

## Use of DCBs in Long Femoropopliteal Lesions: Where Do We Stand?

By Gary M. Ansel, MD

Endovascular treatment has become the standard of care for most cases of symptomatic femoropopliteal peripheral artery disease.<sup>1,2</sup> However, given the anatomic characteristics of the femoral artery, longer lesions are commonly harder to treat and have worse long-term outcomes. Decreased patency and increased need for revascularization in longer lesions have been demonstrated in plain balloon angioplasty, bare-metal stent, and atherectomy studies.<sup>3-7</sup> Drug-eluting stents have demonstrated improvement over their bare-metal counterparts; in one single-center series, there was still a decline in patency but reasonably good freedom from repeat revascularization for very long lesions.<sup>8</sup>

Longer lesions also often possess other characteristics that challenge endovascular treatment, including calcium, in-stent restenosis (ISR), thrombus, and occlusions. Drug-coated balloons (DCBs) have been successfully used to treat lesions shorter than 10 cm, both in randomized controlled trials (RCTs) and larger single-arm registries.<sup>9-18</sup> However, to date, there are only six studies (only one of which is an RCT) showing the results of DCB treatment of lesions longer than 20 cm (Table 1).<sup>19-24</sup> Notably, these long lesions are often occlusive and calcified, and thus their treatment is associated with provisional stenting ranging from 10% to 50%. Despite the challenging nature of these lesions, outcomes appear to demonstrate the safety and effectiveness of DCB use in long lesions.

In response to these clinical results, the recent Society for Cardiovascular Angiography and Interventions (SCAI) guidelines recommended DCBs as the definitive therapy for SFA lesions longer than 20 cm, whether that lesion has calcium, ISR, or a chronic total occlusion.<sup>25</sup> However, until recently, interventionalists have had to use up to four balloons to cover long and diffuse lesions. This incurs both a higher procedural cost to payers and patients, as well

as an increase in procedure time. Shorter balloons also increase the chances of geographic miss, which was shown to negatively impact outcomes in the LEVANT I study.<sup>26</sup> Importantly, care must be taken with long balloons to avoid oversizing in the distal segment.

Beyond cost, there are also other reasons to consider the use of long balloons. First, a relatively recent retrospective single-center analysis of 101 subjects demonstrated fewer type C-F dissections when using long percutaneous transluminal angioplasty (PTA) balloons.<sup>27</sup> Although this study was performed with uncoated balloons, the mechanical principle remains similar, and reducing dissections in long femoropopliteal lesions could reduce the need for stenting and thus placement of a permanent metal implant. Second, if only one balloon is used as compared to two or three, an implanting physician may have time to allow slower balloon inflation and deflation times. The possible importance of this procedural characteristic was discussed as an explanation for the improved standard PTA outcomes in DCB trials by a panel at VIVA 2017 after presentation of the ILLUMINATE EU 2-year results, which had improved PTA outcomes compared to past studies.<sup>28</sup>

Luckily, longer balloons and expanded indications to treat longer lesions are coming onto the market in the United States, allowing interventionalists to more easily treat a broader set of lesions. In the United States, there are three balloons currently approved to treat femoropopliteal lesions: Stellarex™ DCB (Philips), Lutonix™ DCB (BD Interventional), and IN.PACT™ Admiral™ DCB (Medtronic). The Stellarex™ DCB is approved to treat lesions up to 180 mm, with balloon sizes up to 120 mm. The Lutonix™ DCB is approved to treat lesions up to 300 mm with balloon sizes up to 150 mm. In May 2018, the IN.PACT™ Admiral™ DCB received FDA

**TABLE 1. USE OF DCBs IN LONG LESIONS (< 20 CM)**

Study Name	Baseline Characteristics					12-Month Outcomes			
	Number of Subjects	Mean Lesion Length	Chronic Total Occlusion	In-Stent Restenosis	Calcified	Primary Patency	FF CD-TLR or TLR	Stenting	Amputation
LEVANT long lesions <sup>19</sup>	118	21.3 cm	52.1%	NR	88.1%	68.9%	87.8%	39.8%	NR
SFA-Long <sup>20</sup>	105	25.1 cm	49.5%	Exclusion criteria	63.4%	83.2%	96%	10.5%	0%
IN.PACT Global long-lesion cohort <sup>21</sup>	157	26.4 cm	60.4%	0%	71.8%	91.1%	94%	40.4%	0%
IN.PACT Global CTO cohort <sup>22</sup>	126	22.8 cm	100%	0%	71.0%	85.3%	89.1%	46.8%	0%
Retrospective dual-center DCB vs DES <sup>23</sup>	131	19.4 cm	52.7%	Exclusion criteria	68.7%	76.1%	~80%–85%	18.3%	NR
Retrospective single-center single-arm study <sup>24</sup>	260	24 cm	65.3%	37.2%	69%	79.2%	85.4%	23.3%	1.4%

Note: Definitions vary across all studies; table provided for qualitative comparisons only.

Abbreviations: CTO, chronic total occlusion; DCB, drug-coated balloon; DES, drug-eluting stent; FF CD-TLR, freedom from clinically driven target lesion revascularization; NR, not reported; TLR, target lesion revascularization.

approval to treat femoropopliteal lesions up to 360 mm in length, and as of June 2018, 200- and 250-mm balloons were approved for clinical use.

With these longer balloons available for clinical use, treatment options for peripheral artery disease have expanded. Interventionalists look forward to evaluating the long-term DCB results in patients with longer femoropopliteal lesions.

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**Disclosures: Advisor for Abbott Vascular, Boston Scientific Corporation, Medtronic, Philips & Volcano Philips, Gore & Associates, and Surmodics; a compensated board member of VIVA Physicians, a 501(c)(3) not-for-profit education and research organization; equity investor in Primacea; receives royalties from Cook Medical.**

# Medtronic

## IN.PACT™ Admiral™ Brief Statement

### Indications for Use:

- The IN.PACT™ Admiral™ Paclitaxel-Coated PTA Balloon catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions with lengths up to 360 mm in superficial femoral or popliteal arteries with reference vessel diameters of 4-7 mm.
- Contraindications
- The IN.PACT™ Admiral™ DCB is contraindicated for use in:
  - Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
  - Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Patients with known allergies or sensitivities to paclitaxel
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure.

### Warnings

- Use the product prior to the Use-by Date specified on the package.
- Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
- Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
- Do not move the guidewire during inflation of the IN.PACT™ Admiral™ DCB.
- Do not exceed the rated burst pressure (RBP). The RBP is 14 atm (1419 kPa) for all balloons except the 200 and 250 mm balloons. For the 200 and 250 mm balloons the RBP is 11 atm (1115 kPa). The RBP is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
- The safety and effectiveness of using multiple IN.PACT™ Admiral™ DCBs with a total drug dose exceeding 34,854  $\mu$ g of paclitaxel in a patient has not been clinically evaluated.

### Precautions

- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents.
- The safety and effectiveness of the IN.PACT™ Admiral™ DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure or following treatment failure has not been evaluated.

- The extent of the patient's exposure to the drug coating is directly related to the number of balloons used. Refer to the Instructions for Use (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty including thrombosis, vascular complications, and/or bleeding events
- Vessel preparation using only pre-dilatation was studied in the clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT™ Admiral™ DCB.
- This product is not intended for the expansion or delivery of a stent

### Potential Adverse Effects

- The potential adverse effects (e.g. complications) associated with the use of the device are: abrupt vessel closure; access site pain; allergic reaction to contrast medium, antiplatelet therapy, or catheter system components (materials, drugs, and excipients); amputation/loss of limb; arrhythmias; arterial aneurysm; arterial thrombosis; arteriovenous (AV) fistula; death; dissection; embolization; fever; hematoma; hemorrhage; hypotension/hypertension; inflammation; ischemia or infarction of tissue/organ; local infection at access site; local or distal embolic events; perforation or rupture of the artery; pseudoaneurysm; renal insufficiency or failure; restenosis of the dilated artery; sepsis or systemic infection; shock; stroke; systemic embolization; vessel spasms or recoil; vessel trauma which requires surgical repair.
- Potential complications of peripheral balloon catheterization include but are not limited to the following: balloon rupture; detachment of a component of the balloon and/or catheter system; failure of the balloon to perform as intended; failure to cross the lesion.
- Although systemic effects are not anticipated, potential adverse events that may be unique to the paclitaxel drug coating include but are not limited to: allergic/immunologic reaction; alopecia; anemia; gastrointestinal symptoms; hematologic dyscrasia (including leucopenia, neutropenia, thrombocytopenia); hepatic enzyme changes; histologic changes in vessel wall, including inflammation, cellular damage, or necrosis; myalgia/arthralgia; myelosuppression; peripheral neuropathy.
- Refer to the Physician's Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.
- Please reference appropriate product Instructions for Use for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at [www.manuals.medtronic.com](http://www.manuals.medtronic.com).

### CAUTION:

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

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