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Benefits of Cryoplasty Compared to DCB

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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

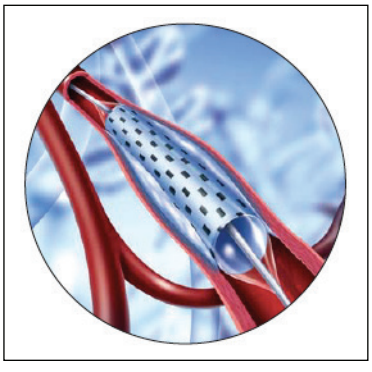

Figure 1. The PolarCath balloon.

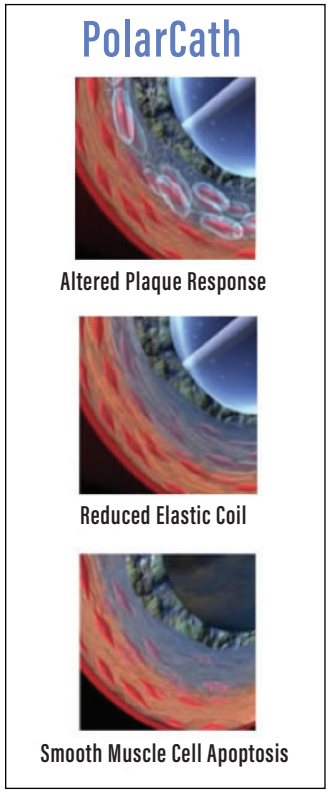

Figure 2. The PolarCath balloon's mechanism of action.

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. ■

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