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Basic Science Review

Drug-Eluting Stents for Coronary Bifurcations: Bench Testing of Provisional Side-Branch Strategies

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The objective of this study was to bench-test provisional bifurcation stenting strategies to provide insights on how best to perform these with drug-eluting stents (DESs). Bifurcation stenting with DESs reduces restenosis compared with bare metal stents (BMSs). Outcomes with a single DES are better than with two DESs but if the main branch is stented, there needs to be a reliable strategy for provisionally stenting the side-branch with full ostial scaffolding and drug application. Stents were photographed in a phantom after deployment with different strategies. With provisional T-stenting, placement of the side-branch stent without gaps is difficult. The internal (or reverse) crush strategy fully scaffolds the side-branch ostium but is experimental. The culotte technique providing excellent side-branch ostial coverage is easier to perform with open-cell or large-cell stent design. In general, kissing balloon postdilatation improves stent expansion, especially at the ostium, and corrects distortion. However, a main-branch kissing balloon of smaller diameter than the deploying balloon causes distortion. Final main-branch postdilatation or sequential postdilatation prevents distortion after the internal crush strategy.

Key words: stents; drugs; restenosis; angioplasty; coronary disease; revascularization

INTRODUCTION

Drug-eluting stents (DESs) reduce restenosis after coronary bifurcation stenting when compared with historical bare metal stent (BMS) controls [1]. Those restenoses that did occur when two stents were used were at the ostium of the side-branch and believed to be due to gaps in coverage, scaffolding, and drug application (Fig. 1) with the conventional T-stenting strategy [1]. This led to the development of the innovative crush technique [2], which ensures that the ostium is covered by stent struts [3]. With the crush technique, the side-branch stent is deployed so that part of it lies within the main branch. Then a main-branch stent is deployed, crushing that portion of side-branch stent within the main branch against the vessel wall. This should be followed by kissing (simultaneous main- and side-branch) postdilatation to correct distortion and expand fully the stent at the side-branch ostium [3].

Coronary bifurcations treated with a single DES had better outcomes than those treated with two stents [1]. However, half of the patients randomized to a single-stent strategy crossed over to the two-stent arm so that those who received a single stent were a selected low-risk group.

The crush technique with DES for bifurcations is safe and quick. It reliably covers the side-branch ostium. However, it is a commitment to a two-stent strategy. Single-stent bifurcation strategies need to have a reliable and safe fallback method for stenting the side branch that ensures adequate strut expansion and coverage of the side-branch ostium. Such strategies with DES might include provisional T-stenting

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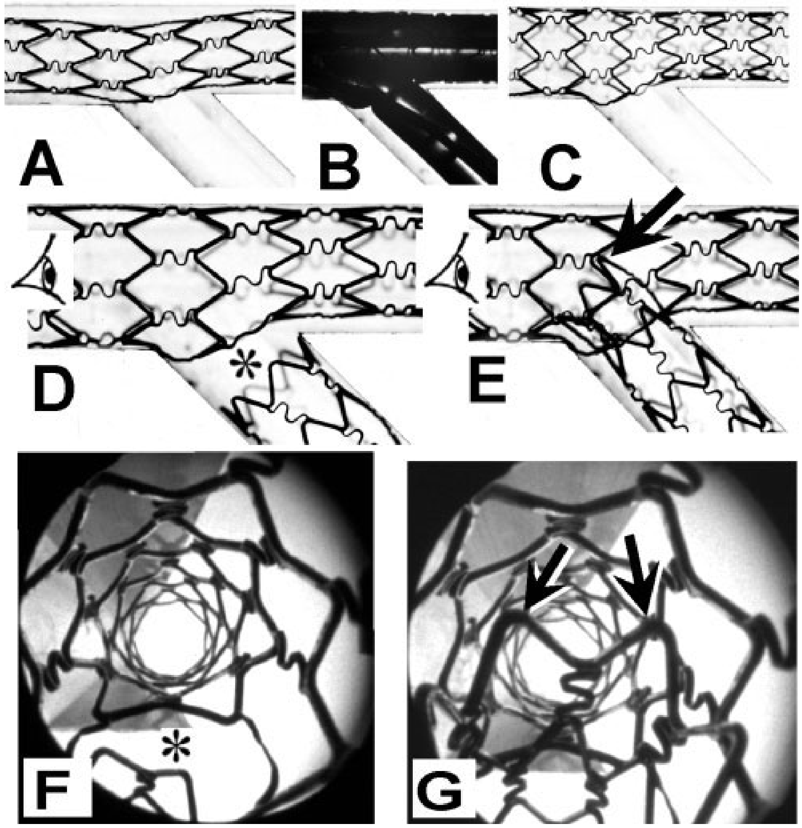

Fig. 1. Provisional T-stenting. Shown in A is a slotted-tube design stent (Bx Velocity) following deployment in the main-branch and side-branch balloon dilatation. Kissing balloon inflations (B) further open the side of the stent and push some stent struts into the proximal margin of the ostium (C). In D and F (the corresponding endoscopic view), a side-branch stent, passed through the side of the main-branch stent, was deployed too distally so that there is a gap between stents (asterisk). In E, the stent has been deployed too proximally so that it partially obstructs the main-branch lumen as confirmed endoscopically (G).

[4], culotte stenting [5,6], the internal (or reverse) crush technique, and, in the future, dedicated bifurcation stents that are drug-eluting.

Bench testing has provided unexpected insights into bifurcation stenting [3,7]. This bench study examines how different DES platforms perform with the provisional T-stenting, internal crush, and culotte techniques and clarifies the best ways to perform these techniques with different DES platform designs and postdilatation strategies.

MATERIALS AND METHODS

Testing was performed on the bare metal Bx Velocity (Cordis, Warren, NJ), Express 2 and Liberte (Boston Scientific, Natick, MA), and the Driver (Medtronic AVE, Minneapolis, MN) stents, which are the delivery platforms of the Cypher sirolimus-eluting, the Taxus Express paclitaxel-eluting, the Taxus Liberte paclitaxel-eluting, and the Driver ABT 578-eluting systems, respectively. The Bx Velocity, Express, and Liberte stents are stainless steel slotted-tube designs and the Driver is a chromium cobalt modular-ring design.

Stents were deployed in our previously described phantom and their exteriors photographed at each stage of deployment for each strategy [3,6,7]. In addition, the interiors of the stents were photographed through a pediatric endoscope during stages of deployment [3].

Deployment Strategies Tested

Provisional T-stenting. In this strategy, the side-branch stent was passed in its entirety through the side of the main-branch stent. The side-branch stent was deployed so that the two stents form a T-configuration. We examined deployment of the side-branch stent in an optimal position with minimum gaps, more distally in the side branch so there was a gap between stents, and more proximally so that part lay within the main-branch stent.

Internal (or reverse) crush. The main-branch stent was deployed first. The side-branch stent was passed part way through the side of the main-branch stent and that portion of the side-branch stent lying within the main vessel was crushed inside the main-branch stent by balloon inflation. It differs from conventional crush [2,3] in that the side-branch stent was crushed inside, not outside, the main-branch stent.

Culotte technique. Following main-branch stent deployment (Fig. 4), a second stent was advanced part way through the side of the main-branch stent and

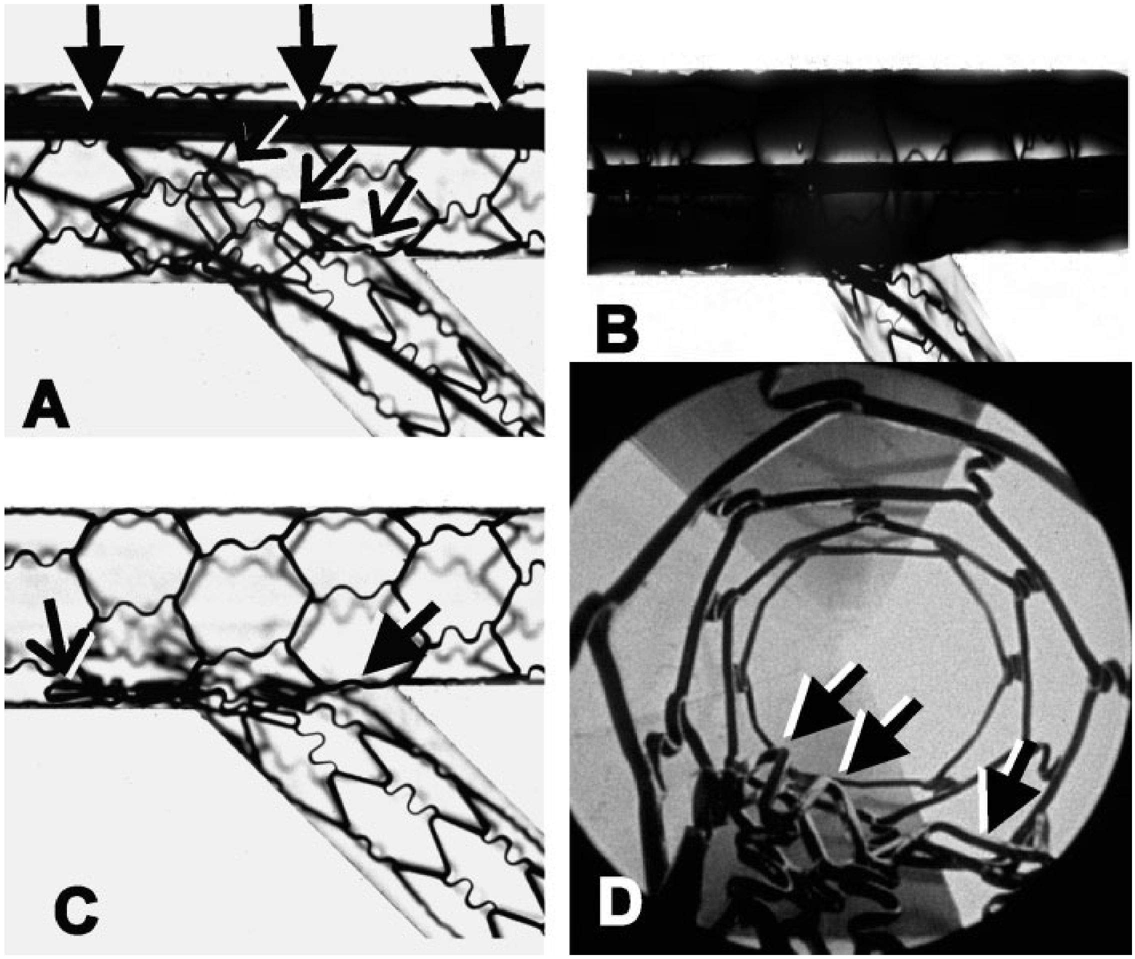

Fig. 2. **Internal or reverse crush provisional side-branch stenting. In A, the side-branch stent (small arrows) is deployed through the side of the main-branch stent. A balloon in the main-branch stent (A, arrowheads) is inflated (B), crushing the proximal portion of the side-branch stent inside the main-branch stent (C, arrows). An endoscopic view demonstrates that the crushed stent is flattened inside the main-branch stent (D, arrows).**

deployed so that the proximal portion of the side-branch stent was expanded inside the main-branch stent and the distal portion was expanded in the side branch [5,6]. The side-branch balloon was withdrawn. A wire and balloon were then passed through the side of the side-branch stent into the distal main branch for postdilatation. Finally, kissing (simultaneous side- and main-branch) balloon postdilatation was performed.

Maximum Achievable Cell Size

To determine the maximum cell size achievable with balloon dilatation through the side of a stent, a 3.5 mm balloon was passed through the sides of each stent and inflated to 20 atm. Following balloon removal, each stent was photographed, cell size measured, and a correction made for magnification.

Postdilatation Strategies Tested

We studied the effect of kissing balloon postdilatation on the different stent deployment strategies. We tested the effect of postdilatation with a main-branch kissing balloon of narrower caliber than the deploying balloon.

RESULTS

Provisional T-Stenting

With provisional T-stenting, it was difficult to place the side-branch stent precisely and it was possible to place this stent either too distally (Fig. D and F), leaving gaps in scaffolding and drug application, or too proximally (Fig. E and G), with potential obstruction of the main-branch stent.

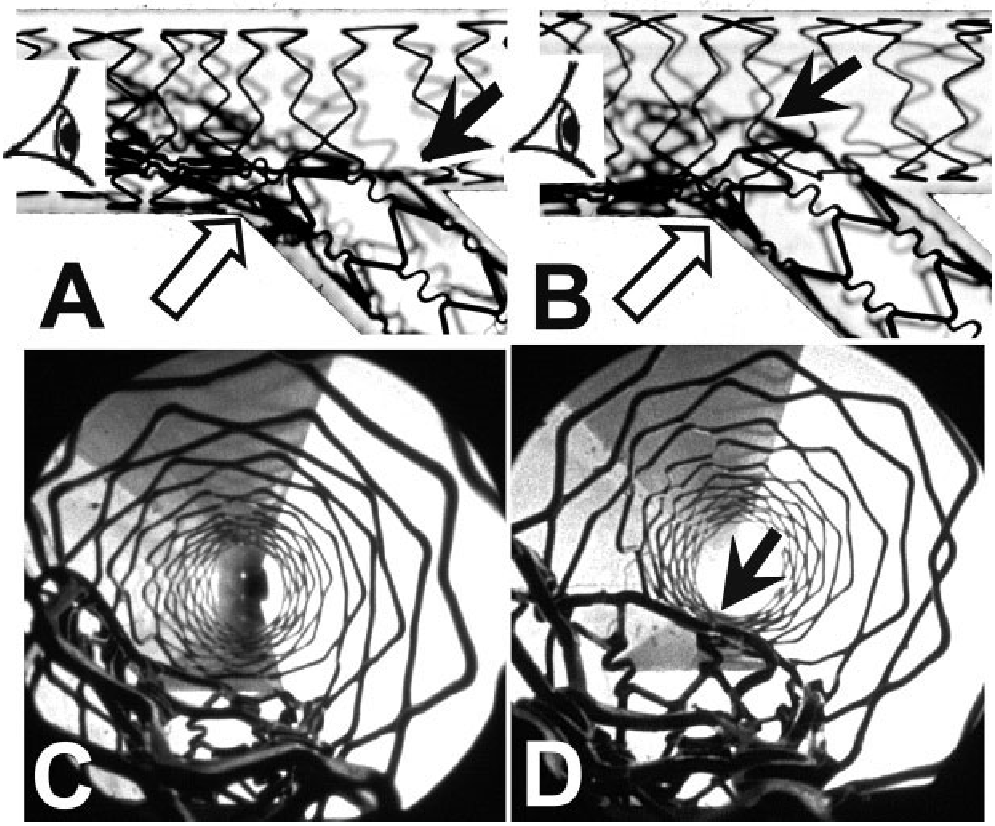

Fig. 3. Internal crush provisional side-branch stenting with distortion caused by kissing balloon postdilatation. In A and C (the corresponding endoscopic view), a Bx Velocity stent was crushed inside a Driver stent. After kissing balloon postdilatation, the stent at the distal margin of the side-branch ostium is distorted and protrudes into the main-branch lumen (black arrows, B and D). The side-branch stent is well expanded at the side-branch ostium even before kissing balloon postdilatation (open arrow, A).

Internal or Reverse Crush Provisional Side-Branch Stenting Strategy

A slotted-tube stent such as the Bx Velocity stent when internally crushed (Fig. 2A and B) within a stent of the same (or different) design was well applied to the wall and did not protrude into the main-stent lumen (Fig. 2C). This was confirmed by endoscopy (Fig. 2D). In contrast, the modular design (Driver) when used in the side branch was not well flattened inside the main-branch stent and struts protruded into the lumen.

The internal crush strategy using the slotted-tube design stents (Bx Velocity and Express) provided coverage of the side-branch ostium with freedom from gaps. The side-branch stent was well expanded at the ostium even without postdilatation (Fig. 3A).

After internal crushing and in contrast to other stenting strategies, kissing balloon postdilatation caused distortion (Fig. 3). The distorted portions of stents at the distal margin of the ostium were pushed into the main-vessel lumen, potentially causing obstruction (Fig. 3B and D). This finding was true of all stent designs tested and not related to the sequence of balloon deflation. Kissing balloons did, however, retain or improve the expansion of the side-branch stent at the ostium (Fig. 3A and C). In addition, they released the side-branch from jail by widening the gaps between struts, potentially improving subsequent side-branch access. The main-branch distortion could be repaired by main-branch redilatation with an appropriately sized balloon. An alternative postdilatation strategy after internal crush that releases the side branch from jail and prevents main-branch distortion is sequential side-branch and then main-branch postdilatation.

Culotte Strategy With Liberte Stent

Deployment of the side-branch stent through the side of the main-branch stent caused distortion of the latter (Fig. 4A and B). Balloon inflation in the main branch through the side of the side-branch stent enlarged gaps between struts but distorted the side-branch ostium (Fig. 4C, arrow). Kissing balloon postdilatation (Fig. 4D) repaired distortion and fully expanded the stent at the side-branch ostium (Fig. 4E). Examination of the interior of the stents showed that kissing balloon postdilatation produced full luminal caliber in both branches with full scaffolding and potential drug application at the ostium (Fig. 4F and G).

Maximum Diameter of Cell

The maximum cell diameter achieved by dilating through the side of a stent were 2.5 $\times$ 3.0 mm for the

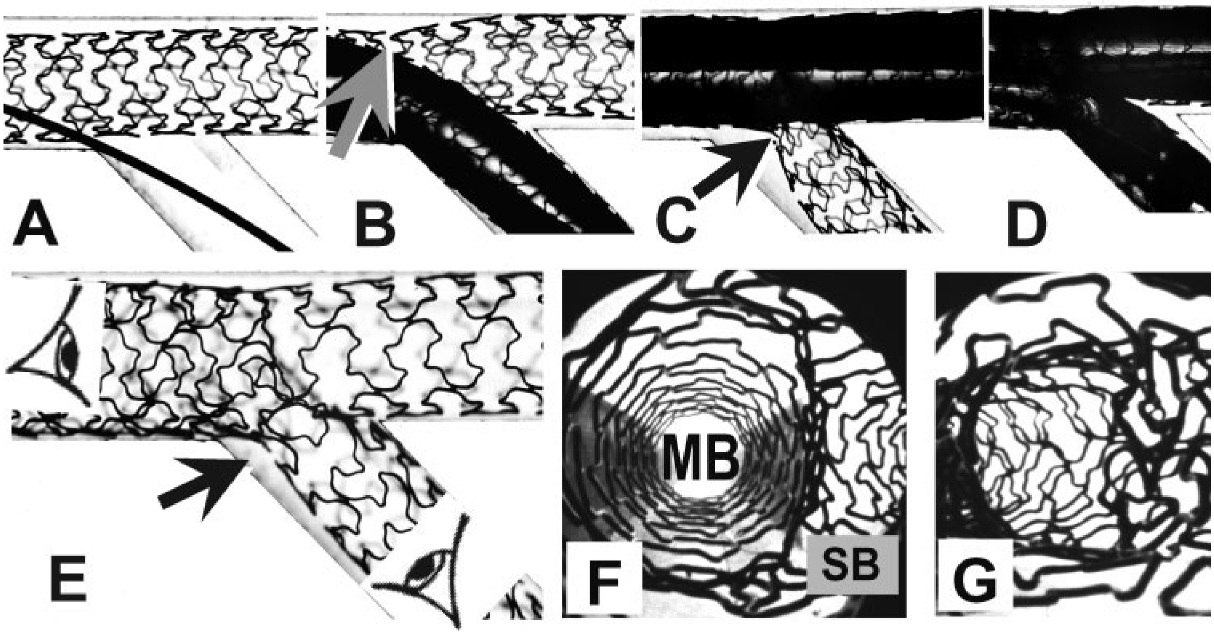

Fig. 4. Culotte technique provisional side-branch stenting with Liberte stents. Following deployment of a stent in the main branch (A), a second is deployed in the side-branch distorting the main-branch stent (B, arrow). Main-branch redilatation distorts the side-branch ostium (C, arrow). Following kissing balloon postdilatation (D), the side-branch stent is fully expanded at the ostium (E, arrow). This is confirmed by the endoscopic main-branch view (F). The main and side branches are widely patent without obstructing stent struts (F and G). MB, main branch; SB, side branch.

Bx Velocity, 3.3 × 3.3 mm for the Express, and 3.4 × 3.6 mm for the Liberte respectively (Fig. 5).

DISCUSSION

Restenosis in coronary bifurcations treated with DESs is much less common than with BMSs [1]. In addition, it is likely that refinements of stenting strategies and stent technology will reduce restenosis even further. Bifurcation stenting can be technically difficult but is likely to become easier.

The interventionist needs DES bifurcation techniques that are safe, easy to perform, cost-effective, and have a low repeat intervention rate. The major safety challenge is to ensure that the side branch is protected and has a satisfactory final result with or without stenting. Deploying a side-branch stent through the side of a main-branch stent can be technically challenging and may not be achieved. If a side-branch stent is deployed, it must be fully expanded with full scaffolding of the side-branch ostium. Postdilatation strategies must ensure that there is full expansion of the main-branch stent (and the side-branch stent if applicable) without stent distortion and with optimization of the potential for subsequent side-branch access by widening gaps between struts separating the side from main branches. Economic cost should be contained.

Provisional T-stenting (Fig. 1) is a widely used strategy that in experienced hands can have excellent outcomes [8]. In the randomized trial of DES stenting [1] with one or two stents, main-branch restenosis was virtually abolished but restenosis occurred at the side-branch ostium when two stents were needed [1]. Restenosis was attributed to gaps between stents (Fig. 1) with deficiencies in scaffolding and drug application. The major difficulty with T-stenting is precise placement of the side-branch stent. Deployment too distally leaves large gaps and deployment too proximally potentially obstructs the main branch. Understanding of these issues led to the introduction of the crush technique to ensure that the ostium is covered without gaps.

The conventional (external) crush technique [2,3] is simple and quick, fully scaffolds the side-branch ostium, but employs two stents, whereas many patients can be treated satisfactorily with only one stent. However, if a single stent is deployed, there needs to be fallback strategies that allow the side branch to be stented safely and effectively if necessary. This bench study provides insights into different provisional side-branch stenting strategies with DESs.

The internal crush technique (Fig. 2) allows provisional side-branch stenting with full stent expansion at the side-branch ostium. Using this strategy without kissing balloon postdilatation (Fig. 3A), the slotted-tube stent was better expanded at the side-branch ostium than after a conventional external crush [3], but the side branch is jailed. Kissing balloon postdilatation after the conventional external crush technique ensures optimum stent expansion without distortion if properly performed [3]. In contrast, kissing balloon inflations after internal crush caused stent distortion (Fig. 3B and D). While these inflations expanded the stents well and released the side branch from jail, the unexpected finding was that stent struts at the distal margin of the ostium were pushed into the main branch (Fig. 3B and D). The distortion was not due to the sequence of balloon deflation. In general, postdilatation with kissing balloon inflations produces optimal bifurcation stent deployment if the postdilating balloons are of the same or larger caliber than the deploying balloons.

The culotte technique with BMS has been largely abandoned because of high restenosis rates [9]. This technique is likely to have a resurgence with DESs because it is a provisional side-branch stenting strategy that can provide full side-branch scaffolding and potential drug application with wide patency of the main and side branches. A limitation of all provisional side-branch stenting strategies is that it may be impossible to pass a stent through the side of the main-branch stent, although this is likely to be easier with modular-ring designs such as the Driver stent [6] or with large-cell slotted-tube designs such as the Liberte stent. In addition, cell size (Fig. 5) limits ostial size and main-branch diameter achievable at the bifurcation.

Dedicated bifurcation stents such as the MultiLink Frontier permit safe side-branch provisional stenting. After main-branch stent deployment, there is a guidewire through the side port into the branch. Their design facilitates easy passage of a stent into the side branch if necessary. A limitation of these designs in common with provisional T-stenting is that it is difficult to place a side-branch stent precisely at the ostium without gaps or without protrusion into the main branch. A further limitation compared with contemporary conventional stents is the larger crossing profile that makes delivery more difficult. In addition, none is currently available coated with an antirestenotic agent.

We have previously described how stent distortion caused by dilating through the side of a stent can be corrected by kissing balloon postdilatation [7]. In general, kissing balloon postdilatation, appropriately performed, improves stent expansion and corrects or prevents distortion. However, there are situations where kissing balloons cause distortion. If the main-branch kissing balloon is smaller in diameter than the deploying balloon, kissing balloons will distort stents [3]. In addition, kissing balloons will cause distortion if used

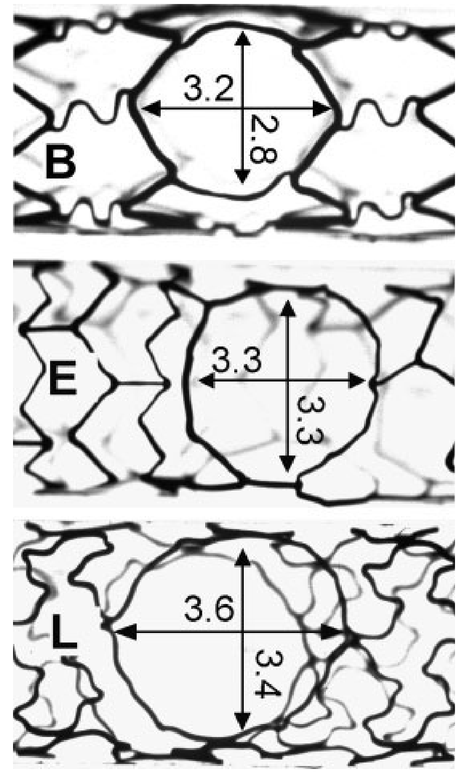

Fig. 5. Following 3.5 mm diameter balloon dilatation through the side of stents, the maximum cell diameters for the Bx Velocity (B), the Express (E), and the Liberte (L) are shown in millimeters.

following internal crush (Fig. 3) by displacing stent into the lumen of the main branch (Fig. 3). The major limitation of bench testing is that bench conditions cannot precisely mimic the in vivo environment.

In summary, restenosis following provisional T-bifurcation stenting with two stents may be due to gaps in scaffolding and drug application at the side-branch ostium. The crush technique with kissing balloon postdilatation fully scaffolds and may reduce restenosis at the ostium. Single-stent deployment has a lower restenosis rate than deployment of two stents, but half of those in the Colombo study [1] randomized to a single stent crossed over to receive two stents. For a strategy of single-stent deployment to be widely accepted in the DES era, there need to be provisional side-branch stenting strategies that are safe, quick, and that can reliably treat the side branch if necessary. All provisional strategies have the limitation that it may not be possible to pass a stent through the side of the main-branch stent to the side branch. T-stenting is limited by difficulties deploying the side-branch stent without gaps. Internal crush using a slotted-tube design in the side branch reliably covers the ostium. The modular-ring design stent did internally crush well. Kissing balloon postdilatation optimizes stent deployment after most strategies (single stent, T-stenting, conventional crush, culotte), but after internal crush causes stent distortion. If kissing balloon postdilatation is performed with a main-branch balloon smaller in diameter than the deploying balloon, stent distortion will result. It is likely in the future that there will be dedicated bifurcation stents coated with antirestenotic medications.

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