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The Petal dedicated bifurcation stent

John A. Ormiston[1]*, MBChB; Frederic De Vroey[2], MD; Mark W.I. Webster[2], MBChB; David E. Kandzari[3], MD

1. Mercy Angiography, Auckland, New Zealand; 2. Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; 3. Piedmont Heart Institute, Atlanta, Georgia, USA

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Description of the Petal dedicated bifurcation drug-eluting stent

The Taxus Petal (Boston Scientific Corporation, Natick, MA, USA) dedicated bifurcation device is a paclitaxel-eluting, side-branch access stent delivered over two coronary guidewires, enabling maintenance of side-branch access throughout the procedure[1,2]. The body of the stent is deployed by inflation of a standard cylindrical balloon, and the side-branch "petal" struts are expanded by inflation of a smaller elliptical balloon (Figure 1). The balloon lumens (main and side-branch) are connected, permitting simultaneous balloon inflation using a single inflation device (Figure 1). The petal strut elements (Figure 1) project approximately 2 mm into the side branch providing mechanical support and applying anti-proliferative drug to the side-branch ostium, a common site for restenosis after bifurcation stenting procedures.[3]

When the Petal is delivered to a bifurcation lesion, separation of markers confirms rotational alignment of the SB elements with the SB (Figures 1 and 2).

The Boston Scientific Petal stent is an improved version of a bare metal Petal stent made by Advanced Stent Technologies[4]. The current laser cut design uses a novel, more radio-opaque platinum chromium alloy that is associated with greater visibility than stainless steel or cobalt chromium (Figure 3). The alloy is also stronger, allowing construction of stents with thinner struts but with maintained radial strength and minimal recoil. The drug (paclitaxel) and polymer (translute) are the same as those coating the Taxus Express and Taxus Liberte stents and evaluated in clinical trials.[5,6] The stent/ delivery system profile allows delivery through a 7 Fr guide catheter.

Bench testing

Bench testing in a relatively simple bifurcation phantom predicted the challenges with passive delivery system rotation experienced in the first-in-human trials with the Petal and other dedicated bifurcation stent systems (Figures 4 and 5). Although observed delivery problems were attributed by some observers to limitations of the phantom model, bench testing unequivocally demonstrated that a major restriction to passive rotational alignment was guidewire bias. In particular, the guidewire in the side branch was always closely apposed to the vessel wall opposite to the branch, immediately upstream of the bifurcation and directed the side branch component of the stent away from the side branch (Figure 4).

In addition, guidewire wrap or twisting frequently prevents device advancement and delivery (Figure 5). If wire wrap is observed, withdrawing and re-advancing either the main branch or side branch wire may solve the problem, albeit with at least temporary loss of guidewire position. The need to withdraw and re-advance a wire partially negates the advantage of a two-wire system that aims

* *Corresponding author: Mercy Angiography, Mercy Hospital, Newmarket, PO Box 9911, Auckland 1031, New Zealand*
E-mail: johno@mercyangiography.co.nz

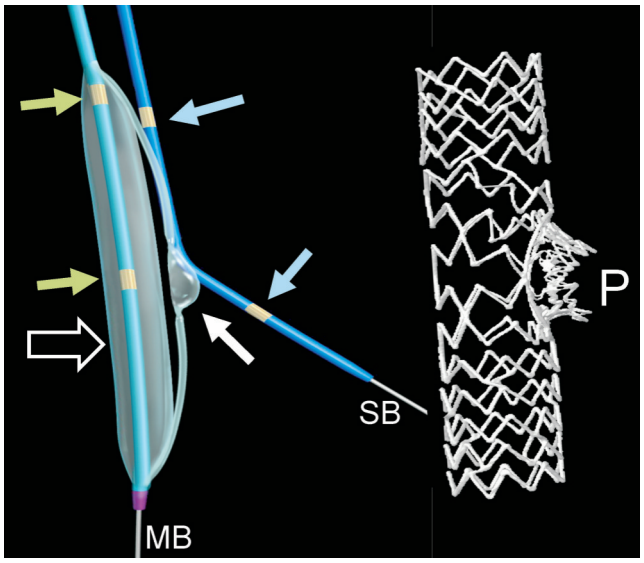

Figure 1. Delivery balloons, wires and markers (left panel) and petal stent (right panel). The Petal stent delivers over a main branch wire (MB) and a side-branch (SB) wire. A tear-drop shaped side-branch balloon (solid white arrow) that deploys the petal-shaped elements (P) is connected to the lumen of the cylindrical main branch balloon (open arrow) permitting deployment is by a single inflation device. Blue arrows indicate the side-branch marker bands and green arrows the main branch marker bands.

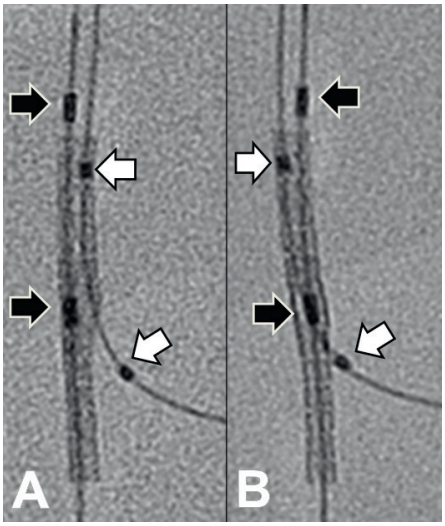

Figure 2. Separation of markers shows rotational alignment. In A, the side-branch markers (white arrows) are clearly separated from the main branch markers (black arrows) indicating correct rotational alignment with the side branch in this projection, which profiles the side-branch origin. In B, the markers are not separated indicating that the device is not correctly aligned with the side branch.

at maintaining access to the side-branch at all times. Passive rotational alignment is also limited by the oval cross-section of the device, which is particularly likely to limit rotation in clinical instances of tortuosity, eccentric plaque or vessel calcification. Bench testing predicts that a delivery system shaft that can be actively rotated under fluoroscopic control may overcome these problems, even in simulated very tortuous vessels.

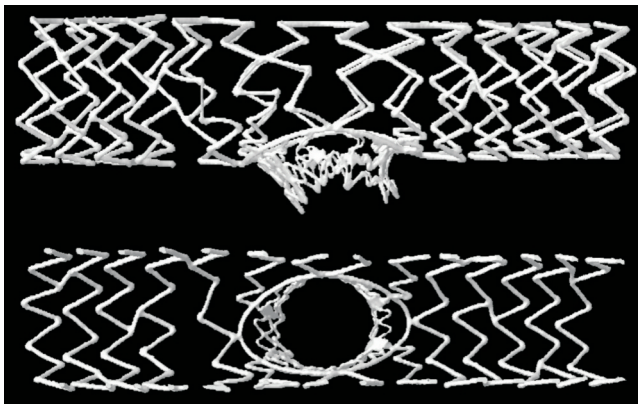

Figure 3. Microcomputed tomographic image of a deployed Petal dedicated bifurcation stent viewed from the side (upper panel) and from inside the stent looking towards the petal elements (lower panel).

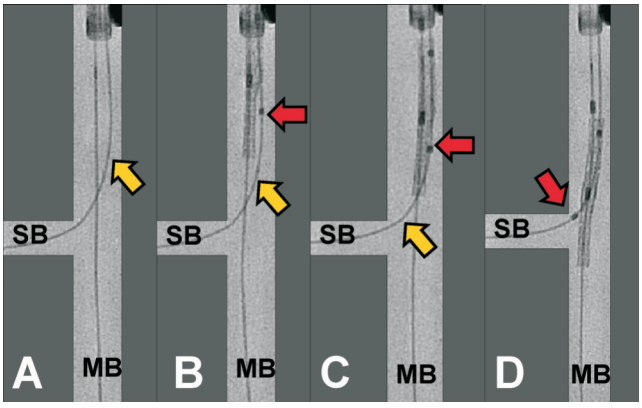

Figure 4. Wire bias prevents device delivery. A bench deployment shows that wire bias directs the side-branch component of a two wire dedicated bifurcation stent away from the side branch (SB) ostium preventing rotation and alignment. In A, the yellow arrow shows the SB wire apposed to the vessel wall opposite to the SB, in the immediate upstream vessel. In B, the stent delivery system is advanced from the guide catheter) and the SB component (red arrow) is directed away from the SB. As the device is advanced further (C and D), the SB component (red arrow) has not passively rotated so that SB alignment and stent delivery were not possible. This problem is most marked with wide SB angles and with proximal SBs. MB: main branch; SB: side-branch

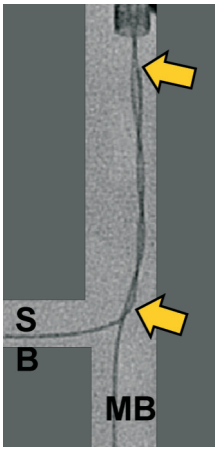

Figure 5. Wire wrap (twisting of wires between the stent delivery system and the bifurcation) prevents delivery.

Clinical trial

The Taxus Petal trial was a first human use study that evaluated the safety and feasibility of the Taxus Petal paclitaxel-eluting bifurcation stent in 28 patients in New Zealand, France and Germany.[2] It was a prospective, single-arm, multicentre study with a composite primary endpoint of 30-day death, myocardial infarction (MI), and repeat target vessel revascularisation. Angiographic and intravascular ultrasound follow-up was performed at six months with planned annual clinical follow-up to five years. The mean patient age was 61 years, and 18% had medically-treated diabetes. The mean lesion length was 13.8 mm in the main branch and 4.4 mm in the side-branch. A Taxus Petal was successfully implanted in 25 (89%) of patients. However, on a per device basis, only 74% (25/34) of Petal deployments were successful. The 30-day primary endpoint occurred in one patient (4%), who had an in-hospital non-Q-wave MI. At one year, the target vessel revascularisation was 11% (3) and target lesion revascularisation was 7% (2). There were no deaths, Q-wave MIs, or stent thromboses. Mean in-segment late loss (assessed in 21 patients) was 0.47 mm in the proximal main branch, 0.41 mm in the distal main branch, and 0.18 mm in the side branch.

The key finding of the Taxus Petal trial was that clinical and angiographic outcomes were favourable, provided that the device could be delivered to the bifurcation. The delivery system often required some passive rotation into the correct alignment, which was not always achieved, particularly in instances of vessel tortuosity or calcification. In many patients, device rotation was limited by wire bias and wire wrap (Figures 4 and 5). Furthermore the oval cross-sectional shape and larger diameter of the device, compared with conventional drug-eluting stents, likely also contributed to suboptimal delivery. Our experience is that there are similar delivery issues with the Medtronic Branch dedicated bifurcation stent, that is also delivered over two wires and requires passive rotation to advance into position at the bifurcation.

Potential design changes since the Petal first-in-human trial: a rationale for continued development of this technology to address an unmet need

Many bifurcation lesions can be treated successfully with conventional drug-eluting stents, using a provisional one-stent strategy. When a suitable angiographic result is achieved with a single drug-eluting stent, such a provisional strategy is associated with at least similar clinical outcome and lower resource use compared with a dedicated two-stent strategy.[7,8] Nonetheless, there are several common instances including the presence of extensive side-branch disease or side-branch compromise following main vessel stenting that require either planned or provisional side-branch stent placement. Conventional bifurcation techniques that stent across the side-branch, require a second wire placement through the stent struts to regain side-branch vessel access. Trapping ('jailing') the initial guidewire in the side branch by the main vessel stent may facilitate rewiring, but does assure it. Advancing a balloon or another stent delivery system through the struts of a deployed stent may also be difficult, particularly when the alignment of the guidewire to the stent struts is unfavourable.

In contrast, the Petal stent maintains access to the side-branch vessel while preserving the option for a single- or two-stent technique. Specifically, the Petal is delivered over two guidewires, maintained in the main branch and side branch throughout the procedure. Unlike main branch stenting with a conventional stent, the Petal facilitates provisional side-branch stenting because rewiring through stent struts is not needed and side-branch entry is not obstructed, allowing easier balloon and stent access. Because the petal elements cover the first 2 mm of the side-branch ostium, the Petal stent may successfully treat focal ostial disease without the requirement for a second stent placement. In contrast to a conventional stent, the petal elements facilitate placement of a second stent in the side branch if necessary without gaps in scaffolding or drug application. The Petal stent may also be useful for those patients in whom elective stenting of both the main branch and side branch is the best revascularisation option. One example would be a patient with a Medina 1,1,1 classification bifurcation lesion with significant disease extending distal to the side-branch ostium, and both downstream vessels supplying important myocardium.

Potential iterative improvements and clinical indications

The limitations of passive rotation evident in the first-in-human clinical study appear to be overcome by modifying the Petal delivery catheter shaft such that torque applied to the proximal end is transmitted to the balloon and stent.[2] Active rotation can be used to rotate the 180° needed to overcome guidewire bias, or the more extensive rotation needed to unravel guidewire wrap. Preliminary benchtop and animal studies have shown that multiple wire wraps can be successfully unwound, and the device delivered to the bifurcation even in very tortuous anatomy. Use of the modified shaft is intuitive and easily learned. It is likely that clinical stent delivery would also be considerably improved.

Aside from procedural outcomes, anti-restenotic efficacy of the Petal system may also be improved through application of alternative anti-proliferative agents and polymer coatings. In non-bifurcation lesions, for example, recent trials have demonstrated superior angiographic and clinical safety and efficacy outcomes with sirolimus- and everolimus-eluting stents compared with paclitaxel-eluting stents.[9-11] Although unstudied as yet, extrapolation of these outcomes associated with sirolimus derivatives to a bifurcation stent platform is hypothesis-generating.

In addition, potential design changes will allow for a lower profile petal device so that it can be delivered through a 6 Fr guiding catheter.

Finally, as our understanding of bifurcation treatment evolves, percutaneous revascularisation for unprotected left main disease has become increasingly more common as an alternative to bypass surgery for selected patients[12,13]. In this lesion subset, the Petal design may be particularly advantageous as the device is best suited to wide rather than narrow distal (B angle) bifurcation angles. Side-branch ostial coverage may be especially beneficial in this indication in view of recent studies with intravascular ultrasound

demonstrating extension of atherosclerotic plaque from the ostia of the left anterior descending and left circumflex arteries into the left main segment yet sparing the carina.[14] Further, when left main bifurcation restenosis does occur, it's most common at the ostium of the left circumflex artery, representing a treatment challenge for conventional stent therapies. Optimal lesion and stent expansion, and stent wall apposition and bifurcation scaffolding, are therefore mandatory to minimise the risk of subsequent stent thrombosis or restenosis.

In summary, the Petal dedicated bifurcation stent is drug-eluting, delivers over two wires thus protecting the side branch and has petal struts that project into the side branch for up to 2 mm supporting and applying drug to the site where restenosis is most common. The Taxus Petal FHU trial showed that clinical and angiographic outcomes were favourable, provided that the device could be delivered to the bifurcation. Shaft design modifications that transmit torque from the proximal hub to the stent distally can overcome the delivery issues caused by wire bias and wire wrap.

References

1. Johnson T, Kay I, Ormiston J. A novel paclitaxel-eluting dedicated bifurcation stent: A case report from the first human use Taxus Petal Trial. *Cathet Cardiovasc Interv.* 2009;73:637-640.

2. Ormiston J, Lefevre T, Grube E, Allocco D, Dawkins K. First human use of the TAXUS Petal paclitaxel-eluting bifurcation stent. *EuroIntervention* 2010;6:46-53.

3. Lansky A, Tulnenburg J, Costa M, Maeng M, Koning G, Popma J, Cristea E, Gavit L, Costa R, Rares A, Van Es GA, Lefevre T, Reiber JH, Louvard Y, Morice M. Quantitative angiographic methods for bifurcation lesions: a consensus statement from the European Bifurcation Group. *Cathet Cardiovasc Interv.* 2009;73:258-266.

4. Ormiston J, Webster M, El-Jack S, McNab D, Simpson-Plaumann S. The AST Petal dedicated bifurcation stent. First-in-human experience. *Cathet Cardiovasc Interv.* 2007;70:335-340.

5. Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, Dudek D, Fort S, Schiele F, Zmudka K, Guagliumi G, Russell ME. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery disease. *Circulation.* 2003;108:788-794.

6. Turco M, Ormiston J, Popma J, Mandinov L, O'Shaughnessy C, Mann T, McGarry T, Wu C-J, Chan C, Webster M, Hall J, Mishkl G, Cannon L, Baim D, Koglin J. Polymer-base, paclitaxel-eluting TAXUS Liberte stent in de novo lesions. The pivotal TAXUS ATLAS trial. *J Am Coll Cardiol.* 2007;49:1676-1683.

7. Steigen T, Maeng M, Wiseth R, Erglis A, Kumsars I, Narbute I, Gunnes P, Mannesverk J, Meyerdierks O, Roevatn S, Niemela M, Kervinen K, Jensen J, Galloe A, Nikus K, Vikman S, Ravkilde J, James S, Aoroe J, Ylitalo A, Helqvist S, Sjogren I, Thayssen P, Virtanen K, Puhakka M, Airaksinen J, Lassen J, Thuesen L. Randomized study on simple versus complex stenting of coronary bifurcatin lesions: the Nordic bifurcation study. *Circulation.* 2006;114:1955-1961.

8. Hildick-Smith D, de Belder A, Cooter N, Curzen N, Clayton T, Oldroyd K, Bennett L, Holmberg S, Cotton J, Glennon P, Thomas M, MacCarthy P, Baumbach A, Mulvihill N, Henderson R, Redword S, Starkey I, Stables R. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions:The British Bifurcation Coronary Study: Old, new and evolving strategies. *Circulation.* 2010;121:1235-1243.

9. Stone G, Midei M, Newman W, Sanz M, Hermiller J, Williams J, Farhat N, Mahaffey K, Cutlip D, Fitzgerald P, Sood P, Su X, Lansky A. Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: A randomized trial. *JAMA.* 2008;299:1903-1913.

10. Stone G, Rizvi A, Newman W, Mastali K, Wang J, Caputo R, Doostzadeh J, Cao S, Simonton C, Sudhir K, Lansky A, Cutlip D, Kereiakes D. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. *N Engl J Med.* 2010;362:1663-1674.

11. Smits P. A comparison of drug-eluting stents for percutaneous coronary intervention-Background, rationale, design of the COMPARE trial. *European Cardiology.* 2010;5:69-70.

12. Kandzari D, Colombo A, Park S, Tommaso C, Ellis S, Guzman L, Terstein P, Tamburino C, Ormiston J, Stone G, Dangas G, Popma J, Bass T. Revascularization for unprotected left main disease: Evolution of the evidence basis to redefine treatment standards. *J Am Coll Cardiol.* 2009;54:1576-1588.

13. Kushner F, Hand M, Smith S, King S, Anderson J, Antman E, Bailey S, Bates E, Blankenship J, DE. C, Green L, Hochman J, Jacobs A, Krumholz H, Morrison D, Ornato J, Pearle D, ED P, Sloan M, Whitlow P, Williams D. 2009 Focused updates. *J Am Coll Cardiol.* 2009;54:2205-2241.

14. Oviedo C, Maehara A, Mintz G, Araki H, Choi S-Y, Tsujita K, Kubo T, Doi H, Templin B, Lansky A, Dangas G, Leon M, Mehran R, Tahk S, Stone G, Ochiai M, Moses J. Intravascular ultrasound classification of plaque distribution in left main coronary artery bifurcations. Where is plaque really located? *Circ Cardiovasc Interv.* 2010;3:105-112.