating the neointimal response.

(Courtesy of Baljeet Uppal, MD.)

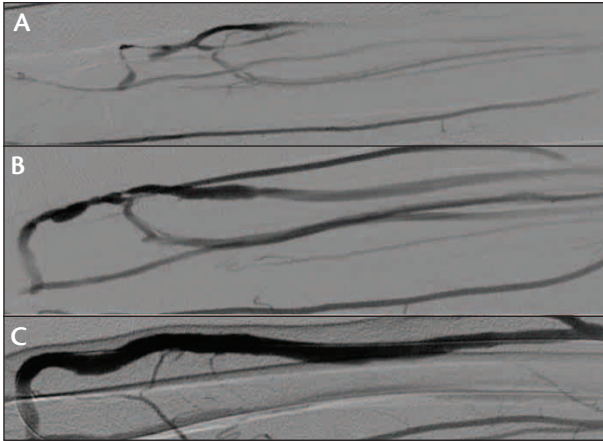
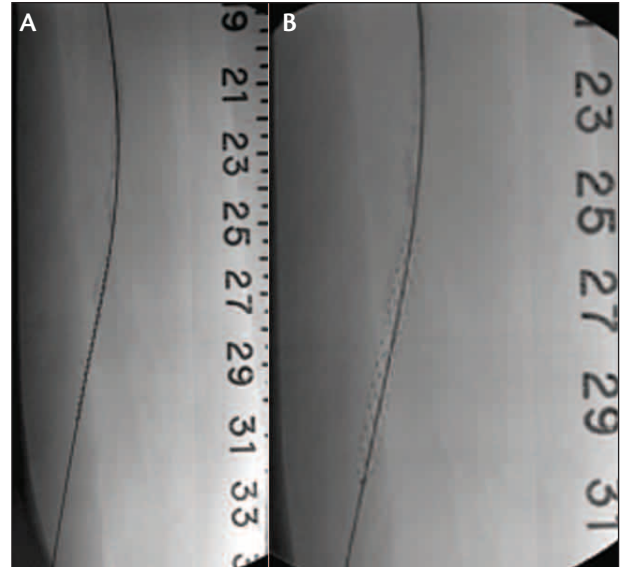


Figure 4. Initial fistulagram showing a near occlusive lesion of the proximal segment of the fistula (A). Fistulagram obtained after crossing with a Fathom® Guidewire and predilation with a 3- X 40-mm Sterling® ES Balloon (B). Fistulagram obtained after CryoPlasty Therapy with an 8- X 40-mm PolarCath® Balloon showing excellent arteriographic result (C).

Fava and colleagues studied 15 patients with application of CryoPlasty Therapy in arterial occlusive disease and reported a 93% (14/15) technical success rate.² Angiographic follow-up at 14 ± 4 months showed the primary patency rate to be 83% (10/12). Laird et al then reported initial safety data in connection with their multicenter registry of 102 patients with femoropopliteal disease with a wide array of disease processes.³ Technical success was reported as 94.1% (96/102) with a primary patency rate of 70.1% at 9 months by Doppler ultrasound (23/77) and a clinical patency rate of 75% by Kaplan Meier estimate at 3.4 years for the 70 patients followed to 3.4 years.⁴

In my experience, I have used CryoPlasty Therapy as the primary option in locations where I am unlikely to stent, such as common iliac arterial lesions, the CFA, the profunda femoris artery, ostial lesions, the popliteal artery, and the tibial arteries. In these locations, my use of CryoPlasty Therapy has preserved my options for future surgical treatment should they be needed. I have found long-length lesions of entire segments of arteries, such as the SFA, tibial



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Figure 5. The PolarCath Balloon has radiopaque markings designed to facilitate accurate placement and fluoroscopic guidance (A) and inflation (B).

arteries, and autogenous bypass graft and dialysis accesses, to be especially amenable to CryoPlasty Therapy. I have also found that treating complex lesions can require a combination of devices and strategies, including balloon angioplasty and debulking technologies. ■

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1. Tatsutani KN, Joye JD, Virmani R, et al. In vitro evaluation of vascular endothelial and smooth muscle cell survival and apoptosis in response to hypothermia and freezing. *CryoLetters*. 2005;26:55-64.
2. Fava M, Loyola S, Polydorou A, et al. Cryoplasty for femoropopliteal arterial disease: late angiographic follow-up of initial human experience. *J Vasc Interv Radiol*. 2004;15:1239-1243.
3. Laird J, Jaff MR, Biamino G, et al. Cryoplasty for the treatment of femoropopliteal arterial disease: results of a prospective, multicenter registry. *J Vasc Interv Radiol*. 2005;16:1067-1073.
4. Laird JR, Biamino G, McNamara T, et al. Cryoplasty for the treatment of femoropopliteal arterial disease: extended follow-up results. *J Endovasc Ther*. 2006;13(suppl 2):II52-II59.

POLARCATH® PERIPHERAL DILATATION SYSTEM

Prior to use please see the complete “Directions for Use” for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator’s Instructions.

INDICATIONS:

The PolarCath System is indicated to dilate stenoses in the peripheral vasculature (iliac, femoral, popliteal, infrapopliteal, renal and subclavian arteries) and for the treatment of obstructive lesions of polytetrafluoroethylene (PTFE) access grafts or native arteriovenous dialysis fistulae. The PolarCath System is also indicated for postdeployed stent expansion of self-expanding peripheral vascular stents.

CONTRAINDICATIONS:

None.

WARNINGS:

Use of this device in coronary or carotid arteries has not been evaluated. Use of this device for stent delivery has not been evaluated. Use of this device for non-PTFE access grafts has not been evaluated. It is unknown whether the cold temperatures generated by the catheter will have any adverse effects on the material integrity and long term performance of these non-PTFE grafts.

POTENTIAL ADVERSE EFFECTS:

Possible adverse events include but are not limited to the following:

- Allergic reaction to contrast media
- Arteriovenous fistula
- Death
- Embolism
- Gas embolism
- Hemorrhage/hematoma
- Pain and tenderness
- Pseudoaneurysm formation
- Pyrogenic reaction
- Restenosis of the dilated vessel
- Sepsis/infection
- Thrombus
- Total occlusion
- Vessel dissection
- Vessel perforation

PRECAUTIONS:

- A thorough understanding of the technical principles, clinical applications, and risks associated with percutaneous transluminal angioplasty is necessary before using this device.
- Only PTFE arteriovenous graft material has been tested for compatibility with the PolarCath Dilatation System. To determine compatibility, testing was conducted to evaluate the tensile mechanical strength of PTFE samples treated with CryoPlasty® Therapy compared to those treated with conventional balloon angioplasty in a simulated environment. No difference was found between the two systems.

CAUTION:

Federal law (USA) restricts this device to sale by or on the order of a physician.



Your Primary, Durable Treatment Strategy

**For the results you want now.
For the options you may need later.**

CryoPlasty® Therapy with the **PolarCath® Peripheral Dilatation System** is a clinically proven first-line treatment for SFA and infrapopliteal lesions. The system is designed to initiate both mechanical and biological responses to produce beneficial vascular effects while preserving the anatomy for future interventional procedures. Keep your options open – choose the PolarCath System first. Call **1.888.272.1001** or visit **www.bostonscientific.com**.

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