# Insights From The Portland DES Symposium

Part I: Treating complex coronary bifurcation lesions in the era of the drug-eluting stent requires careful planning and a strong knowledge base of the technology, components, and techniques.

**BY ANDREW J. CARTER, DO, ON BEHALF OF THE FACULTY MEMBERS***

*This article is the first of a three-part series of coronary topics from The Portland DES Symposium.*

The Portland DES Symposium was conducted on October 2, 2003, to review the current status of clinical trials on drug-eluting stents (DESs), discuss the impact of DESs on the practice of percutaneous coronary intervention (PCI), and identify methods to optimize clinical outcomes with DESs. The basic components of the CYPHER (Cordis Corporation, a Johnson & Johnson company, Miami, FL) and the TAXUS (Boston Scientific Corporation, Natick, MA) stent are summarized in Table 1. In-depth reviews of these DESs are beyond the scope of this article, but a summary of clinical trial results is available for review (Table 2).[1-6]

## THE DES

The introduction of the DES has generated the hope of expanding the clinical indications for PCI to high-risk patient and lesion subsets that, in the past, have been deferred to surgical revascularization, in part, because of a prohibitive risk for restenosis. The management of some of these patient and anatomic subsets to include left main stem obstruction, multilesion, or multivessel disease often requires techniques to address the performance of PCI at a coronary artery bifurcation. In the era of the DES, acute and long-term clinical results, such as stent thrombosis and restenosis, may be even more dependent on operator implant technique than with bare-metal stents for the treatment of bifurcation lesions. The presently available data suggest a requirement for complete lesion coverage with sirolimus- and

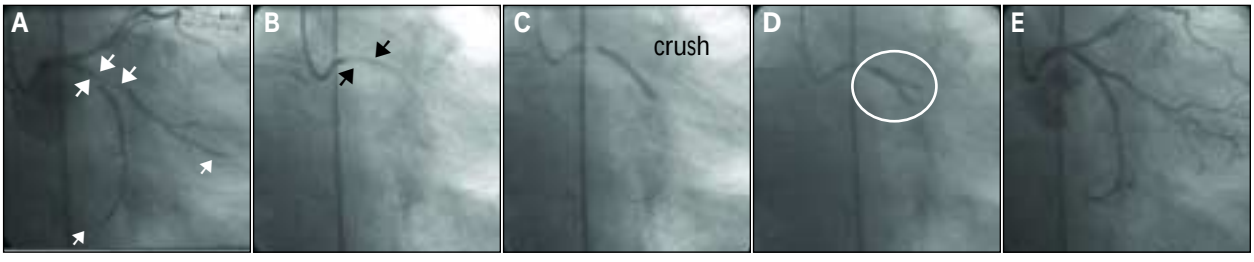


**Figure 1. A complex, noncalcified, ulcerated stenosis of the left circumflex and obtuse marginal branch in an RAO caudal projection (A). An 8-F, Amplatz Left II guiding catheter (Cordis Corporation, a Johnson & Johnson company, Miami, FL) was selected to provide optimal support and lumen to accommodate two CYPHER stents. The CYPHER stents are positioned in the left circumflex (3.5 mm diameter, 28 mm length) and obtuse marginal branch (3 mm diameter, 28 mm length) with 5 to 10 mm overlap (arrows) in the parent artery proximal to the carina of the bifurcation with a double wire technique (arrowheads) (B). After deploying the CYPHER stent in the obtuse marginal branch, the stent delivery system and guidewire were removed from the vessel to eliminate the possibility of device entrapment in the coronary artery with the crush technique. The left circumflex stent was then expanded, crushing the proximal obtuse marginal branch stent between the parent vessel stent and vessel wall (C). High-pressure postdilation of the stents was conducted with noncompliant balloons after re-establishing guidewire position in the obtuse marginal branch (D). The final angiographic result (RAO caudal projection) demonstrates an excellent result with less than 5% residual stenosis (E). (Courtesy of P. Au, MD.)**

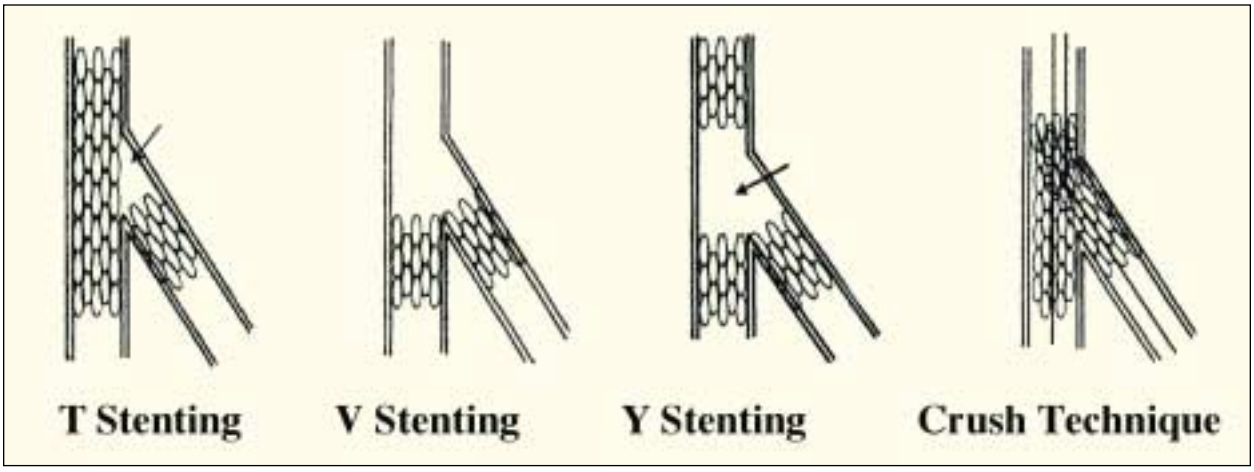


**Figure 2. Conventional stenting techniques for management of bifurcation lesions. The arrows indicate regions susceptible for gaps or geographic miss with DES prone to develop restenosis. (Adapted from Colombo et al.[7,9]).**

paclitaxel-eluting stents because of the limited diffusion capacity for these hydrophobic compounds in the arterial wall. The early clinical experience with the DES has spurred new techniques, such as the crush technique, to ensure complete coverage of the bifurcation to reduce the likelihood of DES restenosis because of a gap or incomplete coverage of the lesion. Throughout the course of The Portland DES Symposium, several panel members discussed aspects of managing symptomatic coronary bifurcation lesions with DES. The faculty emphasized the current known limitations of bare-metal stent and DES technology for this application, specifically angiographic late loss exceeding 1.25 mm, binary restenosis rates in excess of 50%, and target lesion revascularization rates approaching 40% for bare-metal stents.[7] The coronary angiograms depicted in Figure 1 demonstrate a noncalcified, ulcerated left circumflex and obtuse marginal branch lesion treated with two CYPHER stents using a modified T-stenting technique. Percutaneous catheter-based treatment of coronary bifurcation lesions necessitates that the operator address several critical aspects of case management (Table 3).

**TABLE 1. COMPONENTS OF THE CYPHER AND TAXUS DES**

| | **CYPHER** | **TAXUS** |
|---|---|---|
| Stent | BX Velocity<br>2.5 to 3.5 mm diameter<br>8, 13, 18, 23, 28, 33 mm length | Express[2]<br>2.5 to 3.5 mm diameter<br>8, 12, 16, 24, 28, 32 mm length |
| Polymer | Polyethylene<br>Polybutylmethacrylate | Polyisobutylene<br>Polysterene<br>Polyethylene |
| Medical Applications | Drug-release ocular and intrauterine devices | Orthopedic implants |
| Drug and Dose (Manufacturer) | Sirolimus 140 µg/cm$^2$<br>(Wyeth-Ayerst, Madison, NJ)<br>FDA approval: yes | Paclitaxel derivative 1 µg/mm$^2$<br>(Indena, Milan, Italy)<br>FDA approval: no |
| Pharmacokinetics | >95% release at 12 weeks | Unknown, 92% drug retention for indefinite period |

**TABLE 2. SUMMARY OF RANDOMIZED CLINICAL TRIALS FOR SELECTED DES**

| | RAVEL[1] | TAXUS II (SR)[2] | SIRIUS[3] | E-SIRIUS[4] | TAXUS IV[5] |
|---|---|---|---|---|---|
| Diabetic (%) | 15.8 | 10.7 | 24.6 | 18.9 | 24 |
| Lesion Length (mm) | 9.6 | 10.5 | 14.4 | 14.9 | 13.4 |
| Stent Length (mm) | 18 | 15 | 21.5 | 23 | 21.9 |
| Post-MLD (mm) | 2.43 | 2.54 | 2.67 | 2.43 | 2.66 |
| Late Loss (mm) | 0 (6 mo) | 0.31 (6 mo) | 0.17 (8 mo) | 0.21 (8 mo) | 0.39 (9 mo) |
| TLR (%) | 2.5 (24 mo) | 4.7 (12 mo) | 4.9 (12 mo) | 4 (9 mo) | 3 (9 mo) |

## TECHNIQUES

Stenting of coronary bifurcation lesions necessitates a carefully planned, stepwise approach to enable successful treatment of the lesion and to minimize the risk for acute procedural complications. The presently available bare-metal and DESs do not have FDA-approved labeling indications for treating coronary bifurcation lesions. Nonetheless, several techniques have been developed for stenting coronary bifurcations with both bare-metal and DESs. Although several different techniques, such as T-stenting, V-stenting, or Y-stenting, have been developed for the management of the bifurcation lesion, each fundamentally strives to facilitate complete coverage of the complex anatomy (Figure 2).

Colombo et al recently described the crush technique developed for DES placement to avoid stent gaps, in particular at the origin of the branch vessel (Figure 2).[8] The crush technique appears suitable to minimize stent gaps in some bifurcation lesions by compressing three layers of parent and branch vessel DES in the overlap regions. Importantly, the effects of multiple overlapping, or stent crush, on drug dose, local arterial toxicity, and efficacy are presently unknown. In theory, stent-based drugs with a broad therapeutic window, such as the cytostatic compound sirolimus, might provide a greater margin of safety than cytotoxic compounds, such as paclitaxel, with known dose-dependent arterial toxicity.[9] Unfortunately, only limited data are currently available on the application of DESs for the percutaneous treatment of the coronary bifurcation lesion.

Colombo et al documented the safety and feasibility of the sirolimus-eluting stent in coronary bifurcation lesions.[10] In this study, 86 patients were randomized to CYPHER in parent and branch vessels versus CYPHER in the parent vessel with bailout stenting of the branch. The primary endpoint of this study was the angiographically determined percentage of diameter stenosis at 6 months. Crossover to a second DES in the branch vessel was required in 22 patients because of suboptimal PTCA. The majority of patients had type I (18.8%) or type II (48.8%) bifurcation lesions involving the LAD and diagonal (approximately 75%) coronary arteries. Modified T-stenting or the crush technique was employed in 60 of the 63 treated bifurcation lesions.

The investigators used high-pressure postdilation with a kissing balloon technique in most cases. At 6 months, coronary angiography documented a late lumen loss of 0.28 mm (in segment) in the parent vessel and 0.63 mm late lumen loss in the branch vessel with modified CYPHER T-stenting. In the subset with a parent CYPHER and PTCA of the branch, late lumen loss was 0.16 mm in the parent vessel and 0.33 mm in the branch vessel. Angiographic in-lesion restenosis (>50% lesion) was present in 21.6% of cases, with the majority occurring at the ostium of the branch (25%) after modified T-stenting. Major adverse cardiac events were observed in 19% of the patients with a CYPHER in the parent and branch vessels and 13% of patients with a parent CYPHER and PTCA of the branch vessel. Stent thrombosis was reported in 3.6% of all cases. These data document the feasibility of CYPHER bifurcation stenting and suggest an improvement in long-term angiographic restenosis as compared with historical data on bare metal stents. Additional data on these and other bifurcation DES strategies may soon be derived from postmarket surveillance registries on CYPHER (RESEARCH, e-CYPHER) and TAXUS (WISDOM).

**TABLE 3. CRITICAL ASPECTS OF CASE MANAGEMENT**

**Therapeutic Options:**

Justification for PCI in lieu of medical management or surgical revascularization

**Adjunctive Therapies:**

Oral antiplatelet agents: ASA 325 mg daily, clopidogrel 75 mg daily for 3 to 6 months or longer after loading dose of 300 to 600 mg

Antithrombin therapy: Procedural anticoagulation with heparin, fractionated heparin, or thrombin inhibitor

Glycoprotein IIb/IIIa inhibitor: Eptifibatide bolus and infusion; abciximab bolus and infusion

**Device Selection:**

Guiding catheter: 7 F or larger ID, excellent support

Guidewire: Single- or double-wire technique

Lesion preparation: PTCA of parent vessel and/or branch with kissing technique; cutting balloon or other for calcified/ostial lesions; debulking with PTRCA or DCA

Stenting technique: Parent vessel with bailout approach for suboptimal PTCA of branch; parent and branch vessel stent (T-stenting, V-stenting, Y-stenting, crush stenting); stent branch with bailout for suboptimal PTCA of parent

Postdilation: Parent and or branch with or without kissing technique; kissing balloon dilation advisable for parent and branch vessel stenting

## CONCLUSION

In the era of the DES, interventional cardiologists must have a fundamental knowledge of the system components and procedural techniques to optimize clinical outcomes for these combined drug and device therapies. It is prudent to embark carefully, based on available clinical data, in the application of DES to unique high-risk patient and lesion subsets, such as bifurcation disease. The development of dedicated DES and delivery systems for the management of anatomic subsets dependent on precise geographic device positioning, such as ostial and bifurcation lesions, will likely enable reliable acute procedural outcomes, optimal drug delivery, and further reductions in restenosis. ■

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