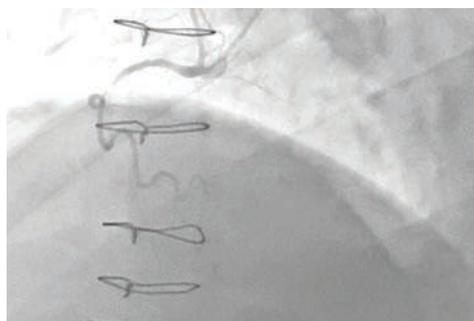


# Cath Lab Digest

A product, news & clinical update for the cardiac catheterization laboratory specialist



## CASE REPORT

### A Useful Addition to Your Complex PCI Toolbox

Leah M. Raj, MD, FACC, FSCAI

**T**AKERU PTCA Balloon Dilatation Catheters (Terumo Interventional Systems) have proven to be a useful tool in complex coronary interventions. Due to its low profile and pushability, the TAKERU balloon catheter can be used in multiple scenarios, including tortuous and uncrossable lesions. In this report, we summarize a case utilizing the low-profile TAKERU balloon catheter.

#### Clinical Case

A 65-year-old gentleman with a history of coronary artery disease treated with coronary artery bypass graft surgery and percutaneous coronary intervention (PCI) to the proximal left anterior descending artery presented with Canadian Cardiovascular Society class III angina despite multiple antianginals (carvedilol 12.5 mg BID, ranolazine 1000 mg BID, and isosorbide mononitrate 60 mg daily).

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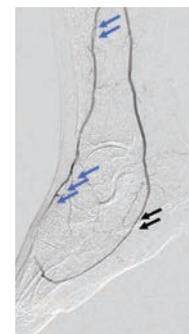
## CUTTING-EDGE TECHNOLOGY

### The MagicTouch PTA Sirolimus-Coated Balloon for the Inhibition of Neointimal Hyperplasia in Lower-Extremity Peripheral Arterial Disease

CLD talks with Edward Choke, MBBS, PhD, FRCS.

#### What are the current challenges in lower-extremity peripheral arterial disease patients?

Due to the increasing incidence of diabetes, we are now seeing more of the severest forms of lower-extremity occlusive peripheral arterial disease (PAD). These occur in the distal arteries located below the knee (BTK) and are often long chronic total occlusions in small-caliber vessels. In its severest form, it leads to chronic limb-threatening ischemia, in which patients develop gangrene or ulcers of the lower extremity, and ultimately loss of limb or life if left untreated.



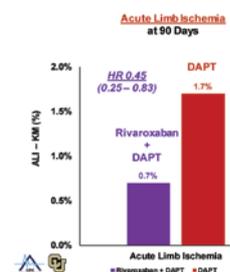
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## CLINICAL TRIAL UPDATE

### Rivaroxaban After Lower-Extremity Revascularization: The VOYAGER PAD Trial

CLD talks with Marc P. Bonaca, MD, MPH.

**T**he phase 3 VOYAGER PAD trial demonstrated the benefit of rivaroxaban (Xarelto, Janssen Pharmaceutical Companies of Johnson & Johnson) (2.5 mg twice daily + aspirin 100 mg once daily) in reducing severe vascular events in peripheral artery disease patients after lower-extremity revascularization.<sup>1</sup>



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# The MagicTouch PTA Sirolimus-Coated Balloon for the Inhibition of Neointimal Hyperplasia in Lower-Extremity Peripheral Arterial Disease

Physicians and industry both recognize that there is a great unmet need to improve the durability of below-the-knee (BTK) vessel patency after conventional balloon angioplasty.

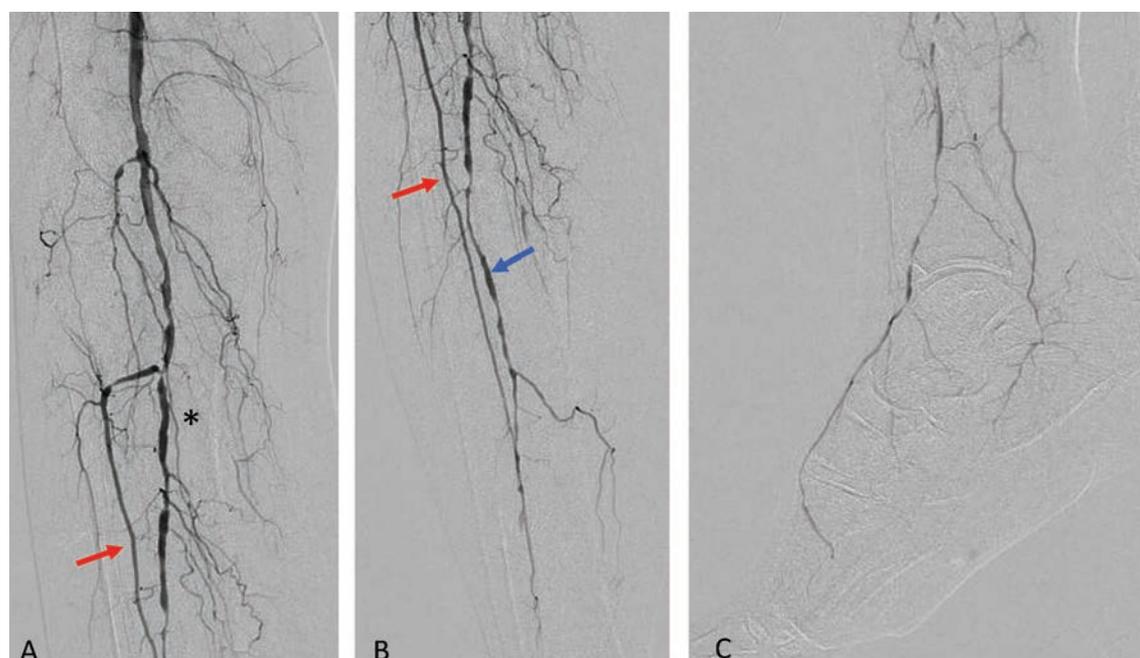
CLD talks with Edward Choke, MBBS, PhD, FRCS.

Improvements in wire and imaging technologies, coupled with advancements of specialty endovascular skills, have enabled us to cross and then open these difficult lesions with conventional balloon angioplasties, with 90% immediate technical success. However, conventional balloon angioplasties have yielded disappointingly low durability in terms of maintaining vessel patency of BTK arteries. In the medium term, many patients experience early restenosis, resulting in frequent repeated angioplasty procedures with the possibility of loss of their limbs or lives.

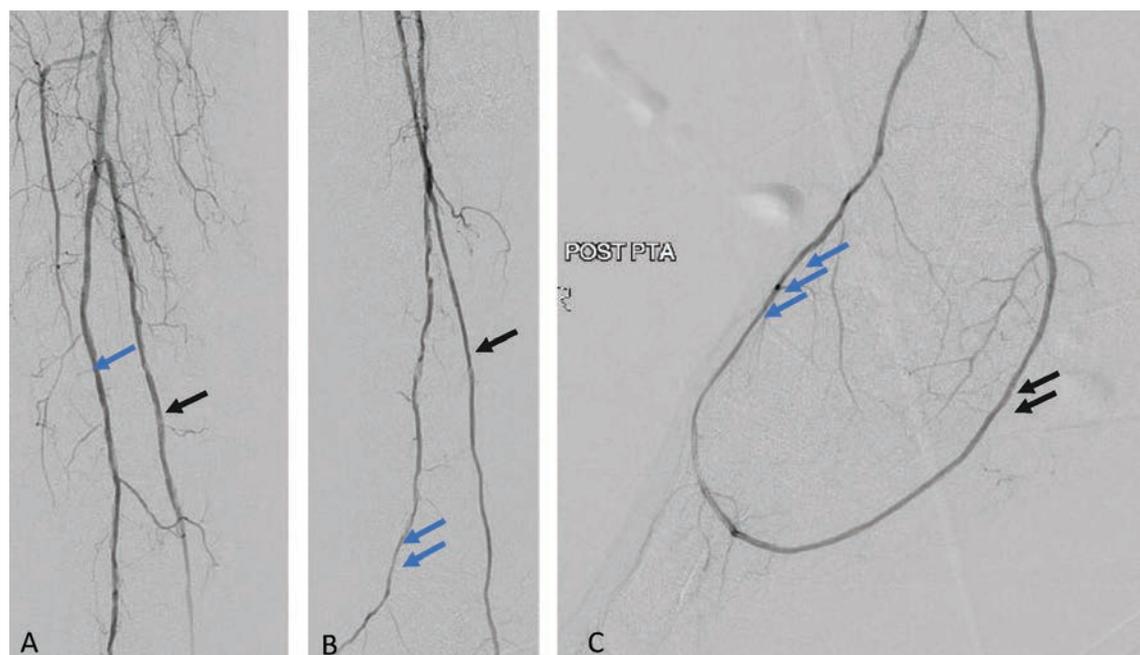
Physicians and industry both recognize that there is a great unmet need to improve the durability of BTK vessel patency after conventional balloon angioplasty. Much effort in the past decade has gone to the search for other adjunctive therapies to improve BTK vessel patency. Paclitaxel-coated balloons have been trialed but with generally unsuccessful results. Whilst paclitaxel-coated balloons have unequivocally demonstrated superiority over conventional balloon angioplasties for femoropopliteal arteries, their effects on BTK artery patency were not as clear-cut, with some trials even reporting higher rates of amputations if paclitaxel-coated balloons are used on BTK arteries. Most recently, another high-profile negative trial was the SAVAL trial, which investigated the utility of paclitaxel-coated BTK stents. Therefore, whilst many improvements have been achieved for the more proximal femoropopliteal arteries, the same cannot be said of BTK arteries, in which the gold standard is still plain old balloon angioplasty (POBA).

**Can you describe the MagicTouch and how you have incorporated its use into your lab? How does its use differ from POBA and paclitaxel-coated balloons? Is the use of intravascular imaging important?**

The MagicTouch PTA (Concept Medical) is a novel sirolimus-coated balloon (SCB) that is designed to deliver sirolimus to occlusive lesions in vessels and then maintain sirolimus concentration within the walls of the vessel in an adequate quantity to inhibit neointimal hyperplasia.



**Figure 1.** (A, B) Pre-angioplasty angiogram demonstrated that anterior tibial artery (ATA) (red arrow), tibioperoneal trunk (TPT) (asterisk), and peroneal artery (blue arrow) were severely diseased. The posterior tibial artery (PTA) was occluded. (C) Pre angioplasty angiogram demonstrated that plantar arch was severely diseased. The dorsalis pedis (DP) was reconstituted from collateral branches from the peroneal artery.



**Figure 2.** (A-C) Angiogram after plain balloon angioplasty demonstrated in-line flows via peroneal (blue arrow) and its collateral (double blue arrows) to DP (triple blue arrows), and PTA (black arrow) to lateral plantar artery (LPA) (double black arrow). ATA treatment was not attempted.

The basic premise of the angioplasty procedure involves the use of POBA to forcefully open the diseased artery. However, this will inadvertently cause vascular injury. This leads to activation of smooth muscle cells, which is the key step in neointimal hyperplasia and restenosis, resulting in poor durability of angioplasties for BTK arteries. An adjunctive step to POBA is therefore needed to prevent the inadvertent neointimal hyperplasia and sirolimus-coated balloons may be the solution.

Sirolimus is a potent antiproliferative drug that inhibits the activation of smooth muscle cells by cytostatic effects on the cell cycle. This is a different mechanism of action to paclitaxel, which has cytotoxic effects and hence pro-apoptotic actions on the smooth muscle cells. Sirolimus is therefore considered to be potentially safer compared to paclitaxel. The anti-restenotic effects of sirolimus have been well-studied in sirolimus-eluting stent devices in the coronary circulation, where it is generally perceived to be a safe drug and one which is more effective than paclitaxel. Sirolimus has other advantageous biological properties over paclitaxel such as its anti-migratory effects on smooth muscle cells and anti-inflammatory effects, which can enhance its anti-restenotic effects on arteries.

It is however significantly more challenging to develop sirolimus-coated balloons. Compared to paclitaxel, sirolimus has poorer adhesion properties and low lipophilicity. The MagicTouch PTA leverages onto proprietary phospholipid carrier technology to improve the lipophilicity and bioavailability of sirolimus. Sirolimus, after transformation into sub-micron sized particles, is encapsulated in phospholipid-drug nanocarriers, resulting in improved lipophilicity, which then allows for better adhesion of sirolimus on the balloon surface. Sirolimus is transferred to the lesion when the MagicTouch PTA is inflated and apposed to the inner surface of the vessel wall.

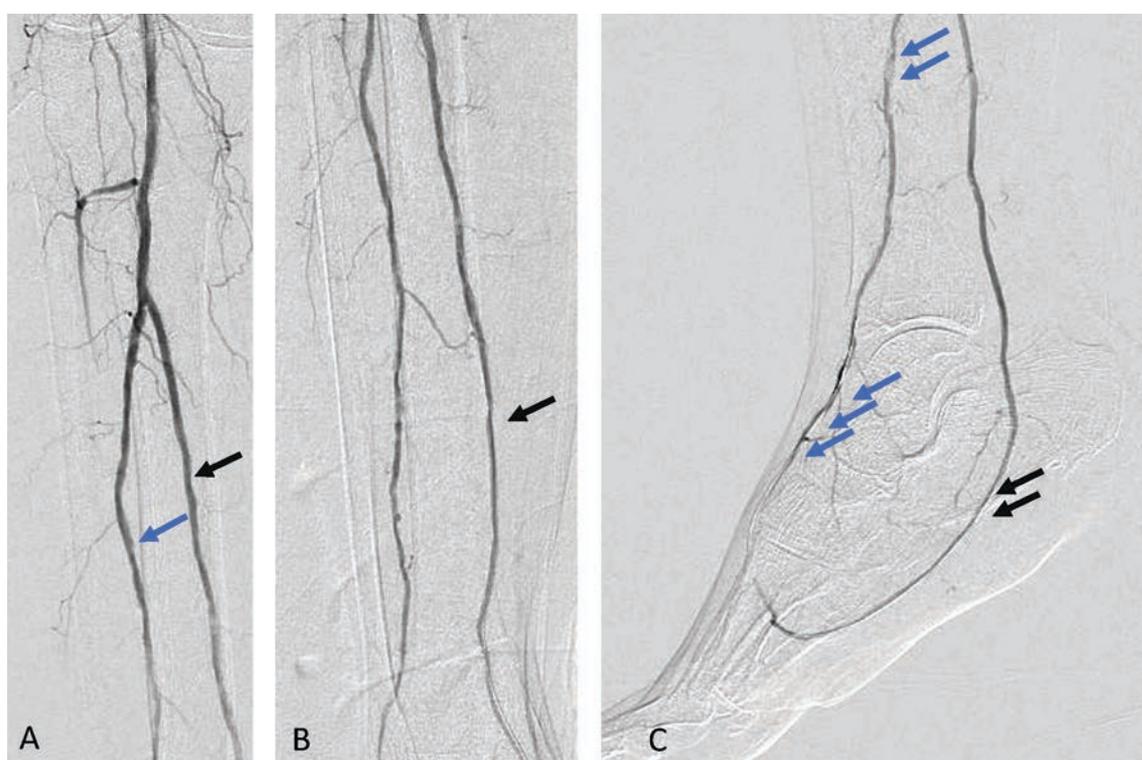
Another major difference is that we have not seen any concerns with distal embolization and slow-flow phenomenon with the use of the MagicTouch sirolimus-coated balloon (SCB), even in very distal and small BTK arteries (Figures 1-4). Conversely, with paclitaxel-coated balloons, 8% rates of slow-flow phenomenon due to distal embolization have been described.<sup>1</sup> This raises concerns of thrombotic risks with the use of paclitaxel-coated balloons in distal BTK arteries.

In my lab, my lower-limb angioplasty practice is almost exclusively for patients with chronic limb-threatening ischemia (CLTI), for both femoropopliteal and BTK disease. I was one of the early adopters of the novel MagicTouch PTA SCB going back to 2017, when I investigated its utility in the first-in-human XTOSI trial. We are currently one of the centers recruiting patients for the multicenter, multinational, randomized, controlled trials of the MagicTouch PTA SCB versus conventional balloon angioplasty for femoropopliteal arteries (FUTURE SFA) and BTK arteries (FUTURE BTK). Outside of



**Figure 3.** (A) Application of MagicTouch PTA sirolimus-coated balloon (Concept Medical) 3 mm x 150 mm to TPT and proximal PTA. (B) Application of MagicTouch PTA sirolimus-coated balloon 3 mm x 200 mm to distal PTA. (C) Application of MagicTouch PTA sirolimus-coated balloon 2 mm x 150 mm to plantar arch.

**We are currently one of the centers recruiting patients for the multicenter, multinational, randomized, controlled trials of the MagicTouch PTA sirolimus-coated balloon versus conventional balloon angioplasty for femoropopliteal arteries (FUTURE SFA) and BTK arteries (FUTURE BTK).**



**Figure 4.** (A-C) Angiogram after MagicTouch PTA sirolimus-coated balloon demonstrated preservation of in-line flows via PTA (black arrow), and peroneal (blue arrow) with its collateral (double blue arrows) to DP (triple blue arrows). There was no distal embolization or slow-flow phenomenon to LPA (double black arrow).

these trials, my patients do also receive the MagicTouch PTA SCB for de novo and recurrent disease in femoropopliteal and BTK arteries after conventional balloon angioplasty. The outcomes from these “real world” patients are monitored in our prospectively maintained HOPE database at our institution.

Recent evidence has suggested that use of intravascular ultrasound (IVUS) was, in general, associated with better outcomes after lower-limb angioplasty. Although there is no direct evidence that IVUS improves the application of drug-coated balloons, intuitively it would seem that accurate sizing of arteries and therefore application of correctly sized drug-coated balloons would facilitate better transfer of sirolimus to the vessel wall.

#### Can you describe the FUTURE BTK trial?

FUTURE BTK (ClinicalTrials.gov NCT04511247) is a randomized, controlled trial of the MagicTouch PTA SCB versus conventional balloon angioplasty for BTK arteries and began enrollment in August 2020. Patients will include CLTI patients in Rutherford classes 4, 5, and 6. The primary efficacy endpoint

were enrolled, of whom 20 patients received the MagicTouch PTA to the femoropopliteal artery and 30 patients received it for BTK disease. The primary endpoint was defined as primary patency at 6 months (duplex ultrasound peak systolic velocity ratio  $\leq 2.4$ ).

The vast majority of patients (94%) in the XTOSI trial had severe CLTI with leg gangrene or ulcers (Rutherford scores 5 or 6). The cohort was a typical CLTI high-risk group, in which 90% had diabetes, 36% had coronary artery disease, 20% had end-stage renal failure, and American Society of Anesthesiologists (ASA) score was 3 or greater in 80%. Mean lesion length treated was 227±81 mm, of which 36% were total occlusions.

The key findings from this trial were the 6-month primary patencies of 88% for femoropopliteal and 74% for BTK arteries. We were particularly encouraged by the 74% 6-month primary patency for BTK, because this represented a potentially significant improvement over previously reported data from Singapore of only 38% and 43% 6-month primary patency for BTK treated by conventional balloon angioplasty and paclitaxel-coated balloons, respectively.<sup>3</sup> The

lower rates of reintervention (target lesion revascularization) at 12 months compared to patients who received conventional balloon angioplasties, and we plan to soon publish these real-world data.

#### What do you hope that physicians take away from research into the MagicTouch?

At this stage, we have the early data from XTOSI trial, which is a small, single-arm pilot study that reported promising results for the MagicTouch PTA SCB, especially for BTK disease. When data from our institution’s prospectively maintained real-world angioplasty database were analyzed, we saw similarly promising outcomes in our day-to-day patients who received the MagicTouch PTA SCB. However, we still, of course, need definitive data from large, multicenter, randomized, controlled trials, which need to be adequately powered in order to determine whether sirolimus-coated balloons are superior to conventional balloon angioplasty. Hopefully this will bring solutions to the current great unmet need for better outcomes in angioplasty for BTK arteries and bring us a step closer to our objective of saving more limbs. ■

*This article is sponsored by Concept Medical.*

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is primary patency at 6 months, defined as duplex ultrasonography-derived peak systolic velocity ratio of  $\leq 2.4$ , in the absence of any target lesion revascularization. It is adjudicated by an independent core lab that is blinded to the treatment group. The personnel performing the duplex assessments are also be blinded to the treatment group. The planned total enrolment is 219 patients from 4 countries: Singapore, Thailand, Taiwan, and South Korea. The results from the FUTURE BTK trial will provide clarity on whether SCB is superior to conventional balloon angioplasty for BTK disease in CLTI patients.

#### Can you discuss your earlier research into the Magic Touch?

The XTOSI first-in-human trial has reached completion and its 12-month results have been published.<sup>2</sup> This was a prospective, single-arm, pilot study investigating the clinical efficacy and safety of the MagicTouch PTA SCB in both femoropopliteal disease and BTK disease. A total of 50 patients

88% 6-month primary patency for femoropopliteal arteries is similar to that achieved by paclitaxel-coated balloons reported in other major trials.

The requirement for reintervention was low, as at 12 months, freedom from clinically driven target lesion revascularization was 94% for the femoropopliteal arteries and 86% for BTK. Limb salvage success at 12 months was high at 94% for the femoropopliteal arteries and 92% for BTK, with high wound healing rates of 84.6%. The 12-month all-cause mortality (14%) and amputation-free survival (82%) were in line with that expected of chronic limb-threatening ischemia cohort.

From these pilot data, we concluded that the MagicTouch PTA SCB shows promising 6-month primary patency rates, especially for BTK disease, with no early safety concerns. We have also seen similarly promising results in our cohort of real-world patients from our institution’s prospectively maintained HOPE angioplasty database. Our analyses suggested that patients who received the MagicTouch PTA SCB had

#### References

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3. Patel A, Irani FG, Pua U, et al. Randomized controlled trial comparing drug-coated balloon angioplasty versus conventional balloon angioplasty for treating below-the-knee arteries in critical limb ischemia: the SINGA-PACLI trial. *Radiology*. 2021 Sep;300(3):715-724.

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