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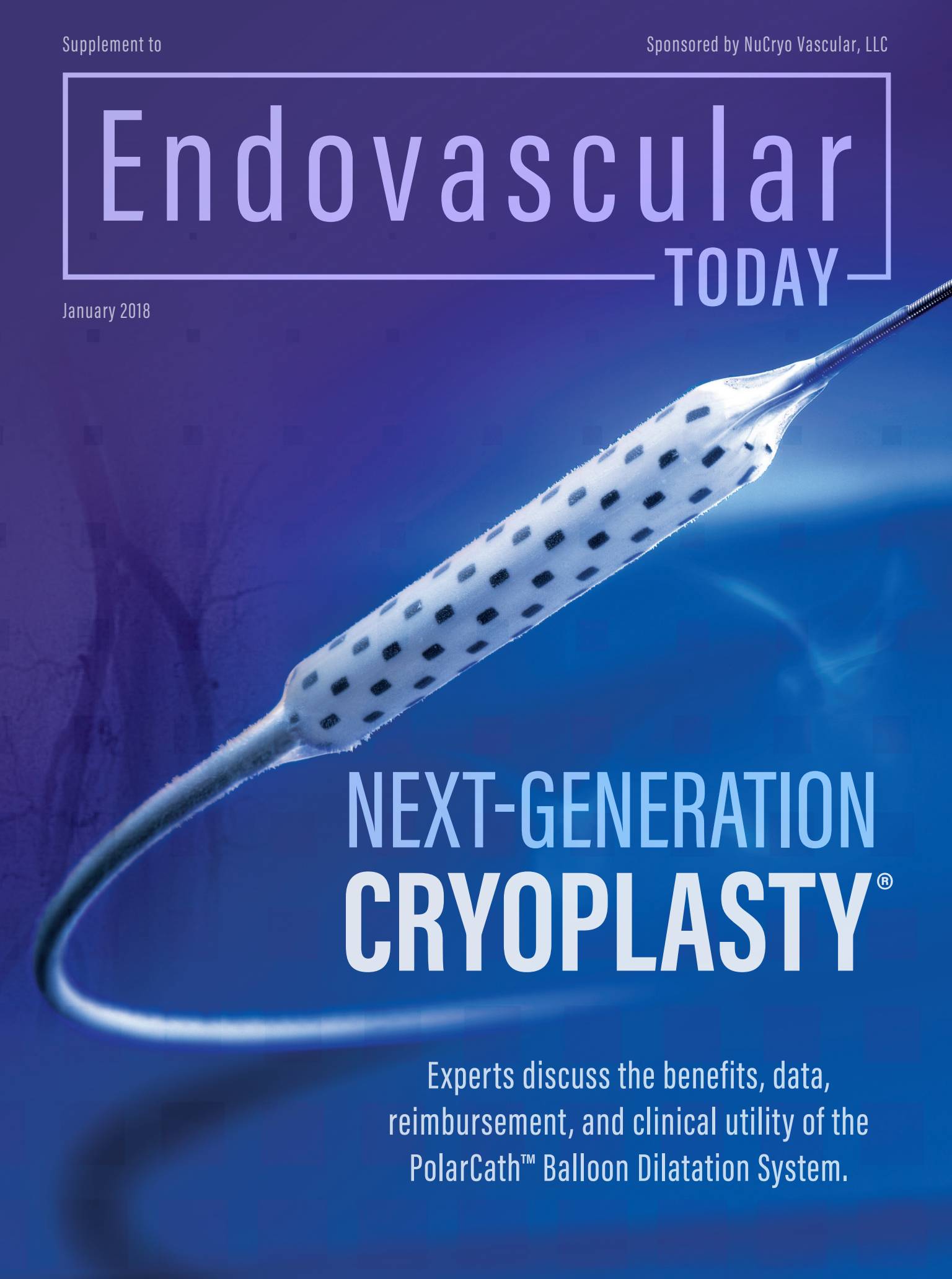

NEXT-GENERATION CRYOPLASTY®

Experts discuss the benefits, data, reimbursement, and clinical utility of the PolarCath™ Balloon Dilatation System.

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The Next-Generation PolarCath System

BY MAHIR ELDER, MD, FACC, FSCAI, FASNC, FAHA, FCCP, RPVI

The PolarCath System (NuCryo Vascular, LLC) is a unique, time-tested biological peripheral dilatation system that combines angioplasty and precise cryotherapy (cooling) to uniformly dilate peripheral vessels and reduce vessel recoil, dissection, and restenosis for the treatment of peripheral artery disease (PAD). The PolarCath System was developed in the late 1990s by Dr. James Joye, an interventional cardiologist in Mountain View, California, in an effort to overcome the limitations of peripheral balloon angioplasty. The PolarCath System received 510(k) approval in 2002, was launched in the United States in 2003, and was acquired by Boston Scientific Corporation (BSC) in 2005. BSC successfully increased their annual revenue of the PolarCath System to greater than $40 million annually, and it quickly became their top-selling peripheral vascular product. BSC decided to discontinue manufacturing and marketing the product in 2012. In 2014, NuCryo Vascular purchased the rights to the PolarCath System to manufacture, reengineer, and relaunch it. Since that time, the PolarCath System has continued to be a proven and viable option for treating PAD.

SCIENCE

Cryoplasty combines the dilatation force of angioplasty with the simultaneous delivery of cold thermal energy to the arterial wall. Both mechanisms are achieved simultaneously by filling the angioplasty catheter with nitrous oxide instead of the usual contrast saline/solution mixture. Cryotherapy has been proven to biologically alter the behavior of arterial cellular components in a benign healing process. Several scientific studies have demonstrated that this cooling process within the vessel results in:

- weakening of the plaque, promoting uniform dilation and reducing vessel trauma;
- alteration of elastin fibers to reduce vessel wall recoil, while collagen fibers remain undisturbed and capable of maintaining architectural integrity;
- induction of smooth muscle apoptosis, which is associated with reduced neointimal formation and, subsequently, less restenosis.

SYSTEM

The next-generation PolarCath Peripheral Dilatation System (Figure 1) currently consists of a sterile disposable catheter; a sterile disposable catheter extension; a non-sterile, disposable nitrous oxide cartridge; and a non-sterile, ***reusable*** cryoplasty inflation unit.

- ***Catheter:*** Coaxial catheter shaft with two concentric, noncompliant balloon systems mounted at the distal tip of the of the shaft.
- ***Nitrous oxide cartridge:*** A cartridge filled with liquid nitrous oxide that, by way of a phase change, inflates the balloon and cools it down to -10° C. One cartridge equals one inflation.
- ***Cryo inflation unit:*** Nonsterile, reusable unit designed to regulate inflation pressure and treatment time of the PolarCath balloon. The operating pressure of the balloon is 8 atm.
- ***Connector:*** Sterile catheter shaft connecting the nonsterile inflation unit to the sterile catheter.

In contrast to the previous system, which was completely disposable, this next-generation system has introduced a reusable cryo-inflation unit (CIU2). The CIU2 is capable of completing 100 inflations and is an advance that has cut the cost per case by nearly half.

DATA

PolarCath has been studied extensively and has proven safety and efficacy.

Cryoplasty or Conventional Balloon Postdilation of Nitinol Stents for the Revascularization of Peripheral Arterial Segments (COBRA)

This 2012 trial was a prospective, multicenter, randomized controlled clinical trial of diabetic patients with complex disease that compared PolarCath to standard percutaneous transluminal angioplasty (PTA) for postdilatation of nitinol stents.[1] In this study, the primary endpoint was binary restenosis at 12 months as determined by duplex ultrasound, defined as ≥ 2.5-fold increase in peak systolic velocity ratio (PSVR) by duplex ultrasound. In lesions averaging 15 cm, many of which (50%) were chronic total occlusions, cryoplasty reduced the rate of restenosis compared to PTA by nearly 50%. These data demonstrated that cryoplasty significantly reduces binary restenosis, especially impressive in a challenging group of patients with diabetes, many of whom presented with 100% total occlusions.

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Above the Knee

The investigational device exemption (IDE) trial for the treatment of femoropopliteal arterial disease was a prospective, multicenter registry published in 2005 that evaluated the efficacy of cryoplasty.[2] There were 102 patients treated with the primary strategy of stand-alone PolarCath therapy in patients with predominantly TASC II B and C lesions, as have been tested in most contemporary stent and DCB trials. Primary patency, as adjudicated by an independent core lab, was 70.1%. In contrast to today's trials, the more stringent PSVR criteria of > 2.0 was used to determine patency. When viewed by current PSVR standards of > 2.5, these data yield a primary patency of 82%, comparable to many published DCB trials (data on file at NuCryo). Additionally, because of the lower dissection rates seen with cryoplasty, bailout stenting occurred in only 9% of patients. The IDE extended follow-up study, published in 2006, demonstrated that clinical patency (calculated by Kaplan-Meier estimate) was well maintained at 75% for over 3 years post treatment.[3]

Below the Knee

The benefits of using PolarCath below the knee (BTK) were highlighted in the BTK Chill study published in 2009.[4] The BTK Chill study was a prospective, multicenter study that examined the use of cryoplasty for BTK occlusive disease in patients with critical limb ischemia. Freedom from amputation at 365 days was 85% with an acute overall technical success rate of 97%. The technical success rate per Rutherford class 4, 5, and 6 was 95.5%, 98%, and 96.4%, respectively. The PolarCath balloon was also proven to be very safe, with clinically significant dissections of 1% in the trial.

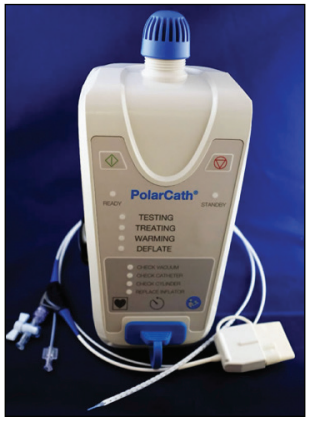
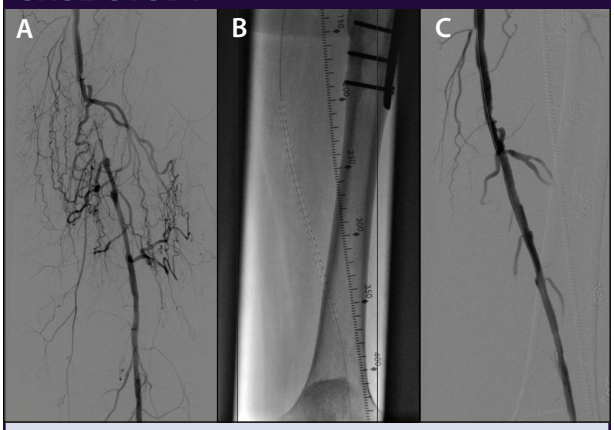


Figure 1. The PolarCath Balloon Dilatation System consists of a sterile disposable catheter; a sterile disposable catheter extension; a non-sterile, disposable nitrous oxide cartridge; and a non-sterile, reusable cryoplasty inflation unit.

REIMBURSEMENT

Cost per case is a real concern in today's practice of medicine. In my experience, cryoplasty has proven to be more economical as compared to DCB technology. Although a pass-through code was created in 2015 to help offset the costs for DCBs, cryoplasty still offered a significant savings when more than two DCBs were needed in a procedure. A single cryoplasty balloon can provide multiple inflations and treatments, unlike DCBs that only allow for a single use. As a result, the total cost associated with the use of a DCB often outweighs the savings intended with the pass-through payment. Furthermore, the Centers for Medicare & Medicaid Services ruled to eliminate that DCB pass-through code in December 2017. Effective January 1, 2018, all DCBS are reimbursed as standard PTA. PolarCath will continue to offer a significant savings over DCBs, given its lower cost point and multiuse ability during each procedure. ■

CASE STUDY



A patient returned to our institution with Rutherford class 3 life-threatening claudication after failed conservative therapy (A). Repeat angiography showed reocclusion of her right superficial femoral artery. She was treated with a 4- X 150-mm cryoplasty balloon (B) and experienced lesion reduction to < 10%, and her symptoms decreased to Rutherford class 1 (C).

1. Banerjee S, Das TS, Abu-Fadel MS, et al. Pilot trial of cryoplasty or conventional balloon post-dilation of nitinol stents for revascularization of peripheral arterial segments: the COBRA trial. J Am Coll Cardiol. 2012;60:1352–1359.
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.
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Benefits of Cryoplasty Compared to DCB

BY AMIT SRIVASTAVA, MD, FACC, FABVM

The PolarCath Balloon Dilatation System (cryoplasty; NuCryo Vascular, LLC) is a specialty angioplasty balloon that offers the unique science of cryogenic cooling to treat peripheral artery disease (PAD). We have observed several benefits in our lab when using the PolarCath balloon (Figure 1) over drug-coated balloons (DCBs), including ease of use, case efficiency, improved clinical outcomes, and a cost savings per case.

Apoptosis (programmed cell death) is the primary mechanism of action for both PolarCath and DCBs. However, the methods used to achieve apoptosis are vastly different (Figure 2). All current DCBs on the market utilize paclitaxel. This technology relies on the ability of paclitaxel to be absorbed into the arterial wall and remain there at a high concentration over an extended period of time. This high concentration of paclitaxel prevents the cell from completing the mitosis cycle and suppresses cell proliferation, causing apoptosis and inhibiting the process of neointimal tissue build up and clinical restenosis. The key components for the mechanism of action of a DCB include (1) balloon inflation, (2) an excipient binding and delivering the drug to the arterial wall, and (3) crystallized paclitaxel acting as the agent that renders the cells incapable of smooth muscle cell proliferation. Paclitaxel, a cytotoxic drug with its lipophilic properties, is passively absorbed through cell membranes, causing the sustained drug effect at the target site for approximately 28 days.

In contrast, the PolarCath balloon is the only cryogenic balloon available in the peripheral market. PolarCath simultaneously combines the mechanical force of a balloon dilation at a programed 8 atm with the benefits of cryotherapy. Compressed liquid nitrous oxide, used as the dilatation medium, creates an endothermic reaction and allows the cryogenic therapy to occur. The compressed liquid nitrous oxide coverts to a gas, which results in balloon inflation and simultaneous cooling of the vessel wall to -10° C. PolarCath also provides an additional three-component effect on the vessel, including:

1. Altered plaque response: Cooling causes the interstitial saline to freeze. As ice forms and expands, microfractures are created that weaken the plaque. This action contributes to more uniform dilation of the vessel and less medial injury.
2. Reduced elastic recoil: Cooling induces an alteration of the collagen and elastin fibers, reducing vessel wall elasticity, which protects against recoil.
3. Smooth muscle cell apoptosis: Freezing interstitial saline in the medial layer of the vessel wall creates a hypertonic environment. Osmotic forces cause smooth muscle cells to eject water. It is speculated that this dehydration and rehydration upon thawing postinflation is what triggers a documented downregulation in smooth muscle cell genetic signaling. A reduction in smooth muscle cells via this noninflammatory mechanism has been correlated with a reduction in neointimal formation.

Both PolarCath and DCBs are indicated for use in femoropoliteal arterial disease and have similar 1-year patency data, although no head-to-head trials have been completed. Using a peak systolic velocity ratio of 2.5 (the standard in all DCB trials), PolarCath showed a 9-month patency of 82% in its investigational device exemption trial.[1] In addition, PolarCath is the only balloon proven to minimize binary restenosis in diabetic patients after stent placement. The COBRA study is a randomized clinical trial comparing standard percutaneous transluminal angioplasty (PTA) for the postdilatation of nitinol stents. In this trial, PolarCath was shown to minimize binary restenosis by nearly 50% at 12 months compared to standard PTA.[2]

PolarCath has also demonstrated efficacy when treating Rutherford class 4 to 6 critical limb ischemia patients in the BTK Chill study.[3] BTK Chill resulted in a 97% technical success

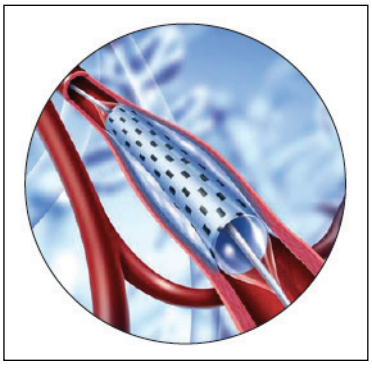

Figure 1. The PolarCath balloon.

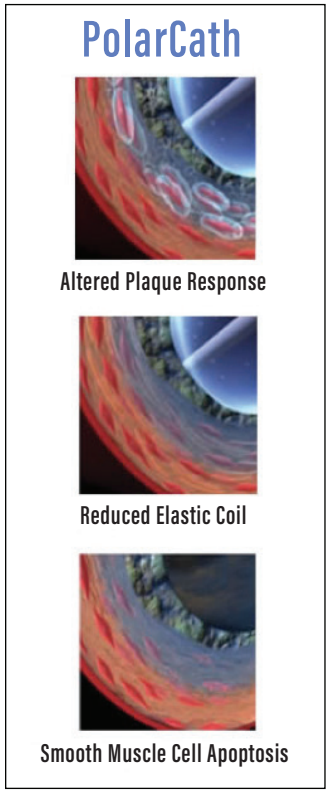

Figure 2. The PolarCath balloon's mechanism of action.

rate with a < 1% dissection rate. On the other hand, DCBs are not approved, indicated, or available in sizes suitable for below-the-knee lesions. The IN.PACT DEEP trial showed DCBs were not beneficial in below-the-knee applications, failing to demonstrate superiority over PTA, and the safety signal detected a trend toward higher major amputation rate in the DCB arm.[4] While ongoing trials for below the knee are in progress, no data have been presented to document its utility in tibial targets.

Other key benefits of PolarCath are the day-to-day indicated applications, ease of use in procedures, and cost savings over DCBs. The use of PolarCath has greatly improved the overall efficiency of my procedures. According to the instructions for use, all DCBs require the lesion to be predilated with a separate balloon and require a dwell time of at least 180 seconds to ensure the drug adheres to the arterial wall. In addition, each DCB can only be used one time. Currently, the longest DCB available is a treatment length of 150 mm. If multiple treatments are needed or if the lesion is > 15 cm, a new DCB is required. In contrast, the PolarCath balloon does not need predilation (no balloon exchanges), does not require a dwell time (apoptosis treatment completed in 20 seconds), and can deliver unlimited apoptosis treatments with a single balloon. These three benefits significantly reduce overall procedural costs by saving time and minimizing costs associated with additional required equipment. Furthermore, PolarCath will offer a significant savings over DCBs with the elimination of the DCB pass-through codes in 2018.

Furthermore, PolarCath has a proven safety profile and eliminates the concerns of paclitaxel showering downstream to other vascular beds. There are reported concerns with the use of DCB, where the DCB excipient and paclitaxel may embolize during delivery and/or inflation. In fact, Aloke Finn, MD, Medical Director at CVPath Institutes recently stated, "all DCBs tested exhibited downstream effects of paclitaxel drug and/or downstream emboli, although differences between different DCBs were seen. This finding of embolic debris from DCB coatings is of potential importance and may be further compounded in patients with claudication and more complex critical limb ischemia with limited flow reserve."[5]

Therefore, because paclitaxel is cytotoxic, this may impact the healing of ulcers or may cause tissue damage such as panniculitis. On the other hand, there are no reported long-term concerns with the use of PolarCath. Cryogenic therapy delivered via the endothermic phase change of nitrous oxide has allowed the PolarCath balloon to maintain the ideal safety profile when treating PAD. ■

1. 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.
2. Banerjee S, Das TS, Abu-Fadel MS, et al. Pilot trial of cryoplasty or conventional balloon post-dilation of nitinol stents for revascularization of peripheral arterial segments: the COBRA trial. J Am Coll Cardiol. 2012;60:1352-1359.
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5. Vascular News. Particulate embolisation after femoral artery treatment with drug-coated balloons. https://vascularnews.com/particulate-embolisation-femoral-artery-treatment-dcbs/. Accessed December 20, 2017.

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The Benefit of Cryoplasty in the Office-Based Lab

The patient and case dynamics to weigh out when utilizing an interventional approach to PAD.

BY GEORGE NASSER, MD, FACC

The PolarCath Balloon Dilatation System (NuCryo Vascular, LLC) is a versatile specialty balloon that offers the unique mechanism of cryogenic cooling to treat peripheral vascular disease. The PolarCath balloon uses the phase change of liquid nitrous oxide to gas to inflate the balloon and cool the arterial wall to -10° C for a controlled 20 seconds. This controlled cryotherapy can induce apoptosis in smooth muscle cells and other cells that participate in the restenosis process.

The peripheral vascular treatment algorithm in my office-based lab is driven by patient presentation, clinical outcomes supported by clinical data, cost, and overall efficiency of the device. As a result, PolarCath is an integral component of my treatment algorithm for peripheral artery disease for the reasons presented in this article.

INDICATIONS

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

CRYOPLASTY VERSUS DRUG-COATED BALLOONS IN THE OFFICE-BASED LAB

Cryoplasty and drug-coated balloons (DCBs) both tout a mechanism of action that minimizes smooth muscle cell proliferation via apoptosis. DCBs in the United States currently use an excipient and paclitaxel, while cryoplasty uses cryogenic therapy at -10° C to induce apoptosis. With a similar mechanism of action to DCBs, cryoplasty offers several other advantages for my peripheral procedures in the office-based lab.

Cost

Currently, cryoplasty catheters are significantly less expensive than DCBs without any additional reimbursement, and thus cryoplasty offers a significant savings. The cryoplasty balloon also offers savings when multiple treatments are needed in a given case. Because the same PolarCath balloon can be used multiple times as compared to the one-time delivery of the DCB, PolarCath offers incremental savings when treating long, diffuse lesions or stenoses requiring multiple treatments. This cost savings will also now be realized in the hospital setting, as all DCB outpatient pass-through codes were eliminated at the end of 2017.

Procedural Efficiency

Cryoplasty also increases the overall efficiency of my peripheral procedures. Because the PolarCath balloon can provide multiple treatments of long segments with the same balloon, the need for multiple balloons is minimized. Additionally, DCBs require long inflations to ensure that the drug is absorbed into the arterial wall. With cryoplasty, multiple segments can be treated in the time required to treat one segment with a DCB. Balloon exchanges for each treated segment are not needed with PolarCath; however, a fresh balloon is needed for each segment treated with a DCB. PolarCath does not have excipient issues, and there is no need for filter placement to prevent distal embolization of excipient. This means less equipment, less complexity, less expense, and less time. As a result, by using cryoplasty, I can save approximately 15 to 20 minutes per case as compared to DCBs, which allows me to spend more time seeing other patients.

CASE REVIEW #1

An 80-year-old woman presented to our clinic with a 1-month history of resting right lower extremity pain consistent with critical limb ischemia. Her comorbidities included hypertension and end-stage renal disease, and she was on dialysis. On examination, she had

preserved pulses in the common femoral arteries with poor distal pulses, right worse than left, which was suggestive of superficial femoral artery (SFA) disease. This was confirmed with a noninvasive study.

She was then taken to the office-based lab for invasive study. Right lower extremity arteriography was performed utilizing an up-and-over approach after retrograde left common femoral artery sheath placement. This confirmed diffuse, high-grade right SFA occlusive disease extending into the P1 segment of the right popliteal artery. The diseased segments were successfully crossed with an exchange-length 0.014-inch guidewire with the distal tip placed in the distal peroneal artery. The SFA stenoses were first debulked by atherectomy. The SFA and proximal popliteal artery were then treated with a 5- X 150- X 150-mm cryoplasty balloon with sequential overlapping inflations. Blood flow was restored, and distal pulses were easily palpable and 3+ after the procedure. At 6-month follow-up, the patient was free of ischemic rest pain, and she had no intermittent claudication.

CASE REVIEW #2

An 80-year-old man presented to my office with complaints of right leg pain with a wound. His medical history included coronary artery disease, hypertension, hyperlipidemia, and aortobifemoral bypass grafting. On examination, the right foot and the distal half of the right leg were cool to the touch, the right foot was ruddy, and there was a nonhealing wound with skin breakdown at the right heel.

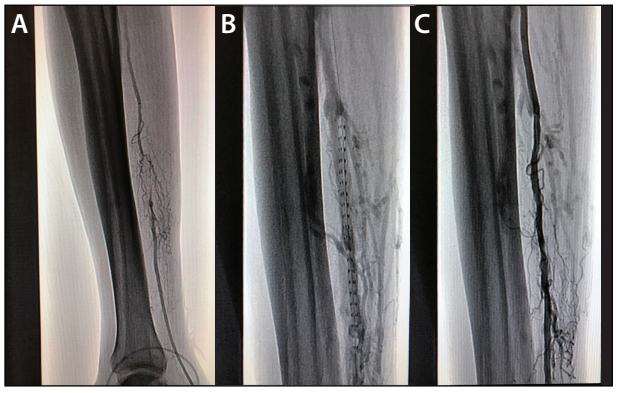

Figure 1. The patient presented with an occluded tibial artery that was treated via pedal intervention (A); cryoplasty was performed with a 2.5- X 150-mm PolarCath balloon (B); and wide patency was achieved (C).

The patient was taken to the office-based lab for invasive evaluation and treatment. After retrograde sheath placement in the left common femoral artery, an up-and-over approach was used for arteriography (Figure 1A). This demonstrated a patent right SFA, occluded anterior tibial artery, patent but diseased peroneal artery, and a total occlusion of the mid-posterior tibial artery. Due to the angulation of the aortobifemoral graft limbs, the patient was sent home and brought back for a pedal intervention.

The posterior tibial artery was accessed utilizing a micropuncture needle under ultrasound guidance. After the total occlusion was crossed, cryoplasty was performed with a 2.5- X 150- X 150-mm balloon (Figure 1B). Wide patency was achieved, and the pedal microsheath was removed with excellent hemostasis (Figure 1C). On follow-up, the wound had completely healed and the ischemic foot changes had resolved.

CASE REVIEW #3

A 68-year-old woman with a prior history of intermittent claudication of the right lower extremity presented to our office. Angiography showed both severe stenoses and aneurysms of the right SFA. She subsequently was treated with placement of a covered stent. After several months, she developed recurrent right lower extremity intermittent claudication; arterial ultrasound showed total occlusion of the stent graft.

She was brought to the office-based lab, placed in the prone position, and a retrograde sheath was placed in the right popliteal artery under ultrasound guidance. The occluded stent was crossed, arteriography was performed proximal to the occlusion, and atherectomy was performed to debulk the stenosis. Cryoplasty was then performed in serial overlapping inflations of the right SFA stent and P1 segment of the popliteal artery utilizing a 6- X 150- X 135-mm cryoplasty balloon. At 3- and 6-month follow-up, she was free of claudication, and 3- and 6- month arterial ultrasounds showed wide patency. ■

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