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Directional Atherectomy and Drug-Coated Balloon Therapy for Leaving Nothing Behind

An Update From VIVA REALITY

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Disclosures: Consultant to Alucent Biomedical, Becton Dickinson, Medtronic, Metavention, Pedra Technology, and Philips.

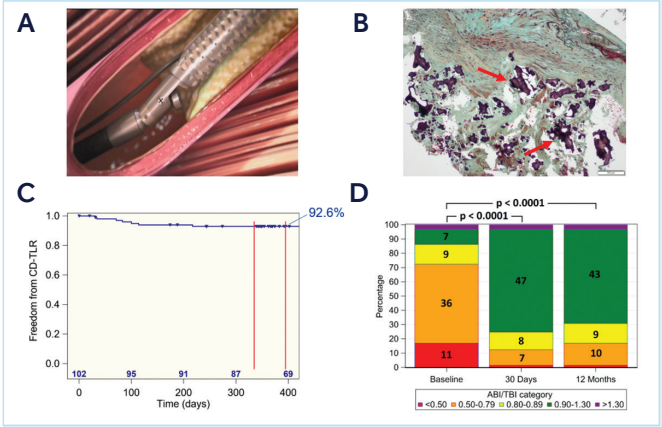

Figure 1. HawkOne directional atherectomy system (A). Histology showing excised calcified atheroma (arrows indicating calcium) (B). Freedom from CD-TLR by Kaplan-Meier estimate in the REALITY study at 12 months (C). Percentage of participants with improved ABI/toe-brachial index at 30-day and 12-month follow-up (D).

REALITY is a unique study that explored the safety and effectiveness of the specific treatment algorithm of vessel preparation using the HawkOne™ directional atherectomy system (Medtronic) prior to IN.PACT™ Admiral™ drug-coated balloon (DCB; Medtronic) angioplasty. Sponsored and conducted by the VIVA Physicians, REALITY focused specifically on complex femoropopliteal lesion morphologies characterized by long lesion lengths and bilateral vessel wall calcification. A large percentage were long chronic total occlusions (CTOs). In these aspects, REALITY sets a new "high bar" in assessing the safety and effectiveness of this treatment strategy in a well-defined patient cohort with complex symptomatic femoropopliteal occlusive disease.

A primary focus of REALITY was the prespecified requirement of high grades of vessel wall calcification as assessed by fluoroscopy. This inclusion criterion presented a challenge to patient recruitment because patients were required to have bilateral vessel wall calcification, and the cumulative bilateral calcification had to involve a significant percentage of total lesion length. In this regard, REALITY enrolled not only long lesions (averaging 18 cm) but also 86.2% of the lesions exhibited grade 3 and 4 bilateral calcification. To assess vessel wall calcification, REALITY used a novel calcification grading scale called the Peripheral Arterial Calcium Scoring System (PACSS) and assessed an individual lesion PACSS index, defined as the mean bilateral vessel wall calcification length, divided by the lesion length, and multiplied by 100. Moreover, REALITY included independent angiographic, duplex Doppler, and histology core lab assessment of all data and clinical events committee adjudication of all clinical events. Therefore, these distinctive elements define the unique contribution of REALITY to better our understanding of the safety and effectiveness of this treatment algorithm in complex femoropopliteal lesions.

During the design phase of REALITY, the complexity of the lesions to be studied made the consideration of a randomized

design difficult. What would be an appropriate control arm for such long, calcified lesions? Recent registry and single-center data have demonstrated excellent 12-month effectiveness of DCB angioplasty in long femoropopliteal lesions and CTOs with varying degrees of calcification; however, acute vessel recoil and/or arterial dissection necessitated provisional bare-metal stenting ranging from 10% to > 40% of participants.[1,2] Furthermore, data from a long lesion cohort reported that the need for provisional stent implantation increased to 51% in lesions > 25 cm.[1] Aside from surgery, which the Trans-Atlantic Inter-Society Consensus II guidelines suggest is appropriate in such lesions, it can be argued that there is no other appropriate standalone endovascular control arm.

The key takeaways from VIVA REALITY are that a vessel preparation strategy using HawkOne directional atherectomy (Figure 1A and 1B) in conjunction with IN.PACT Admiral DCB angioplasty in long, calcified femoropopliteal arteries was both safe and effective up to 12 months. Importantly, from a clinical perspective, the high level of freedom from clinically driven target lesion revascularization (CD-TLR; 92.6%) demonstrates the sustained benefit to patients exhibiting complex femoropopliteal disease through 12 months (Figure 1C). Additionally, the primary patency rate of 76.7%, which includes follow-up beyond the prespecified 12-month endpoint, demonstrates objective evidence in the success of this treatment strategy. Notably, these results were achieved with a very low provisional stent rate (8.8%) given the long, calcified morphology of the lesions treated. Thus, these results reinforce the strategy of using directional atherectomy and DCB to achieve compelling outcomes in challenging calcified lesions while minimizing permanent scaffolding.

Results also demonstrated improved Rutherford classification and ankle-brachial index (ABI) from baseline through 12 months (Figure 1D). Despite the technical nuances to this approach, clinical outcomes were quite compelling and represent an exceptional data field that provides physicians with an important treatment strategy for a very complex patient population. Finally, the REALITY results pertain specifically to the use of the HawkOne directional atherectomy device and the IN.PACT Admiral DCB. It is inappropriate to generalize these findings to other atherectomy devices or adjunct percutaneous transluminal angioplasty technologies used together with other DCBs.

1. Scheinert D, Micari A, Brodmann M, et al. Drug-coated balloon treatment for femoropopliteal artery disease. Circ Cardiovasc Interv. 2018;11:e005654. doi: 10.1161/CIRCINTERVENTIONS.117.005654
2. Tepe G, Micari A, Keirse K, et al. Drug-coated balloon treatment for femoropopliteal artery disease: the chronic total occlusion cohort in the IN.PACT Global study. JACC Cardiovasc Interv. 2019;12:484-493. doi: 10.1016/j.jcin.2018.12.004

A Year in Review

As demonstrated by results from the REALITY trial, the "leave nothing behind" strategy using directional atherectomy and DCB was in the spotlight for treatment of lower extremity occlusive disease during the year 2020. Herein, we present highlights from a selection of last year's published Medical Affairs Corner articles that utilized the directional atherectomy and IN.PACT Admiral DCB strategy for the treatment of femoropopliteal arterial disease—including limb salvage in patients with critical limb ischemia (CLI) during the COVID-19 era, long calcified lesions, and multilevel disease.

Aug 2020

Navigating the Ins and Outs of CLI Care During the COVID-19 Pandemic

Gregory A. Stanley MD, FACS

Dr. Stanley discussed the challenges of CLI care during the COVID-19 pandemic, emphasizing a need for leveraging the most effective endovascular technologies available that provide high patency rates and decreased reinterventions and offer significant wound healing potential. The revascularization strategy used as a part of the limb salvage plan entailed debulking with directional atherectomy followed by DCB angioplasty. A woman in her early 70s was admitted with congestive heart failure exacerbation (ejection fraction, 20%). She had stage 3 chronic kidney disease, diabetes mellitus, coronary artery disease, and previous stroke with right lower extremity paralysis, as well as a 3-month-old left heel wound. Duplex ultrasound of the left lower extremity demonstrated occlusion of the superficial femoral artery (SFA), reconstitution of the popliteal artery with CTO in P1, and monophasic tibial waveforms. MRI demonstrated osteomyelitis of the left calcaneus.

Successful recanalization was performed with directional atherectomy of the SFA and popliteal artery using the HawkOne LX catheter followed by 5- X 250-mm and 5- X 200-mm IN.PACT Admiral DCBs. Before and after revascularization angiograms are shown in Figure 2. This article also reiterated the importance of rigorous follow-up visits (including virtual) and coordination among medical specialty clinics to

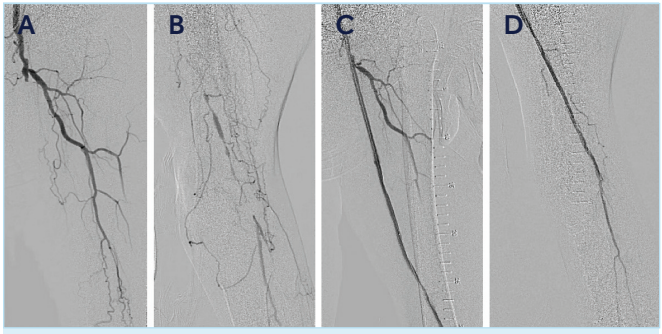

Figure 2. Initial angiograms (A, B) and completion angiograms of the SFA and popliteal artery after directional atherectomy with the HawkOne LX catheter followed by 5- X 250-mm and 5- X 200-mm IN.PACT Admiral DCBs (C, D).

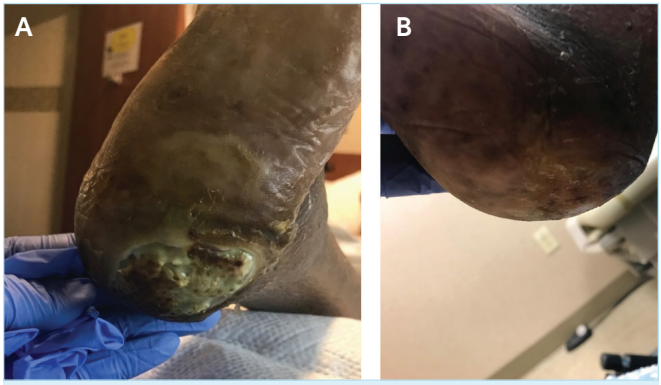

Figure 3. The left foot wound at initial examination (A) and 2.5 months postrevascularization (B) with directional atherectomy and IN.PACT Admiral DCB.

successfully maintain comorbidity equipoise. Over the course of 2.5 months, the patient's left heel wound was healed (Figure 3) and continued to do well.

Sept 2020

Directional Atherectomy and Drug-Coated Balloons for Femoropopliteal Disease: A Case-Based Discussion

Brian G. DeRubertis, MD, FACS

At the forefront of Dr. DeRubertis's revascularization strategy is managing the mechanical and biologic forces that threaten femoropopliteal patency. As discussed in this article, the limitations of stenting in the femoropopliteal segment, especially when used extensively in a "full-metal jacket" manner, are significant. Nitinol stents can suffer fractures, which are almost universally associated with loss of patency, and in-stent restenosis is significantly more difficult to treat compared to native arteries. They carry an increased risk of embolization, and the patency rates after treatment of in-stent restenosis are historically quite dismal. For these reasons, there has been a move away from standard nitinol stent use in recent years toward a "leave nothing behind" approach.

The case example from this article highlighted the versatility of directional atherectomy and its ability to achieve significant luminal gain while minimizing dissections, as well as the need for stent implantation for calcified long lesions. A woman in her late 60s with a history of hyperlipidemia and hypertension presented with an extensive left lateral lower leg pressure ulcer and a 2.5-cm heel ulcer. Diagnostic angiography demonstrated a distal SFA and proximal above-knee popliteal artery occlusion, with reconstitution of the behind-knee popliteal artery (Figure 4A and 4B). The occlusion in the SFA and above-knee popliteal artery was crossed with

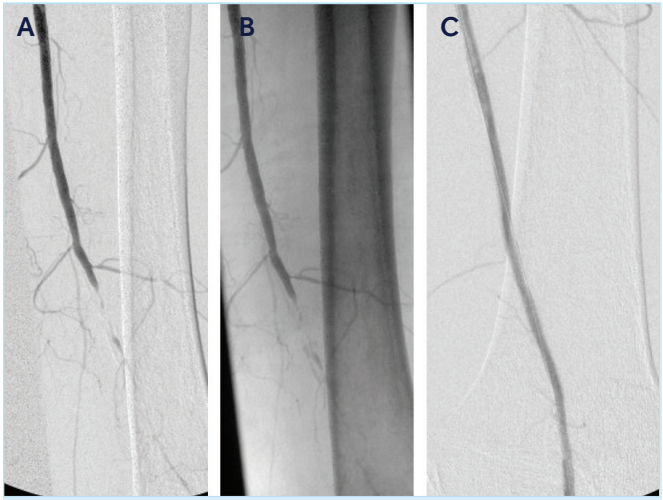

Figure 4. Initial (A, B) and completion (C) angiograms of the SFA and proximal popliteal artery.

a stiff, angled Glidewire™* (Terumo Interventional Systems) and a 0.035-inch Trailblazer™ support catheter (Medtronic). A 6-mm SpiderFX™ embolic protection device (Medtronic) was then delivered into the distal popliteal artery. The distal SFA and proximal popliteal artery were then treated with a TurboHawk™ SX-C peripheral plaque excision system (Medtronic), which was followed by postdilation using a 5- X 150-mm IN.PACT Admiral DCB. Completion angiography demonstrated a widely patent SFA and popliteal artery, without residual stenosis or dissection (Figure 4C). The patient's wounds healed within 2 months after operative debridement, which was performed after revascularization.

Oct 2020

Keeping it REAL: Revascularizing Extremities Against Limb Loss

Paul Michael, MD

Dr. Michael highlighted the importance of endovascular education in CLI care and limb salvage and how to access, cross, open, and keep these vessels patent. Using the following case example, the importance of choosing the right tool for the job when taking on a challenging end-stage peripheral artery disease patient with multilevel disease was demonstrated.

A patient in his mid-60s with diabetes mellitus, coronary artery disease, and hypertension presented with CLI and multilevel disease of right SFA, popliteal, and tibial vessels (Figure 5A and 5B). In addition to his multivessel CLI disease, the COVID-19 pandemic-related situation prevented him from achieving wound management therapy, and his rest pain worsened. Given the proximal long segment, right SFA disease, and distal SFA CTO, a contralateral left common

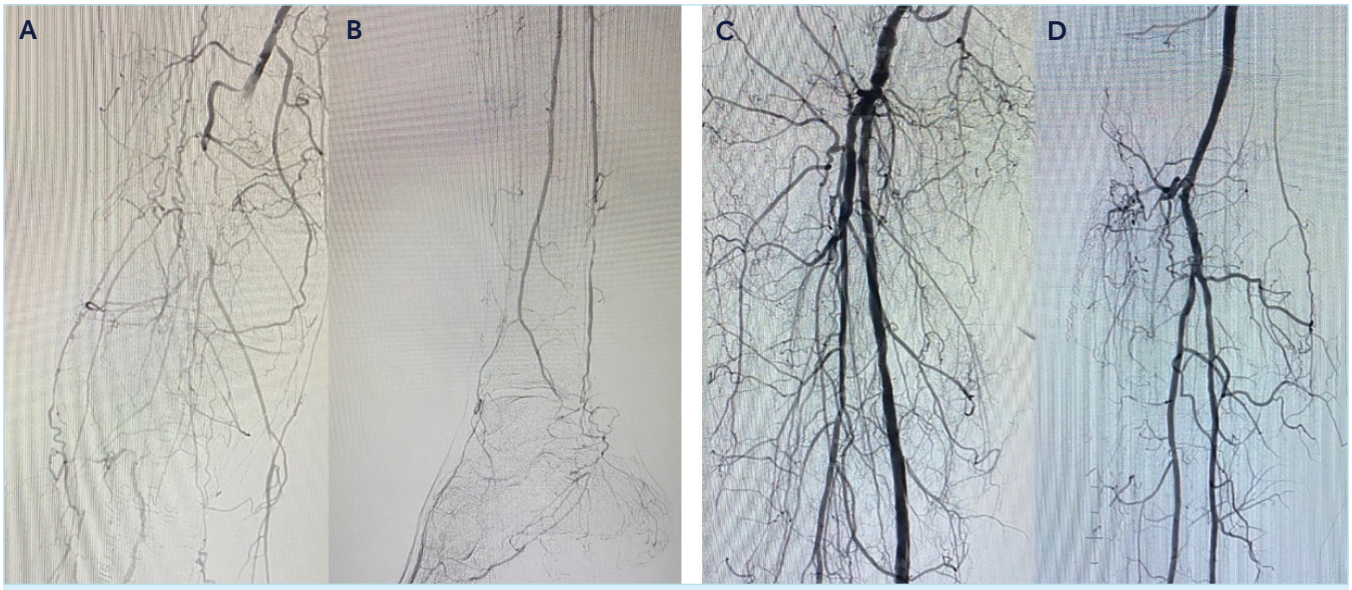

Figure 5. Initial angiograms showing multilevel disease in a CLI patient (A, B). Completion angiograms (C, D) demonstrating successful revascularization with directional atherectomy followed by angioplasty, which can be performed with percutaneous transluminal angioplasty and/or IN.PACT Admiral DCB.

femoral artery approach was taken. Directional atherectomy was chosen to debulk the SFA, popliteal, and posterior tibial artery, allowing for optimal DCB therapy delivery to the SFA and popliteal at the termination of the procedure without the need for excessive scaffolding in a stent-naive patient prone to restenosis.

After successful directional atherectomy of the right SFA and popliteal artery with a 6-F HawkOne directional atherectomy system, the device was exchanged for a TurboHawk SS-CL device to debulk the right posterior tibial artery down to the terminal portion at the level of the ankle. After directional atherectomy, balloon angioplasty of the right lateral plantar artery was performed. The posterior tibial artery was treated with a series of tapered NanoCross™ Elite balloon catheters (2.5-/2- X 210-mm, 3-/2.5- X 210-mm; Medtronic). The proximal posterior tibial artery was treated with a 4- X 300-mm Pacific Xtreme™ balloon catheter (Medtronic) extending into the SFA. For the popliteal and SFA, a 5- X 300-mm and then a 6- X 300-mm Pacific Xtreme balloon were used, followed by 6- X 150-mm IN.PACT Admiral DCB to the terminal and mid-right SFA. In summary, with the use of directional atherectomy followed by prolonged angioplasty inflations with long balloons and antirestenotic DCB therapy, the patient achieved brisk inline SFA and popliteal flow with two-vessel tibial outflow to the wound site. Figure 5 shows the initial and completion angiograms. ■

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HawkOne™ directional atherectomy system Reference Statement

Important Information:
Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

Indications for Use:
The HawkOne directional atherectomy system is intended for use in atherectomy of the peripheral vasculature. The HawkOne catheter is indicated for use in conjunction with the SpiderFX™ embolic protection device in the treatment of severely calcified lesions. The HawkOne catheter is NOT intended for use in the coronary, carotid, iliac or renal vasculature.

CAUTION: Federal (USA) law restricts this product for sale by or on the order of a physician.

TurboHawk™ peripheral plaque excision system Reference Statement

Important Information:
ndications, contraindications, warnings and instructions for use can be found in the product labelling supplied with each device.

Indications for Use:
The TurboHawk peripheral plaque excision system is intended for use in the atherectomy of the peripheral vasculature. The TurboHawk catheter is NOT intended for use in the coronary, carotid, iliac, or renal vasculature.

The TurboHawk catheter is indicated for use in conjunction with the SpiderFX™ embolic protection device in the treatment of severely calcified lesions (LX-C only).

CAUTION: Federal (USA) law restricts this product for sale by or on the order of a physician.

NanoCross™ Elite 0,014" OTW PTA balloon catheter Reference Statement

Important Information:
Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

Indications for Use:
The NanoCross Elite 0.014" OTW PTA balloon dilatation catheter is intended to dilate stenoses in the iliac, femoral, ilio-femoral, popliteal, infra-popliteal, and renal arteries, and for the treatment of obstructive lesions of native or synthetic arteriovenous dialysis fistulae. This device is also indicated for stent post-dilatation in the peripheral vasculature.

CAUTION: Federal (USA) law restricts this product for sale by or on the order of a physician.

IN.PACT™ Admiral™ Paclitaxel-coated PTA balloon catheter 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
- **A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients.**
- 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 dosage exceeding 34,854 µg 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.

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

SpiderFX™ embolic protection device Brief Statement

Important Information:
Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

Indications for Use:
- **Lower Extremity (LE) Interventions**

The SpiderFX embolic protection device is indicated for use as a guidewire and embolic protection system to contain and remove embolic material in conjunction with the TurboHawk™ Peripheral Plaque Excision System, either during standalone procedures or together with PTA and/or stenting, in the treatment of severely calcified lesions in arteries of the lower extremities. The vessel diameter at the filter basket placement site should be between 3.0 mm and 6.0 mm.

- **Carotid Interventions**

The SpiderFX embolic protection device is indicated for use as a guidewire and embolic protection system to contain and remove embolic material (thrombus/debris) while performing angioplasty and stenting procedures in carotid arteries. The diameter of the artery at the site of filter basket placement should be between 3.0mm and 7.0mm.

- **Saphenous Vein Graft (SVG) Interventions**

The SpiderFX embolic protection device is indicated for use as an embolic protection system to contain and remove embolic material (thrombus/debris). The device also acts as the guidewire while performing percutaneous transluminal coronary angioplasty or stenting procedures in coronary saphenous vein bypass grafts with reference vessel diameters of 3.0mm to 6.0mm. The safety and effectiveness of this device as an embolic protection system has not been established in the cerebral vasculature.

CAUTION: Federal (USA) law restricts this product for sale by or on the order of a physician.

TrailBlazer™ support catheter reference statement

Important Information:
Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

Indications for Use:
TrailBlazer support catheter are percutaneous, single lumen catheters designed for use in the peripheral vascular system. TrailBlazer™ support catheters are intended to guide and support a guide wire during access of the vasculature, allow for wire exchanges and provide a conduit for the delivery of saline solutions or diagnostic contrast agents.

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a physician.

Pacific Xtreme™ PTA balloon dilatation catheter Reference Statement

Important Information: Prior to use, refer to the Instructions for Use supplied with these devices for indications, contraindications, side effects, suggested procedure, warnings and precautions.

Indications for Use: The Pacific Xtreme PTA balloon dilatation catheter in 150 mm, 200 mm, 250 mm and 300 mm balloon length is intended to dilate stenoses in femoral, popliteal and infrapopliteal arteries.

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a physician.

Test data is on file at Medtronic Inc. Bench test results may not be indicative of clinical performance.