(Future) Perspectives on Bifurcation Stenting

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Presenter Disclosure Information for Angioplasty Summit 2009

Martin B. Leon, M.D.

Scientific Advisory Board or Equity:
Abbott, Boston Scientific, Cappella, Cordis, Medtronic, TMI, and Tryton

Coronary Bifurcations

Important Observations

- There is marked variability in the morphology of coronary bifurcation and left main lesions.
- This includes varying vessel size (MB and SB), lesion location, lesion length, lesion severity, morphology, and SB takeoff angle.
- *Therefore, multiple stent designs and operator techniques may be required to optimally treat highly variable bifurcation lesions.*

3 Dimensional Casts of Coronaries (Ao to terminal branches)

- Branching
- Curvature
- Tortuosity
- Lesions
- Intersections

Courtesy of Mary Russell

The Ostial Junction of Coronary Arteries (bifurcations)

- *Complex transition zone* from main vessel to side branch with many asymmetric features (incl. oval shape and rapid taper)
- *Anatomic distortion* likely with symmetric (cylindrical) designs
  - Strut protrusion/injury
  - Coverage gaps
  - Incomplete wall apposition

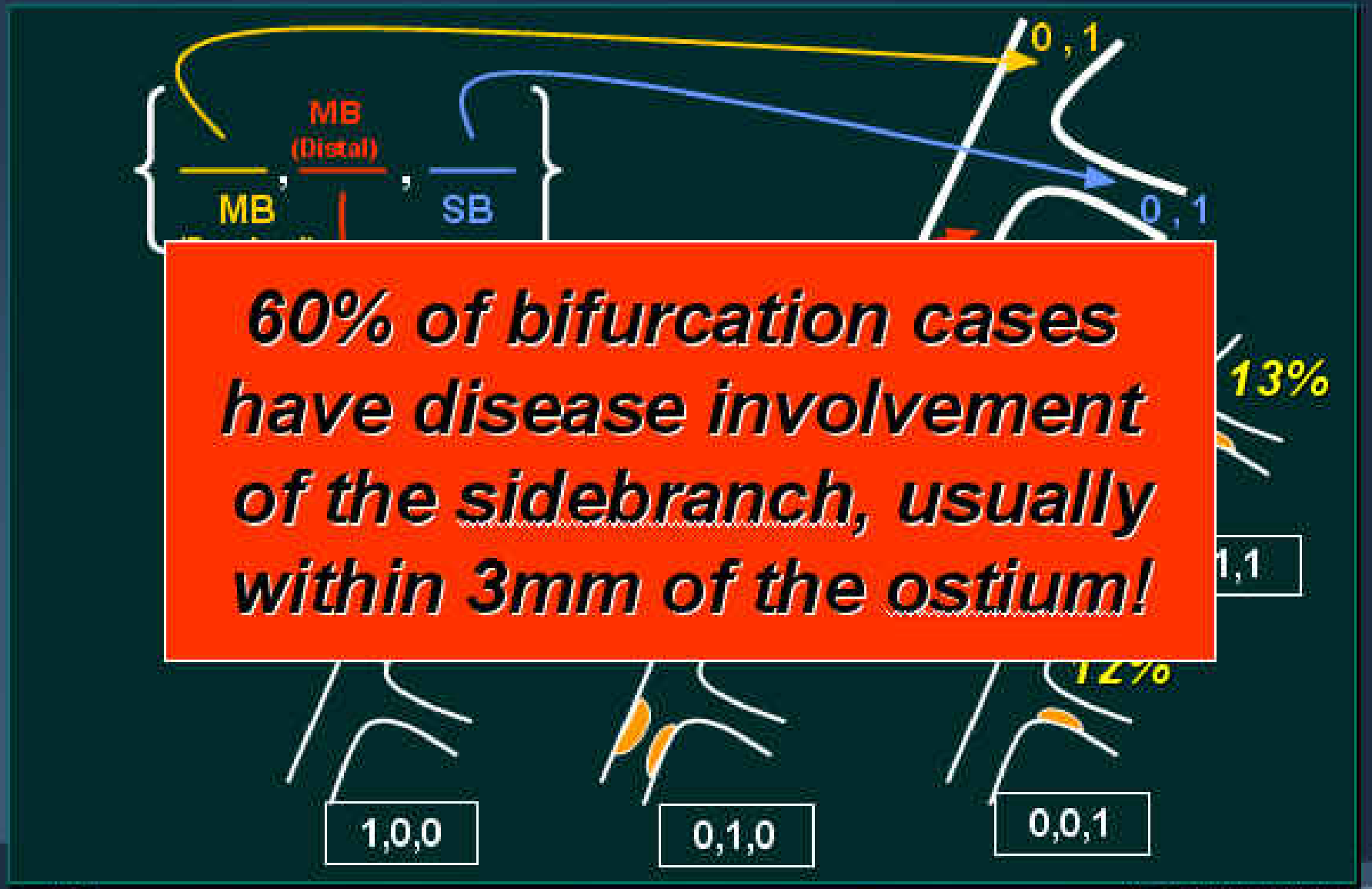
- Matching design to asymmetric ostial geometry may minimize implant injury, enhance scaffolding and improve outcomes

Coronary Bifurcations

Important Observations

- Bifurcations lesions (broadly defined) comprise approximately 25% of all PCI lesions, and in more than half, there is significant disease in the region of the sidebranch
- Sidebranch narrowing in bifurcations is usually confined to the ostial location (< 3mm from carina)

Medina Bifurcation Classification



60% of bifurcation cases have disease involvement of the sidebranch, usually within 3mm of the ostium!

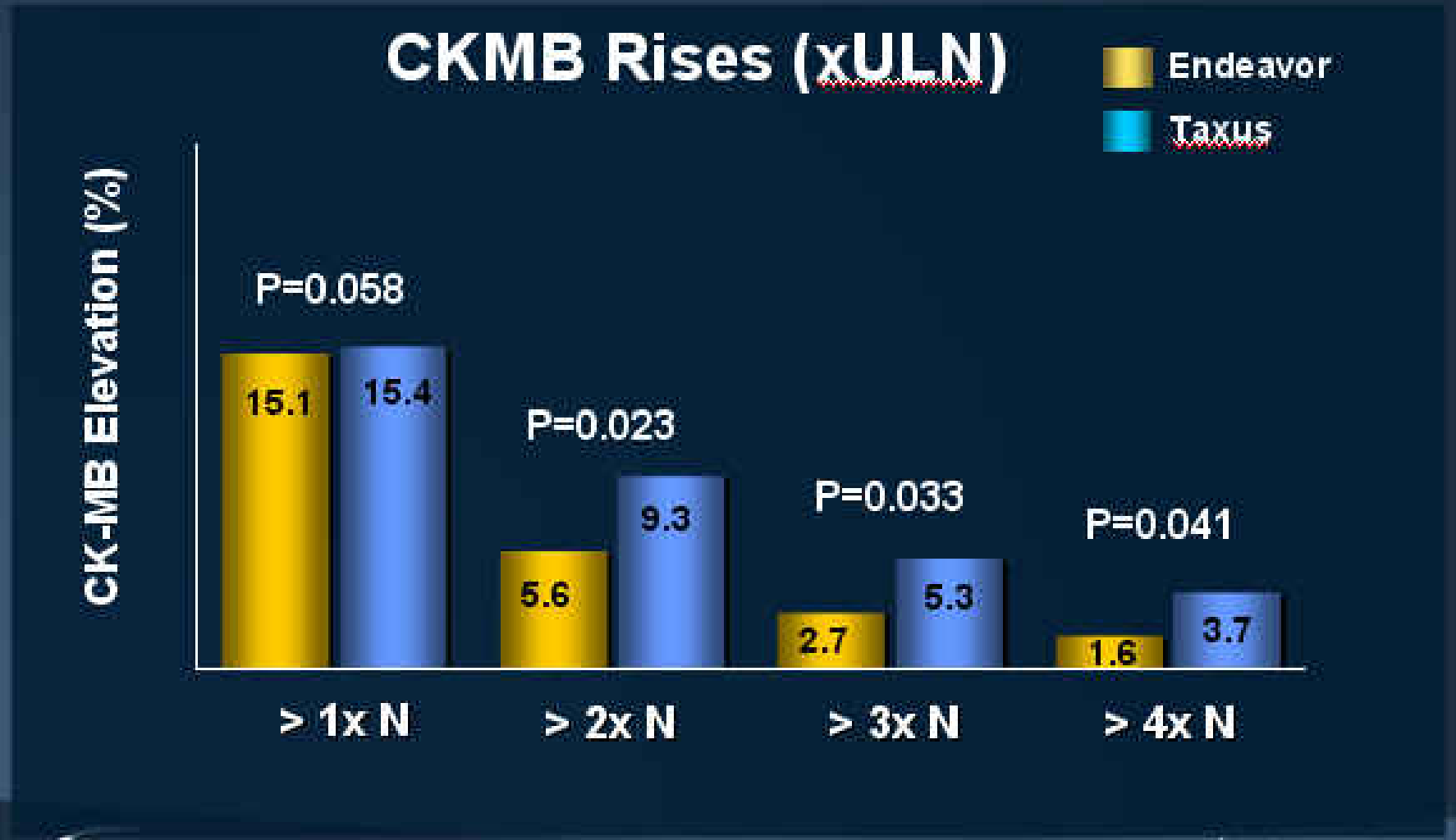
Coronary Bifurcations

Important Observations

- Sidebranch occlusion (even transient) during main vessel stenting is associated with a high frequency of CKMB elevations.
- *Main branch stenting (BMS and DES) often induces plaque shift across covered sidebranches, which may result in transient or permanent obstruction of the sidebranch.*

Endeavor IV

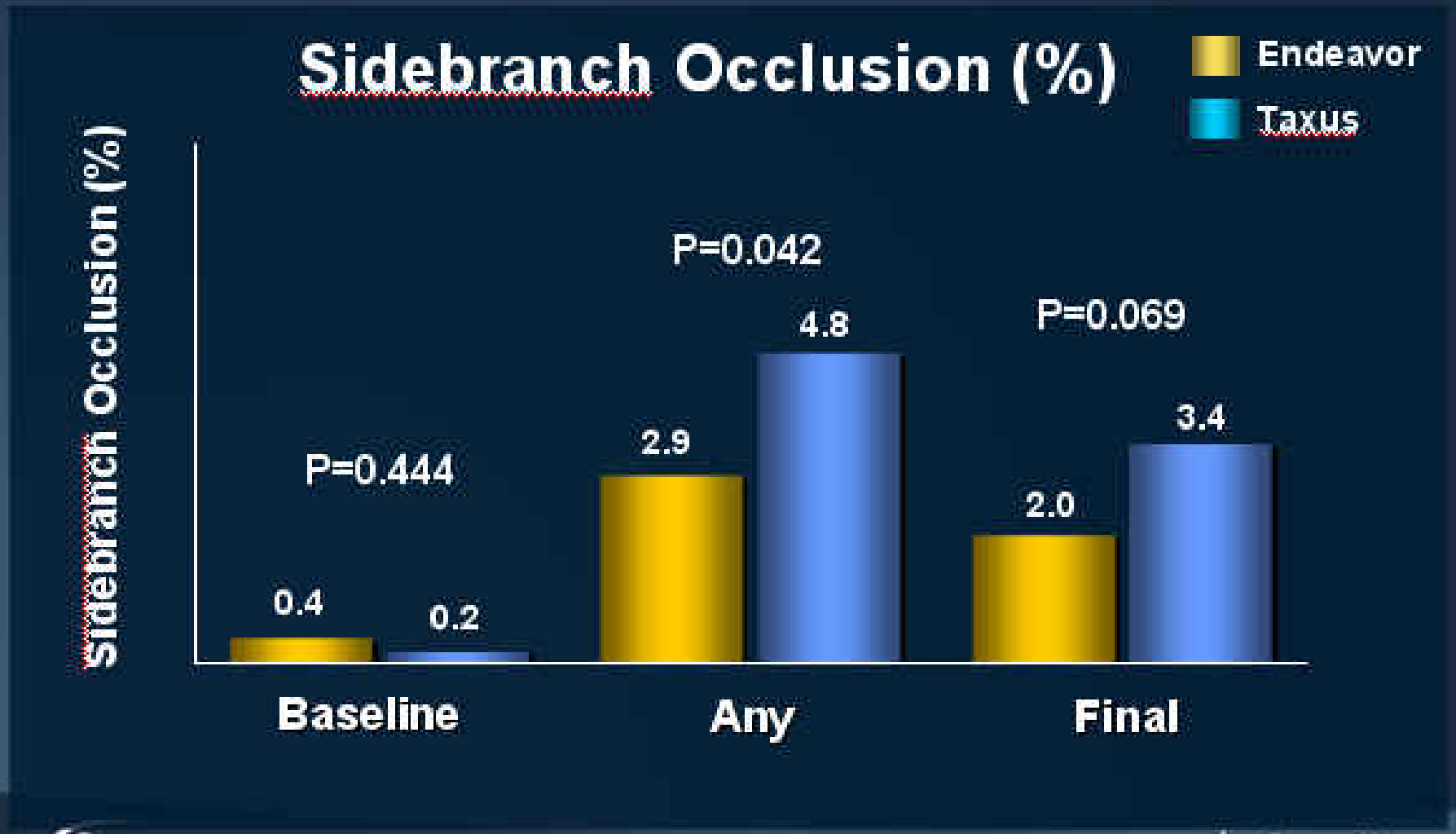
Sidebranch Occlusion Analysis



Popma, J et al; Circulation Intervention 2009

Endeavor IV

Sidebranch Occlusion Analysis



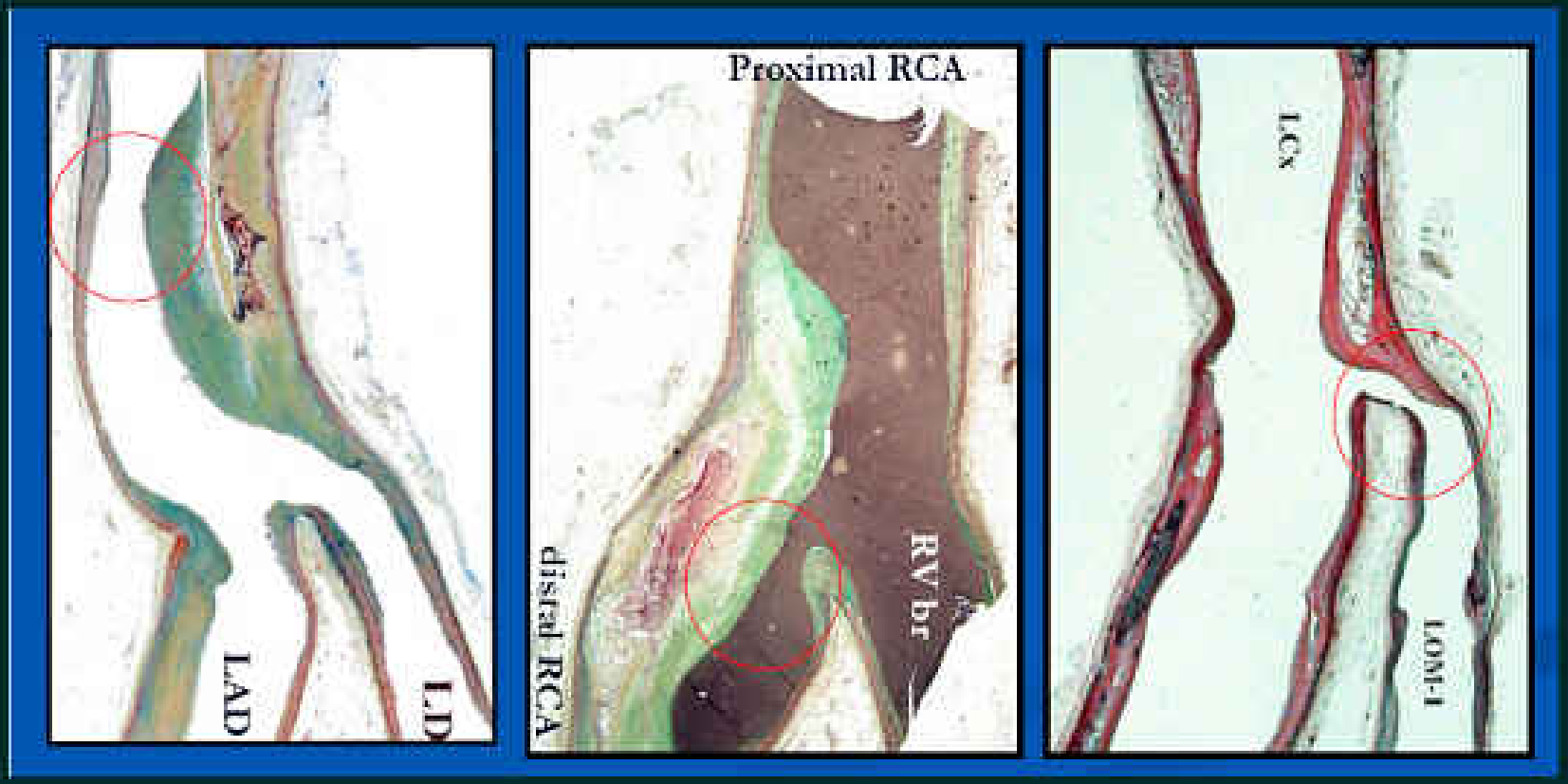
Popma, J et al; Circulation Intervention 2009

Coronary Bifurcations

Important Observations

- High shear stress at the bifurcation flow divider (carina) results in minimal plaque accumulation at the true carina
- However, due to altered flow dynamics after bifurcation stenting, there is a predisposition to recurrent ostial narrowing (neointima + mechanical negative remodelling)
- Main branch DES do not elicit anti-restenosis responses in covered side branches (requires SB ostial DES coverage)

Anatomy of the Bifurcation



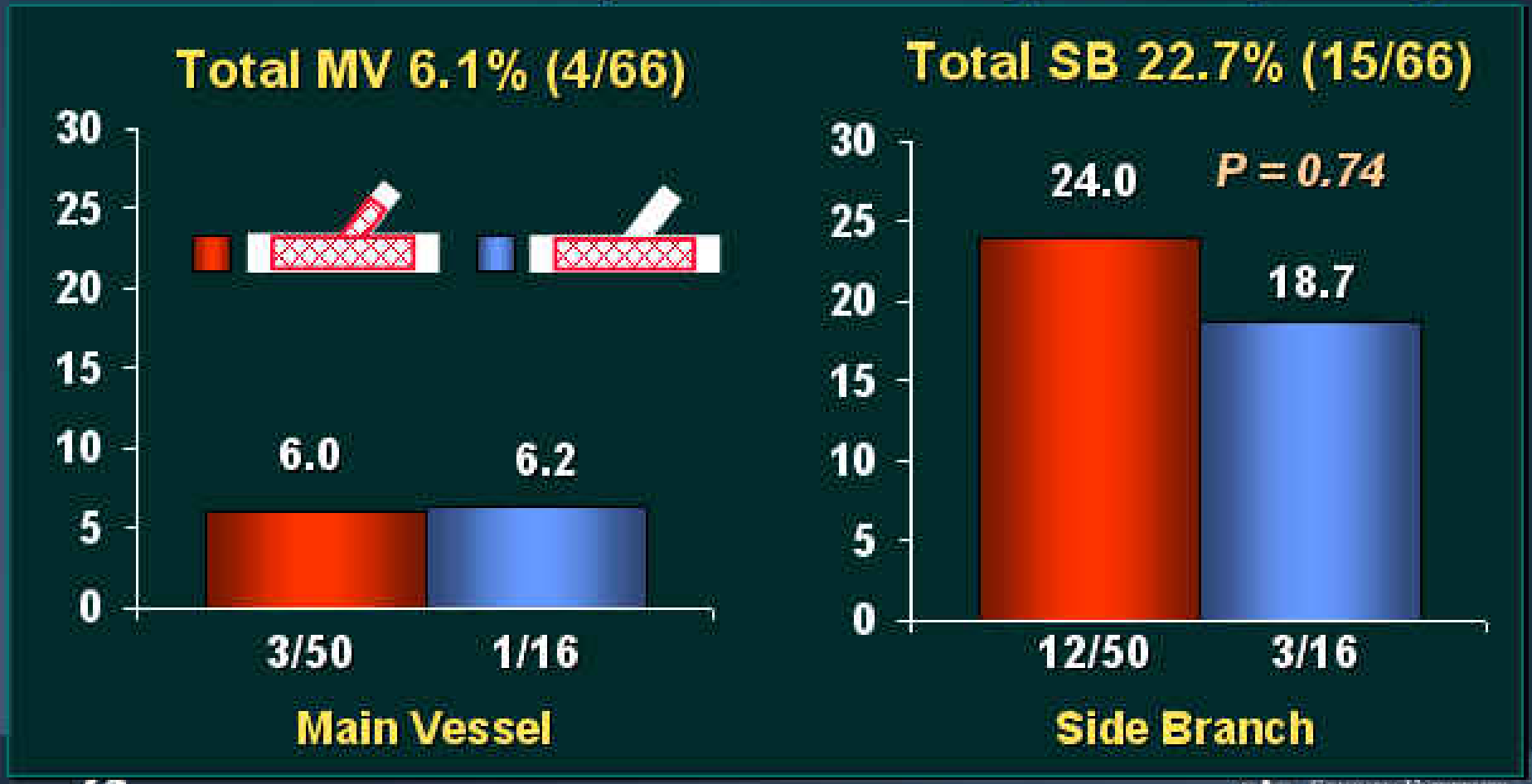
Pathology evidence shows that shear stress is high at the flow divider and therefore DES coverage may not be needed

Courtesy of Renu Virmani

SIRIUS Bifurcation Study

In-lesion Restenosis (treatment received); 78% FU

Total Restenosis (MV and/or SB) 25.7% (17/66)

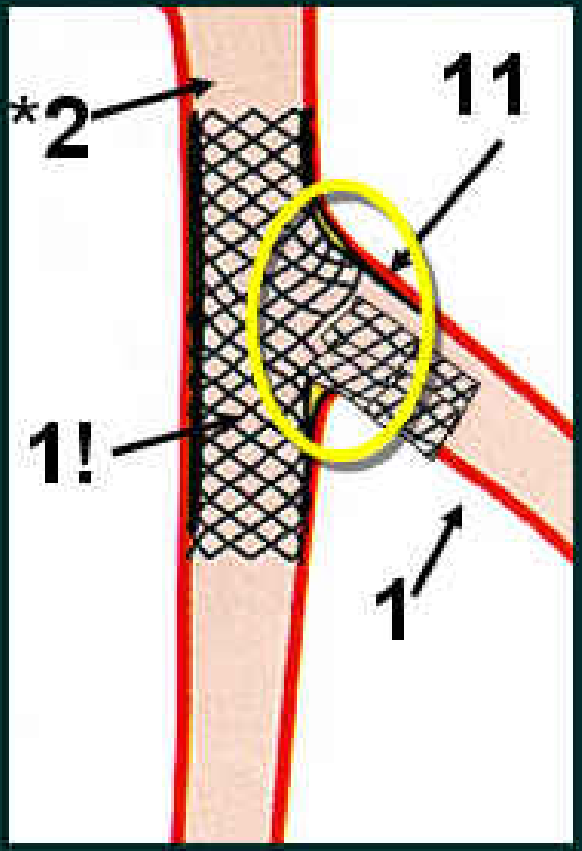


Colombo A et al; Circulation 2004;109:1244-9

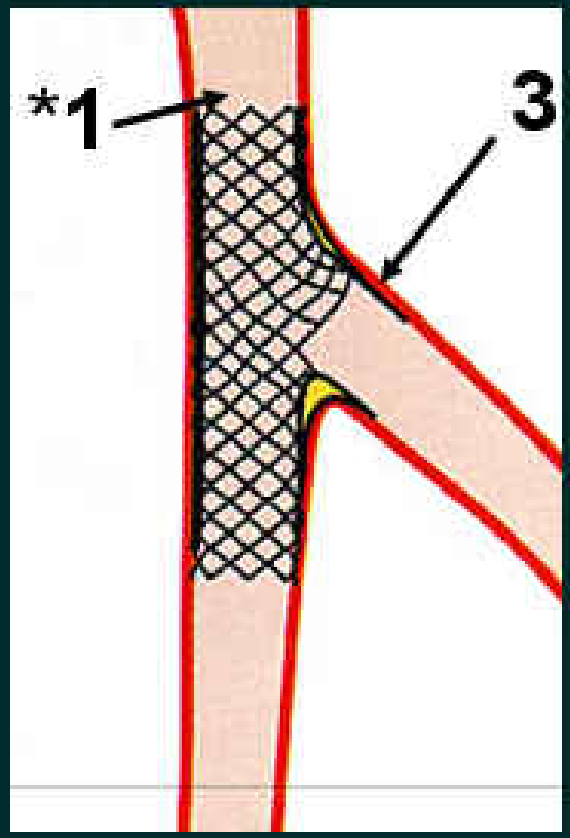
SIRIUS Bifurcation Study

Restenosis Site (17 cases)

Stent + Stent



Stent + PTCA

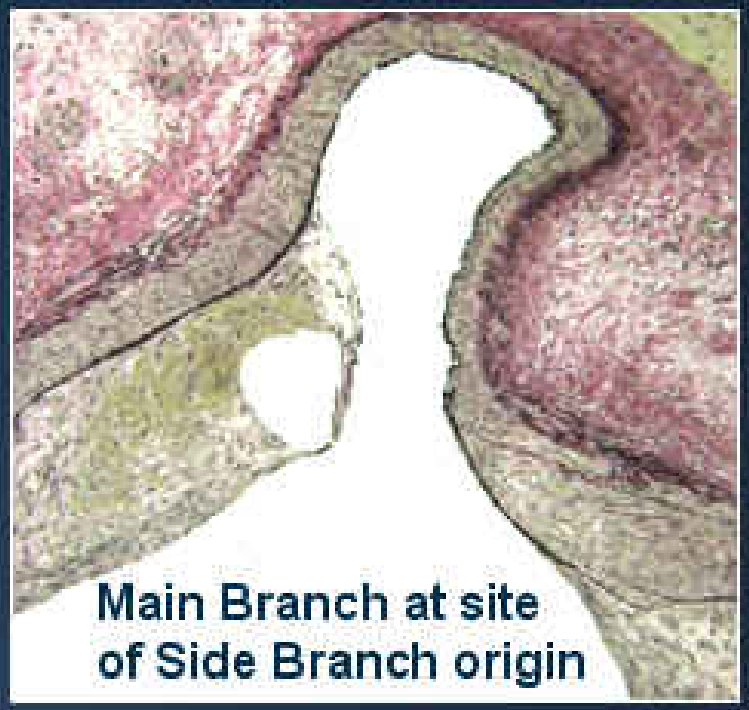


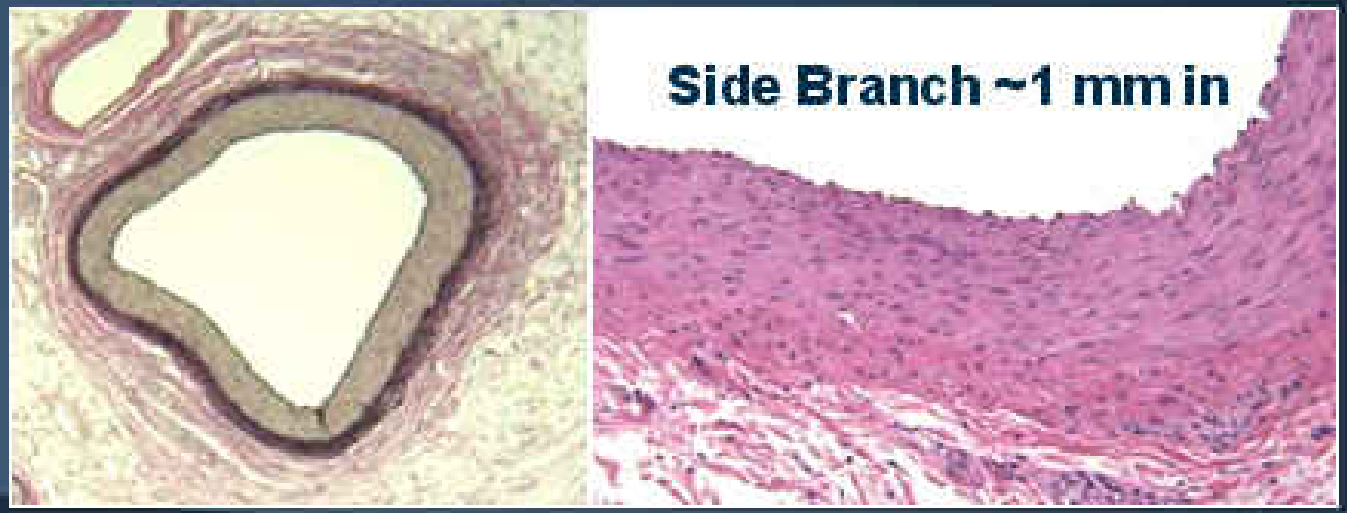
Colombo A. et al; Circulation 2004;109:1244-9

DES (Cypher) drug effects in side branches 30 days after implant (porcine coronaries)

Courtesy of:
AR Groothuis, ER Edelman, P Seifert, J Dooley, and C Rogers

CBSET and Cordis Corporation





Coronary Bifurcations

Important Observations

- *Current operator technique favors a "minimalist" provisional single stent approach under most circumstances, including distal left main disease*
- This is based upon growing data and perceptions (from observational studies and RCTs) indicating that a systematic two stent approach to all bifurcations imposes increased operator technical challenges, increased peri-procedural complications (esp. non-Q MIs and ? ST), and increased late MACE (including sidebranch TVR)

NORDIC Bifurcation Trial (SES)

Study Design

413 patients with bifurcation lesions
(LMCA, LAD. LCx, or RCA)

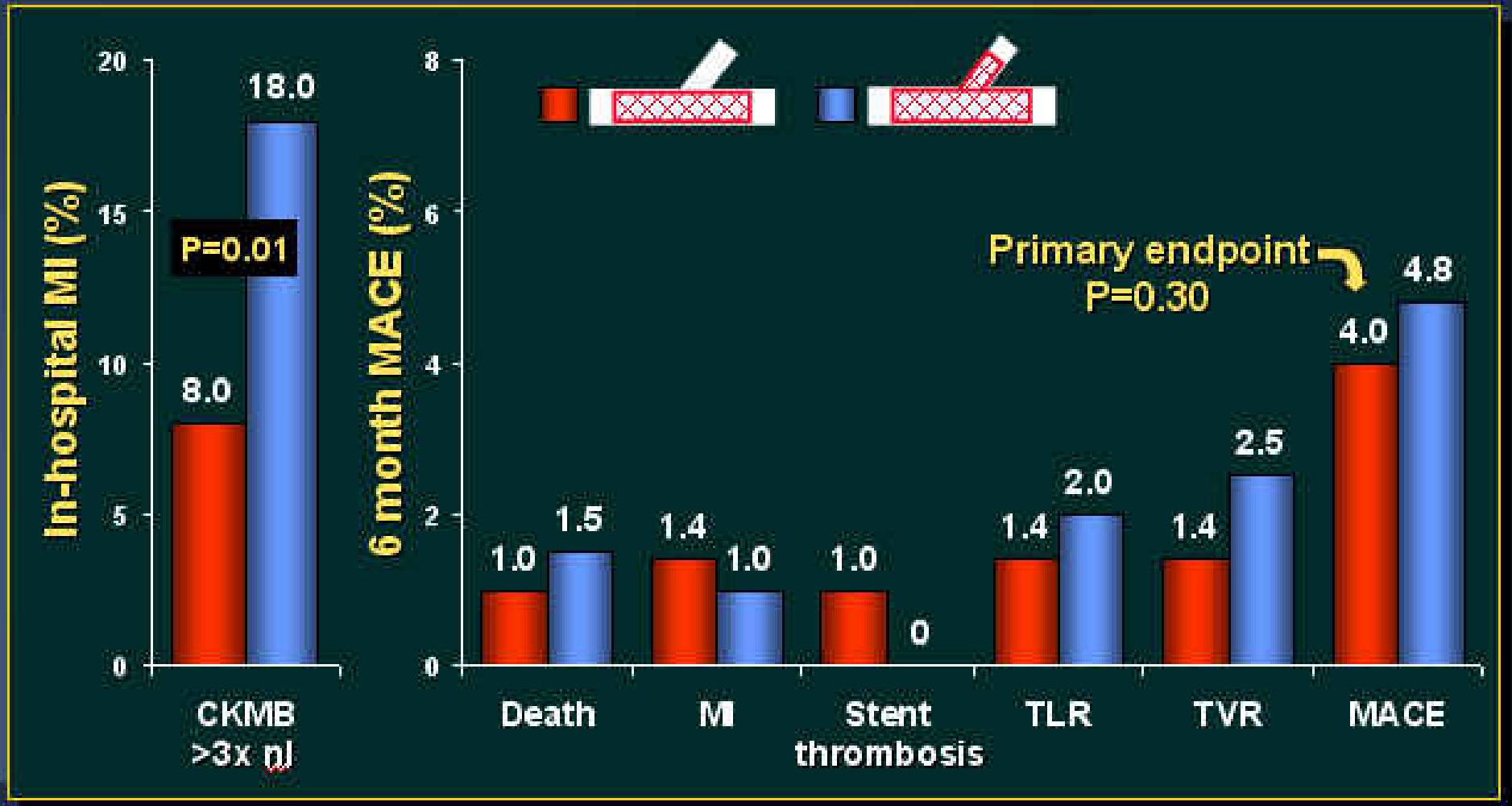
Stenting of both the main vessel and side branch (MV+SB) n=206 pts	Stenting of the main vessel and optional stenting of the side branch (MV only) n=207 pts
(95.1% SB stent)	*(4.3% SB stent)*

- **Primary Endpoint: Major adverse cardiac event (MACE) at 6 months, defined as cardiac death, myocardial infarction (MI), target lesion revascularization (TLR) or stent thrombosis of the index lesion**

Steigen T. et al; ACC 2006 Oral Presentation

Nordic Bifurcation Study (n=413)

Major Endpoints (clinically driven)



BBC - 1

PRIMARY ENDPOINT

Composite (9months) Death, MI, TVF

	Complex	Simple	P value
Death	2 (0.8%)	1 (0.4%)	-
Myocardial infarc	28 (11.2%)	9 (3.6%)	-
Target vessel failure	18 (7.2%)	14 (5.6%)	-
Primary endpoint	38 (15.2%)	20 (8.0%)	0.009 HR 2.0 (1.2 to 3.5)

Hildick-Smith et al. TCT 2008

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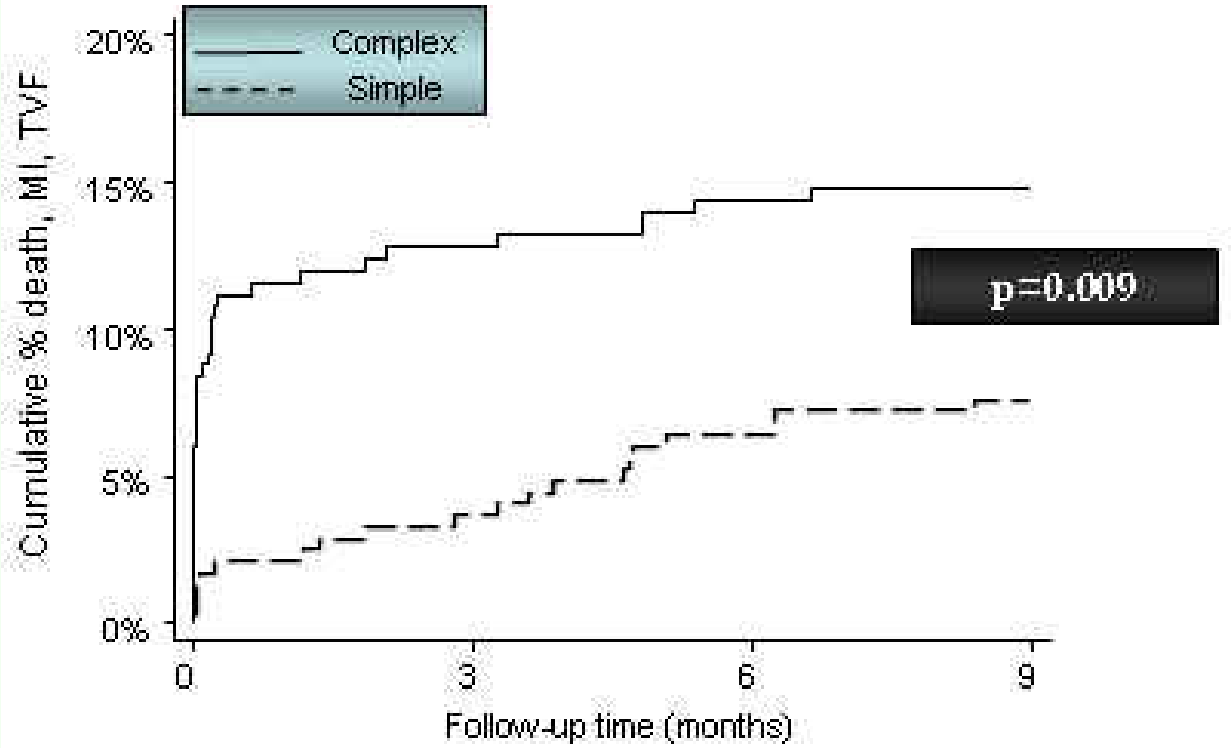
BBC - 1

PRIMARY ENDPOINT

Composite (9months) Death, MI, TVF



Hildick-Smith et al. TCT 2008

BBC - 1

Target Vessel Failure

	Complex	Simple
No. patients	18 (7.2%)	14 (5.6%)
Immediate CABG	2 (0.8%)	0
Inpatient CABG	1(0.4%)	0
Stent thrombosis (ARC definite)	5 (2.0%)	1 (0.4%)
Revascularisation (restenosis)	9	12
Revascularisation (distant lesion)	1	1

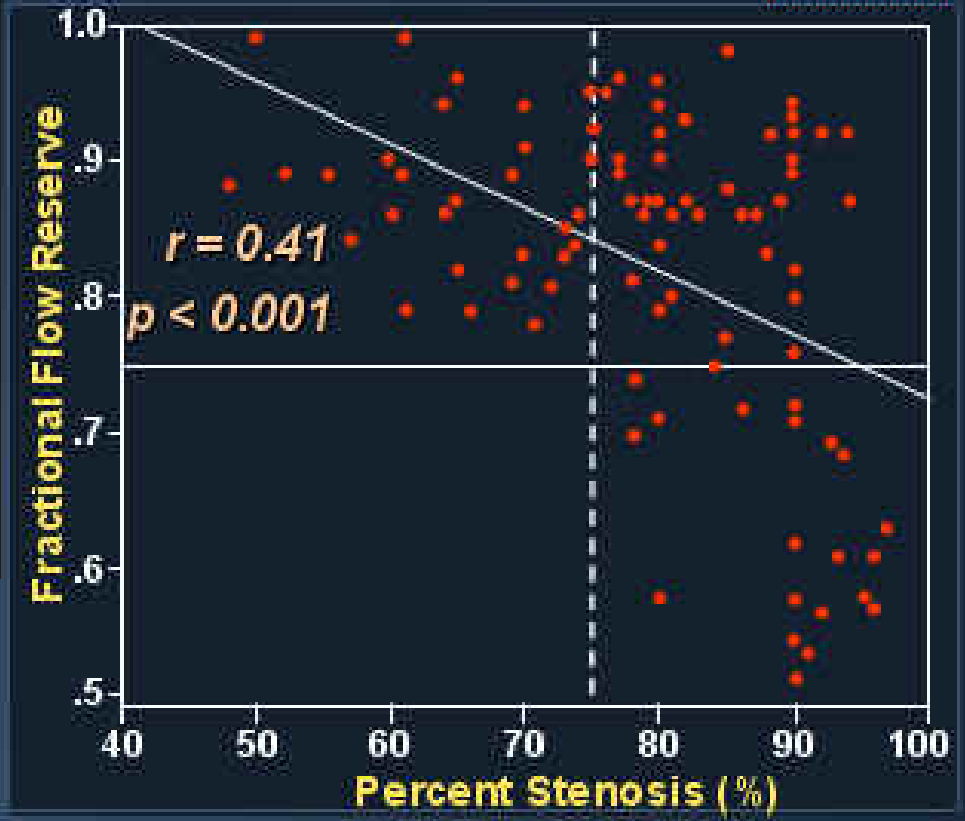
Hildick-Smith et al. TCT 2008

Physiologic Assessment of Jailed Side Branch (SB) Lesions Using Fractional Flow Reserve (FFR)

Variable	% stenosis by QCA <75%	% stenosis by QCA ≥75%
All lesions (n=94)		
FFR <0.75	0	20 (27%)
FFR ≥0.75	20	53
Vessel size >2.5mm (n=28)		
FFR <0.75	0	8 (38%)
FFR ≥0.75	7	13

The optimal cutoff value for percent stenosis to predict functionally significant stenosis was 85% (Sensitivity: 0.80, Specificity: 0.76)

Correlation between FFR and % stenosis



Conclusions: QCA is unreliable in the "functional" assessment of stenosis severity in jailed SBs. Conversely, FFR measurements demonstrate that most of stenotic SBs do not have functional significance

Koo, B.-K. et al. *JACC* 2005;46:633-637

Provisional SB Stenting

Tips and Tricks

- Jailed SB wire technique
- No SB pre-dilatation (selective)
- Stent diameters (distal MB and SB vessel ref)
- Final kissing balloons (correct balloon sizing)
- When to use 2 stents (TIMI flow, % diam sten, dissection grade in SB, physiology)

Coronary Bifurcations

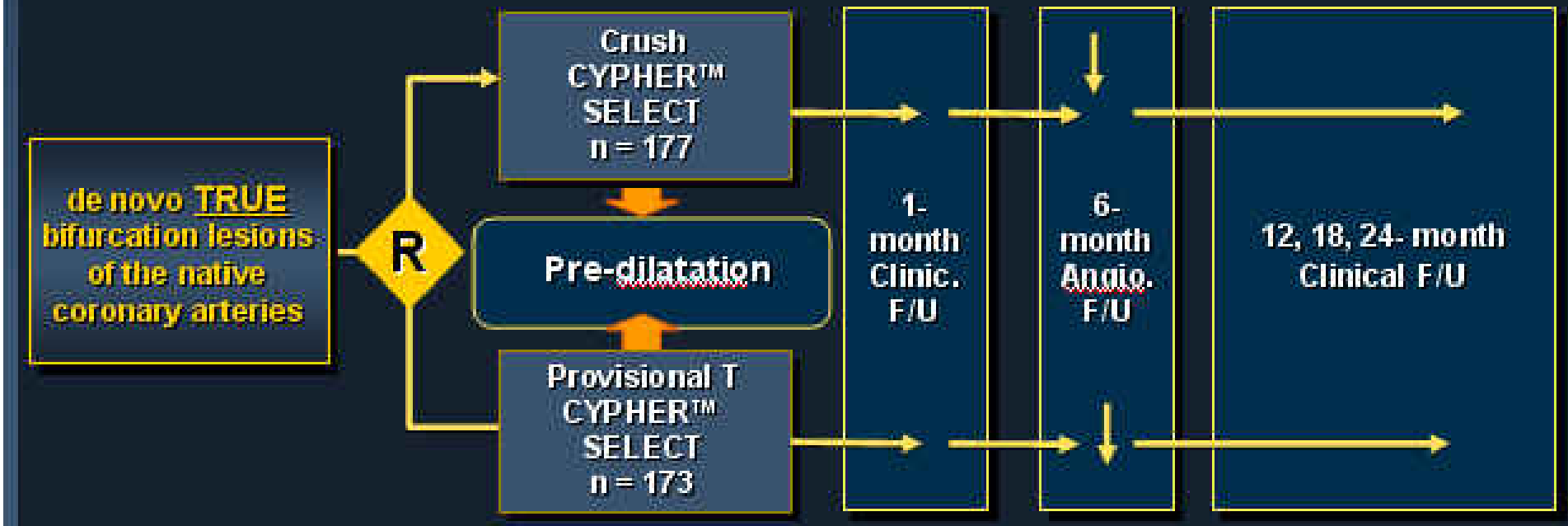
Important Observations

- The reliance on a provisional bifurcation stent strategy may have been *exaggerated* by (1) less rigorous application of essential operator techniques to optimize two-stent results (e.g. HP two-step final kiss), (2) negative experiences associated with the more challenging current two-stent strategies (crush, T, culotte, and kissing stents), and (3) the lack of dedicated user-friendly bifurcation stent designs

CACTUS Trial

Study Design

n = 350 patients



31% (54/173) NEEDED PROVISIONAL STENTING IN THE SB

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CACTUS Trial

Coronary Bifurcation Application of the Crush Technique Using Sirolimus-Eluting stents

Procedural characteristics

	Crush (n=177)		Prov T (n=173)	
	MB	**SB**	**MB**	**SB**
Predilatation (%)	89.8	89.8	90.8	90.8
IVUS (%)	3.4	2.8	4.1	2.3
Total stent length (mm)	23.8 ± 5.9	17.9 ± 5.0	22.2 ± 5.7*	18.1 ± 6.2 (54 lesions)
Max pressure (atm)	15.7 ± 4.3	13.4 ± 3.4	16.4 ± 4.1	12.0 ± 2.4*
Final kissing (%)	92.1		90.2	
IIb-IIIa GP inhibitors (%)	22.6		17.3	

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** = p<0.05 for comparisons between crush and prov T*

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CACTUS Trial

Coronary Bifurcation Application of the Crush Technique Using Sirolimus-Eluting stents

6- month in-segment binary restenosis

Angiographic F.U. performed in 86% of pts in both groups

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Colombo A, EuroPCR 2008

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CACTUS Trial

Coronary Bifurcation Application of the Crush Technique Using Sirolimus-Eluting stents

	Crush	T-Prov	
30 days MACE (days 0-30)			
Q wave MI	3 (1.7%)	2 (1.1%)	1.00
Non-Q wave MI	15 (8.5)	12 (6.9%)	0.69
TLR	3 (1.7%)	1 (0.5%)	0.63
TVR (including TLR)	3 (1.7%)	1 (0.5%)	0.63
Death	0	0	-
6-month MACE (days 31-180)			
MI	1 (0.6%)	1 (0.5%)	1.00
TLR	10 (5.6%)	10 (5.8%)	1.00
TVR (including TLR)	11 (6.2%)	12 (6.8%)	0.83
Death	0	1* (0.5%)	0.49

* = non cardiac death (ischaemic stroke confirmed by autopsy)

CACTUS Trial

Coronary Bifurcation Application of the Crush Technique Using Sirolimus-Eluting stents

Stent thrombosis

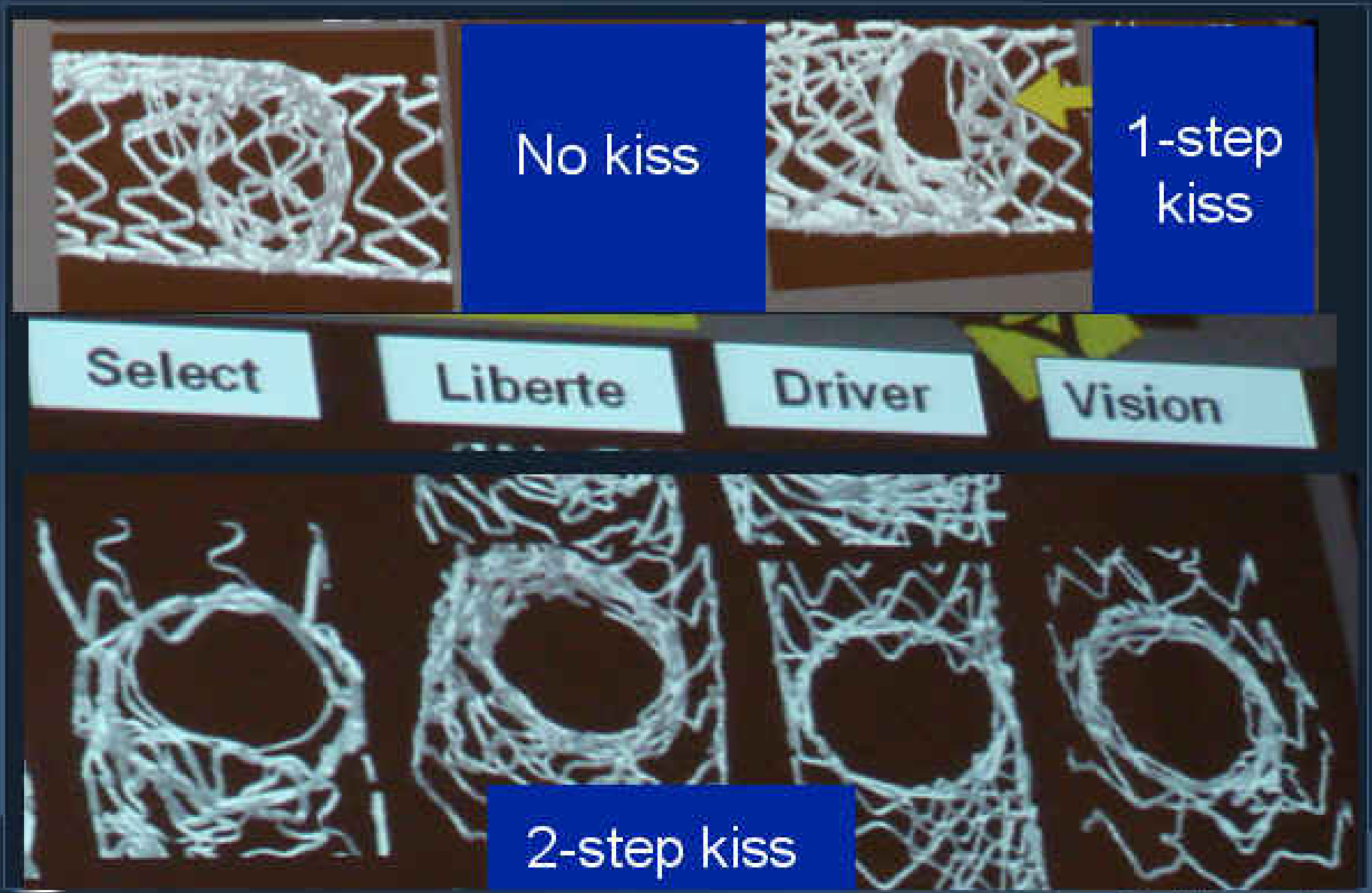
	Total	Acute (first day)	Subacute (days 2-30)	Late (days 31-180)
Crush (n=177)	3 (1.7%)	1 (0.5%)	2* (1.1%)	0
Prov. T (n=173)	2 (1.1%)	0	1 (0.5%)	1 (0.5%) (definite)

P=0.62 for comparisons between crush and prov. T

* One patient did not take thienopyridine therapy after discharge

Colombo A, EuroPCR 2008

"Ormography"- Importance of 2-step kissing



Coronary Bifurcations

Important Observations

- Dedicated bifurcation stent designs have been proposed to manage the highly variable anatomy of coronary bifurcation lesions
- Early FIM and feasibility studies with prototype devices have raised concerns that new dedicated bifurcation devices are not user-friendly and have technical limitations
- *Nevertheless, iterative design enhancements, DES versions, and ⬆operator experience have combined to improve outcomes, offering hope for the future!*

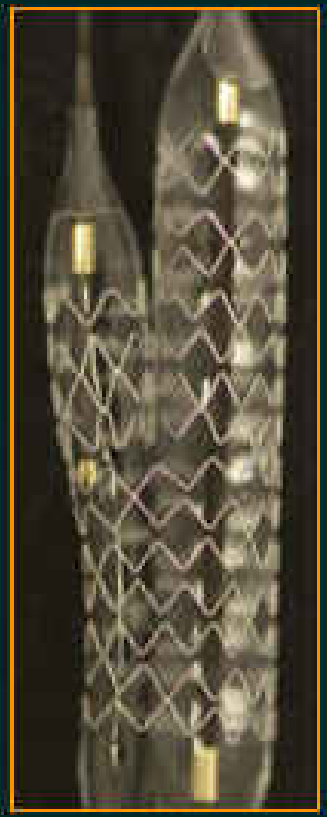
Dedicated Bifurcation Stents

General Categories

- Complete bifurcation "Y" stents
- Sidebranch access MB stents
- Sidebranch only stents
- Specialty designs (e.g. carina or for LM disease)

Medtronic Bifurcation Stent

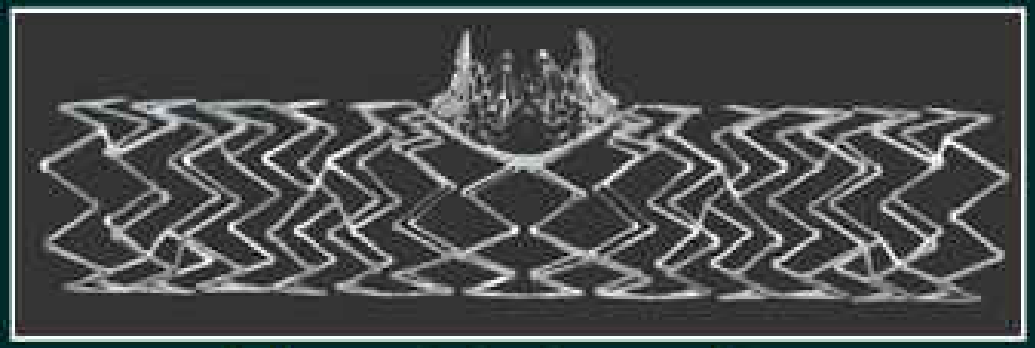
Anatomically designed for treatment of "true" bifurcation lesions



- ***Dual-branch stent***
  - accommodates bifurcation angles from 0 to 70 degrees in 1st generation
- ***Dual balloon, simultaneous inflation***
- ***Side branch – tapered balloon design***
  - matches desired proximal vessel diameter
  - limits vessel trauma – lowers risk of over-expanding proximal vessel
- ***Ostial marker band***
  - can clearly see when device is properly placed

BSC TAXUS Petal

Design Characteristics



Element stent geometry

Stent Advantages

- Special stent feature to cover ostium of sidebranch (~2mm)
- Reduces sidebranch "gap" and need for 2nd stent
- Placing 2nd stent, when necessary, is technically simplified

Delivery System Advantages

- Side Branch wire lumen aids in alignment at ostium
- Side branch "pre-wired", no need to re-access through stent
- Final Petal size determined by post dilatation balloon

TriReme Bifurcation Stent

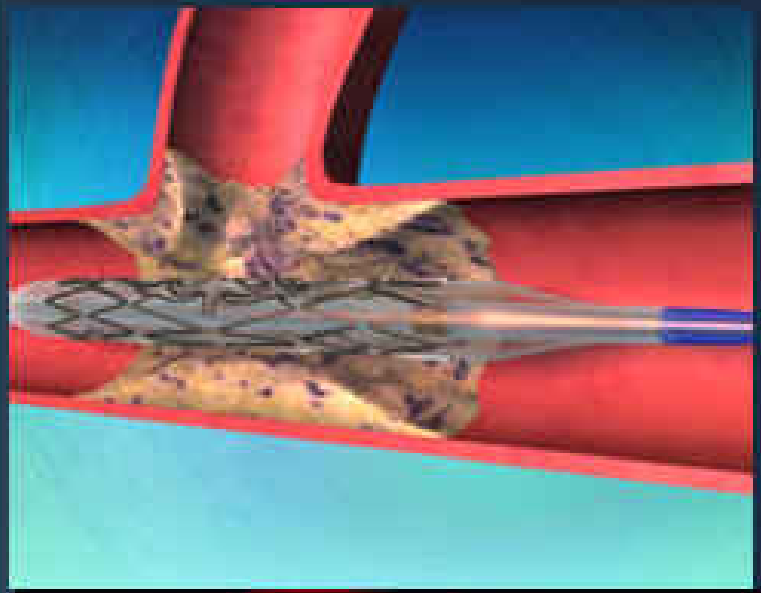
Design Characteristics

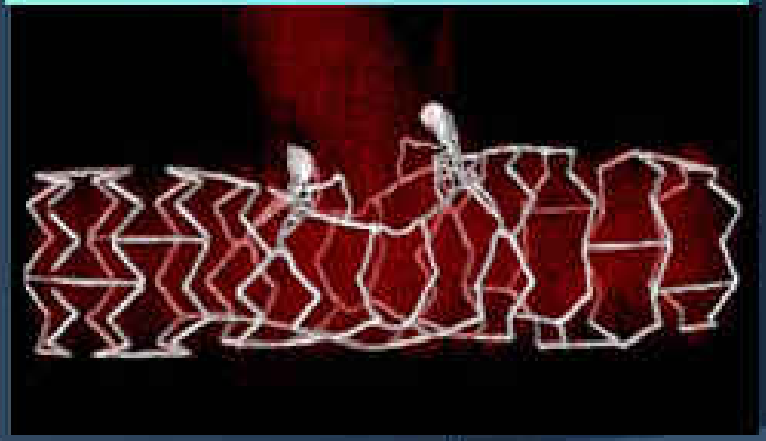
Stent Design

- Central "custom" cell with crowns extending into sidebranch ostium upon balloon expansion (ostial coverage and support)
- Low profile (6 Fr guide compatible)

Delivery System

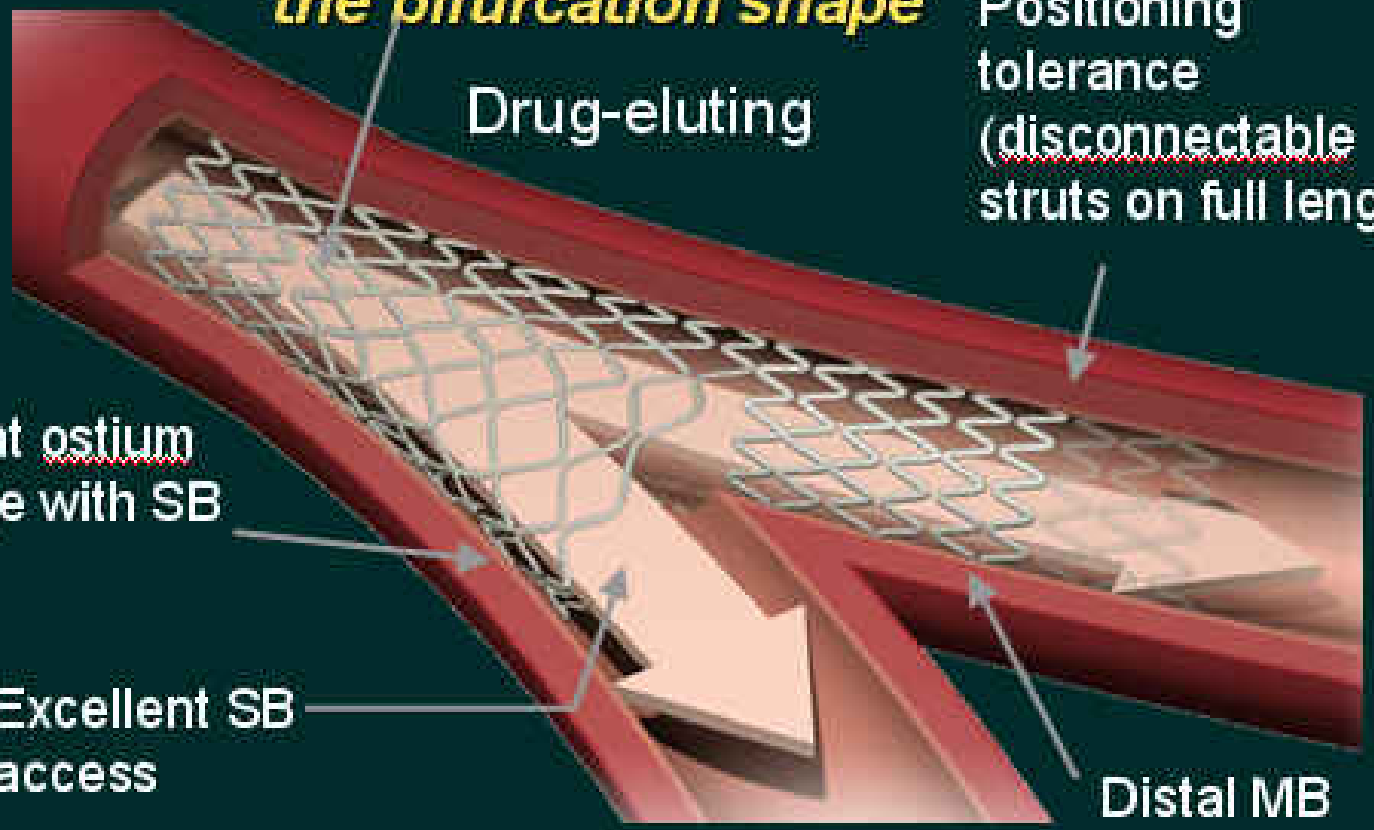
- Rx main branch wire
- Custom "nested" side branch wire advanced thru central cell when proximal to side branch
- Crown markers to assist with axial and rotational alignment





StentYs Bifurcation Stent

Design Characteristics



Single wire 5F delivery system

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FIM Completed

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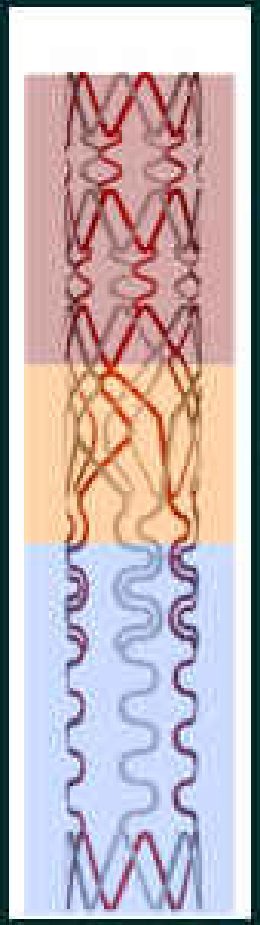
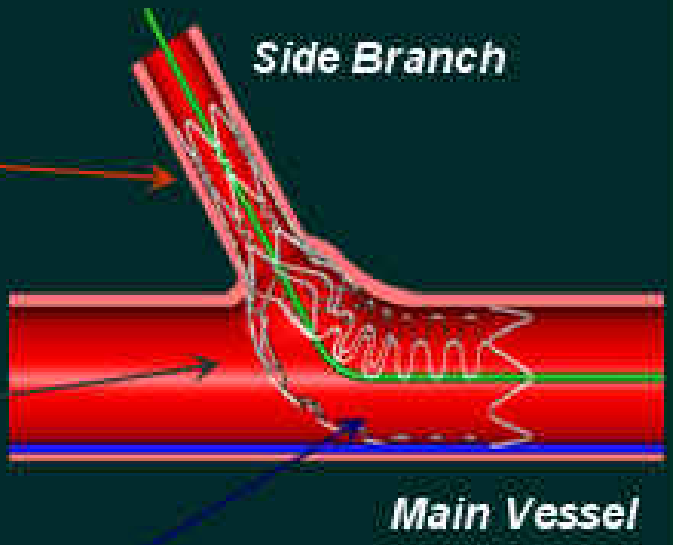
Tryton Side-Branch Stent

Side Branch Region
Standard Design

Transition Zone
Coverage
Hoop Strength

Main Vessel Region
3 Fronds - Minimal Coverage
Wedding Band





Cobalt Chromium
Strut Thickness: 0.003"
Diameter: 2.5 mm

Cappella Sideguard

Ostium Protection Device

Self-Expanding, Balloon-Actuated, Anatomically-Shaped Coronary Side Branch Stent

Balloon-Actuated Catheter System (3.1 Fr)

Self-Expanding Nitinol SB Stent

Anatomically-Shaped Design

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Devax AXXESS PLUS

Carina Expansion for Bifurcations

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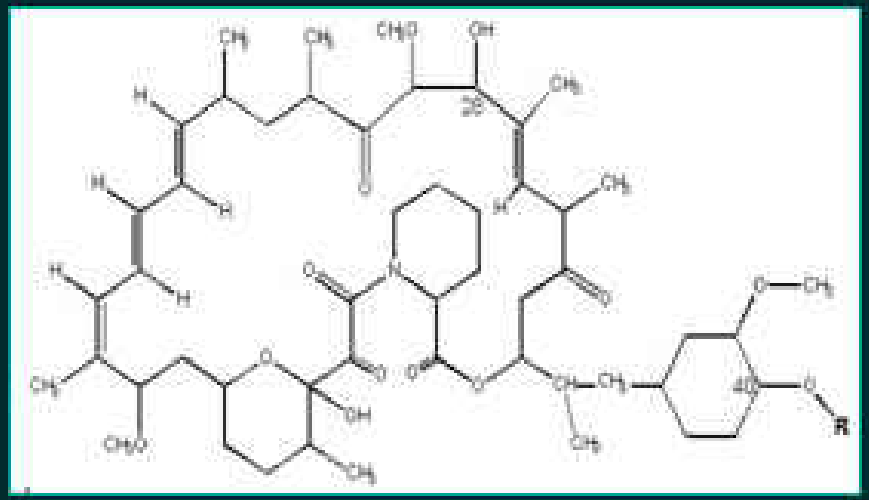

AXXESS
Stent

PLUS

Biolimus-A9
Anti-proliferative &
Bioerodable Polymer

DIVERGE: Drug Stent Intervention for Treating Side Branches Effectively

Prospective, Single-arm, Multicenter Registry

Patients with de novo bifurcated lesions in native coronary arteries N=300

PCI using Axxess™ stent System

Angio F/U at 9 mo in 300 pts
Annual clinical F/U for 5 years

PRIMARY Endpoint: 9-mo MACE: death, MI, iTLR
SECONDARY Endpoints: device success, binary restenosis, late loss

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DIVERGE - Clinical Results

Cumulative 9 Month MACE	
N completing follow up (%)	99.3% (300)
All-cause MACE	7.7%
Any death	0.7%
Q wave MI	1.0%
Non-Q wave MI	3.3%
Ischemia-driven TLR - ALL BIFURCATION	4.3%
Exclusively side branch driven	1.3%

DIVERGE - 9 Mo QCA Results

At Follow Up		MV (N=140)	SB (N=140)
Late Loss (mm)	In-stent LL (Axxess only)	0.18	-
	In-stent LL (all stents)	0.29	0.29
	In-lesion LL	0.20	0.17
Restenosis *Per Vessel*	In-stent - Axxess Only	0.7%	–
	In-stent - Cypher	2.3%	4.8%
	In-lesion restenosis (all stents + edges)	3.6%	4.3%
Overall Bifurcation Restenosis	In-stent - *PV + SB*	5.0% (7/140)	
	In-stent or edges, within *PV + SB*	6.4% (9/140)	

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Coronary Bifurcations

Final Thoughts

- Provisional bifurcation SB stenting is the consensus strategy for most cases – technique issues critical
- Two stent approaches required in ~ 20-30% of cases; e.g. diffuse SB disease, ostial "failure"; indications and technique for 2 stents remain controversial (recent trends = TAP, mini-crush, culotte)
- Bifurcation disease is markedly variable and a "family" of dedicated bifurcation stents may be required to manage all lesions; design preference and DES integration/need (esp. SB stents) still requires further clarification and clinical trial validation

THIRD ANNUAL

LEFT MAIN AND BIFURCATION SUMMIT

June 4-5, 2009

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New York, NY

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