



**20th Angioplasty Summit
TCTAP 2015
Boston Scientific Symposium**



SYNERGY[®] : A Novel Solution Designed to Heal

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National University of Singapore

President, Asia Pacific Society of Interventional Cardiology



National University Heart Centre, Singapore (NUHCS)



Boston Scientific Coronary Stents Pipeline

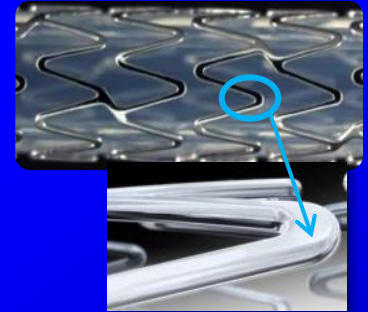
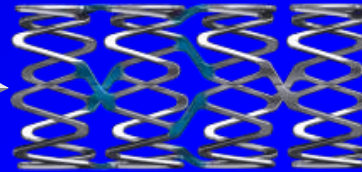
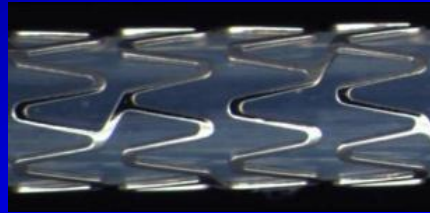
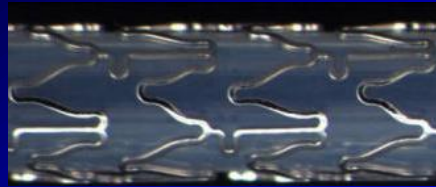
Everolimus

PROMUS™
CoCr Stent

PROMUS Element™
PtCr Stent

Promus PREMIER™
PtCr Stent

SYNERGY™ I&II
Bioabsorbable Polymer
PtCr Stent



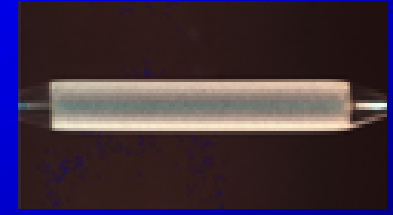
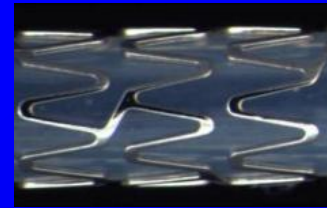
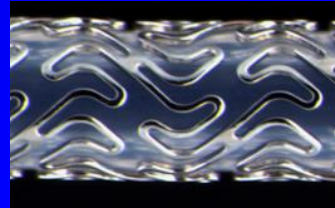
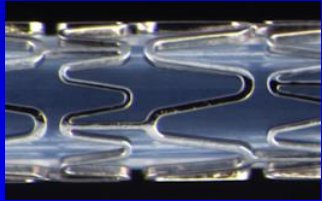
Paclitaxel

TAXUS Express™ Stent

TAXUS Liberte™ Stent

ION™/ TAXUS Element™ Stent

Drug-Eluting Balloon

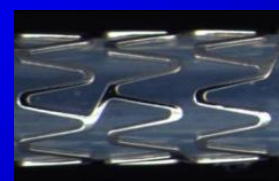
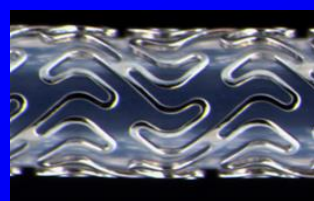
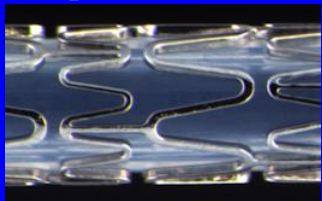


Bare Metal Stents

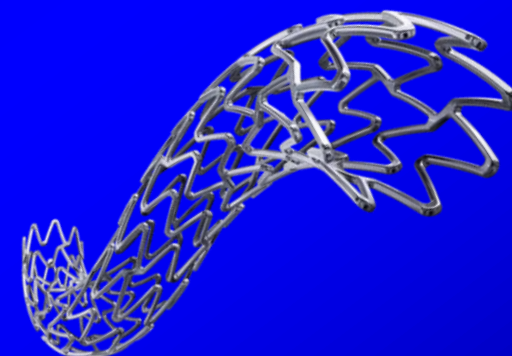
Express™ Stent

Veriflex™ / Liberte™ Stent

OMEGA™ Stent



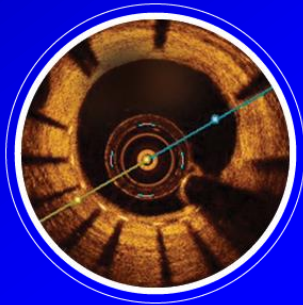
SYNERGY™ Stent: Introduced to Singapore on Christmas Day 2012



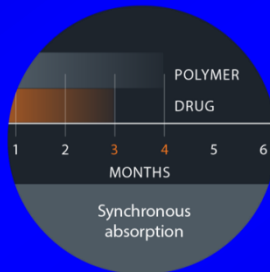
SYNERGY™ Stent System: Healing With Confidence



Designed to Heal



Early Healing

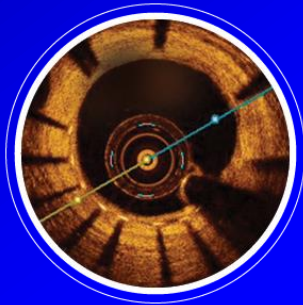


Freedom from Long-term Polymer Exposure

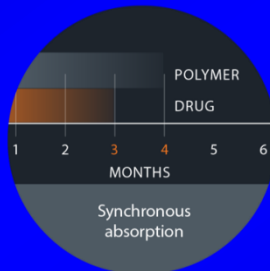
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Designed to Heal



Early Healing

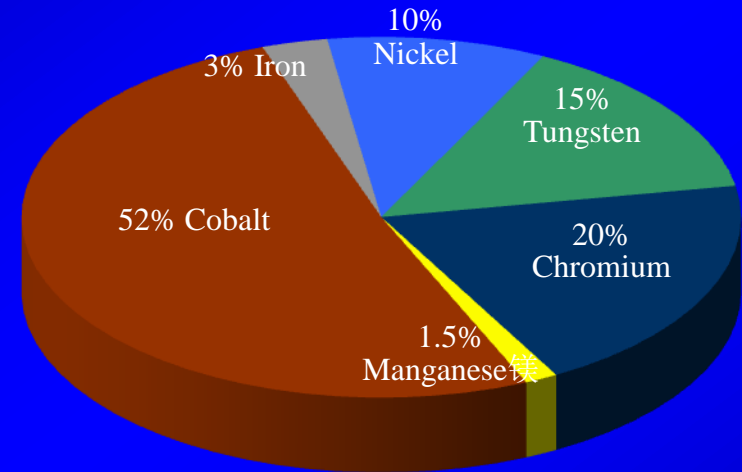
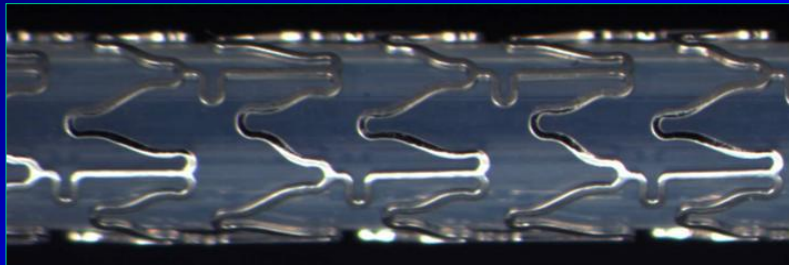


Freedom from Long-term Polymer Exposure

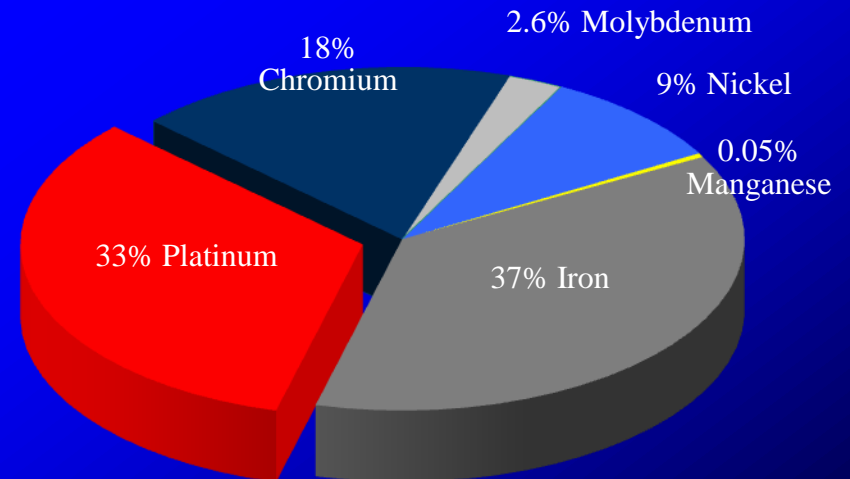
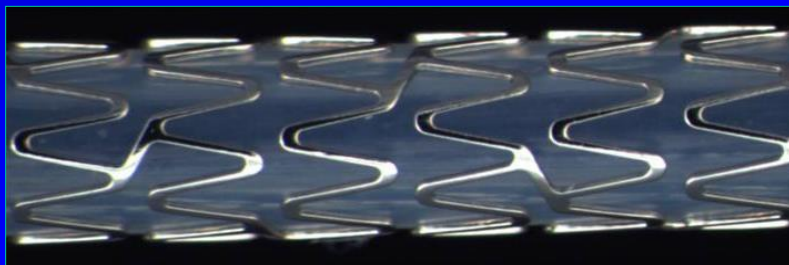
Comparison of Cobalt-Chromium and Platinum-Chromium Stents

Everolimus concentration: 100 ug/cm²
 Polymer: PBMA & PVDF-HFP (7µm thickness)

XIENCE V / PROMUS (CoCr-EES)



PROMUS Element (PtCr-EES)



SYNERGY™ Stent Has Thin Struts and Little Polymer

Durable Polymer Coated Stents	Bioabsorbable Polymer Coated Stents	Bioabsorbable Stent
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Xience V™ Stent
 Xience Prime™1 Stent
 Xience Xpedition™ Stent
 PROMUS Element™1 Stent

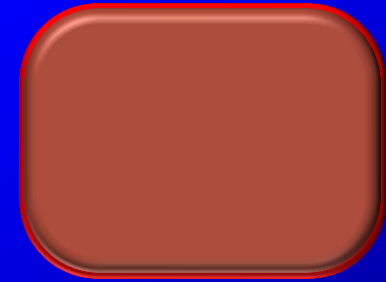
Resolute Integrity™2 Stent

BioMatrix Flex™3 Stent

Nobori™4 Stent

SYNERGY¹ II Stent

ABSORB™ BVS⁵



Strut Thickness

81 μm
(0.0032")

89 μm
(0.0035")

120 μm
(0.0047")

125 μm
(0.0049")

74 μm*
(0.0029")

150 μm
(0.0059")

Polymer

Coating Type & Thickness

Conformable
7-8μm / side

Conformable
6μm / side

Abluminal
11μm

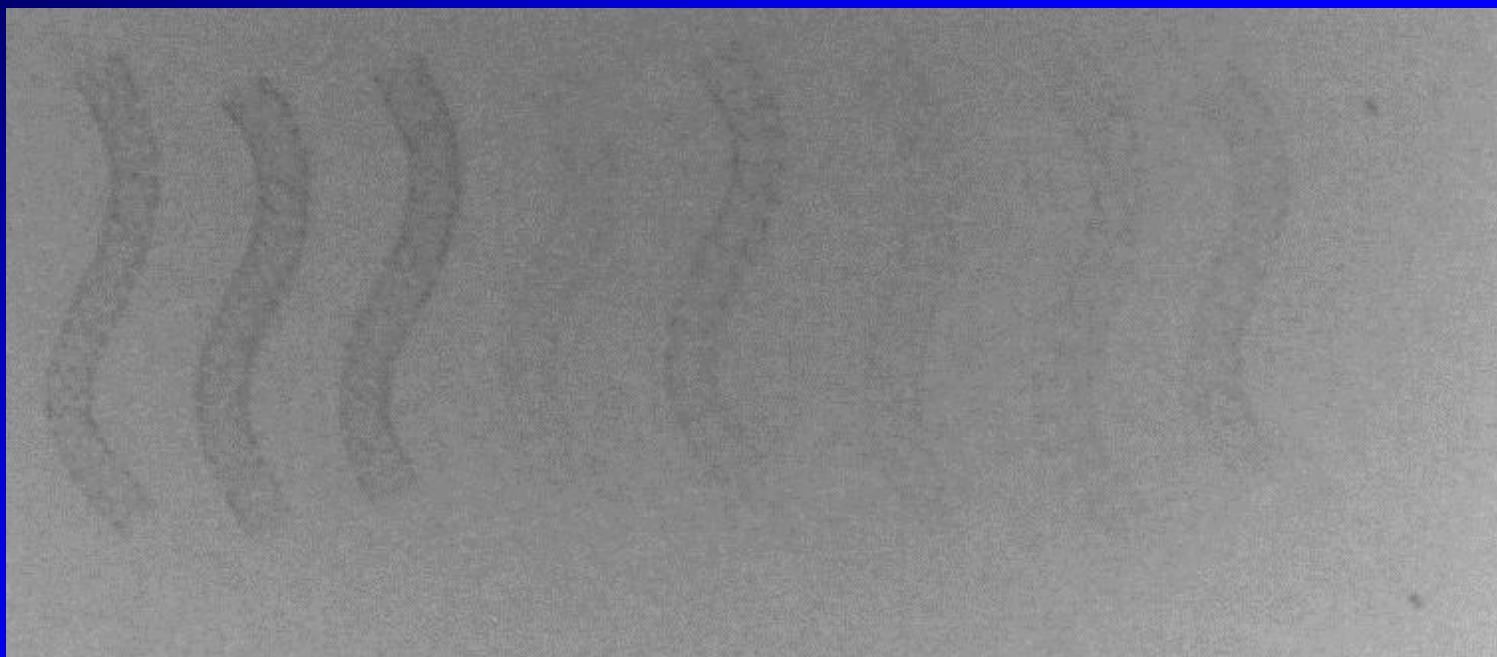
Abluminal
20μm

Abluminal
3-4μm

Conformable
3μm / side

SYNERGY™ II Stent

*Even with Thin Struts the High Density of Platinum Chromium Allows for Greater Visibility**



	SYNERGY II Stent	Promus PREMIER™ Stent	PROMUS Element™ Stent	Resolute Integrity™ Stent	XIENCE™ Xpedition Stent	BioMatrix™ Stent	Nobori™ Stent	Orsiro™ Stent	ABSORB™ BVS Stent
Alloy	PtCr	PtCr	PtCr	CoNi	CoCr	Stainless Steel	Stainless Steel	CoCr	PLLA Polymer
Strut Thickness	74 μm*	81 μm	81 μm	89 μm	81 μm	120 μm	120 μm	60 μm	150 μm

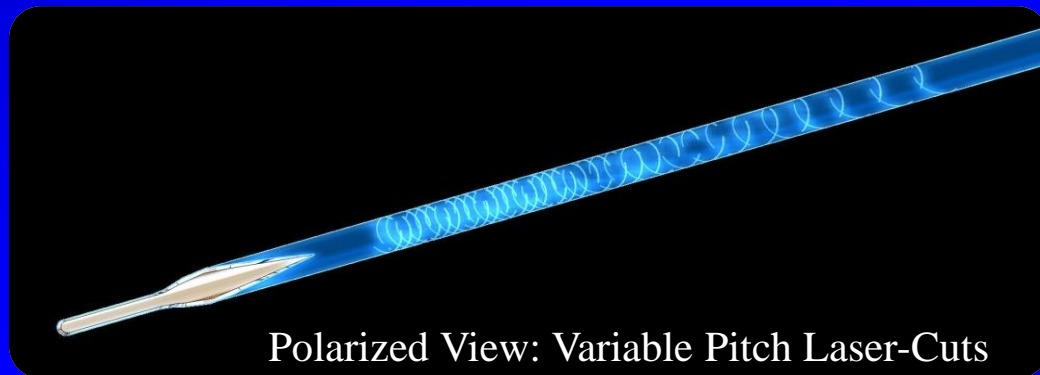
Based on 2.5mm stents. Under 6.0mm copper phantom to simulate body mass

***Strut thickness for small vessel model is 74μm, Workhorse model is 79μm and large vessel is 81μm.**

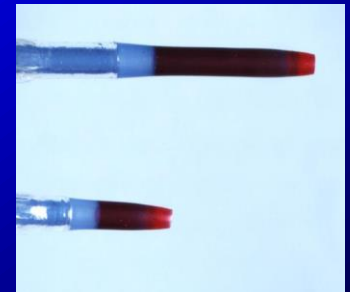
SYNERGY™ II Stent System

Delivery System Overview

- Hypotube extends into midshaft to exit port to improve pushability
 - 10% longer than existing BSC monorail hypotube designs
- Additional length laser cut to maintain midshaft flexibility
 - Variable pitch intermittent laser cuts (~360 cuts over 100mm length)
- Low profile
- Shorter, more flexible tip



SYNERGY Catheter Tip

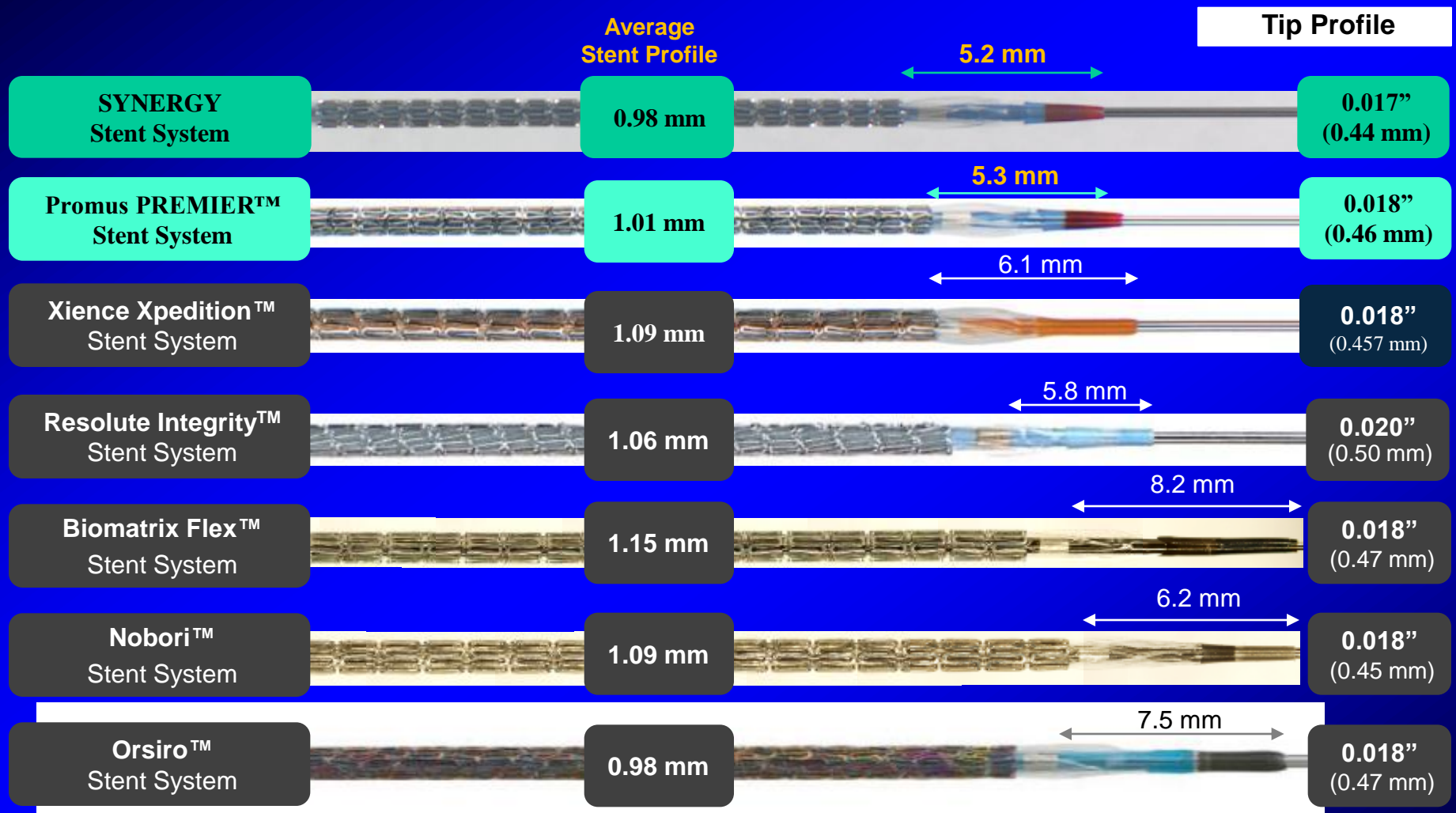


SYNERGY II Catheter Tip

Boston Scientific Data on File

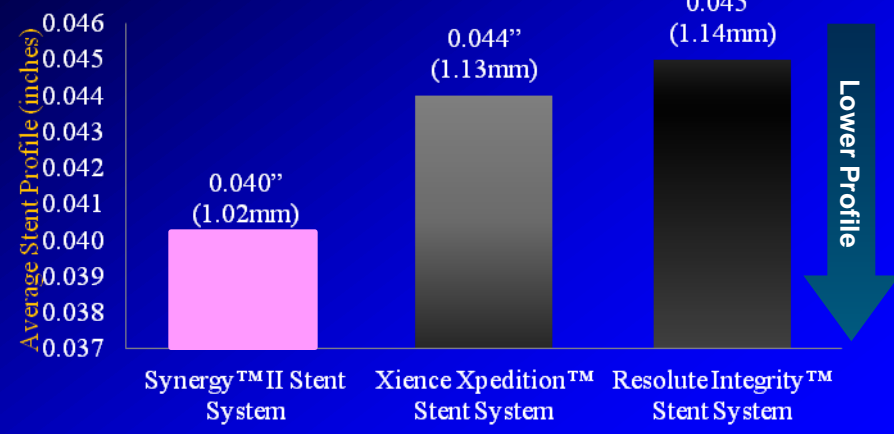
SYNERGY™ Stent System

Low Stent, Tip Profile and Short Tip

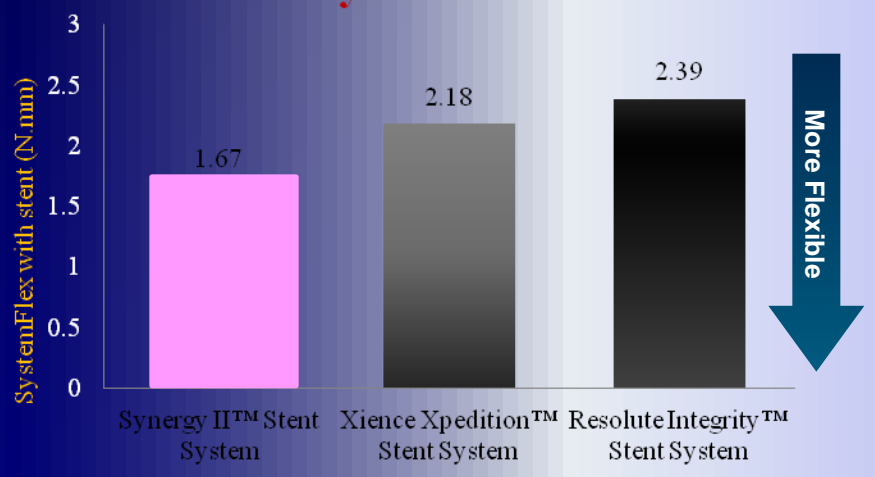


SYNERGY™ II Stent System : Superior Deliverability

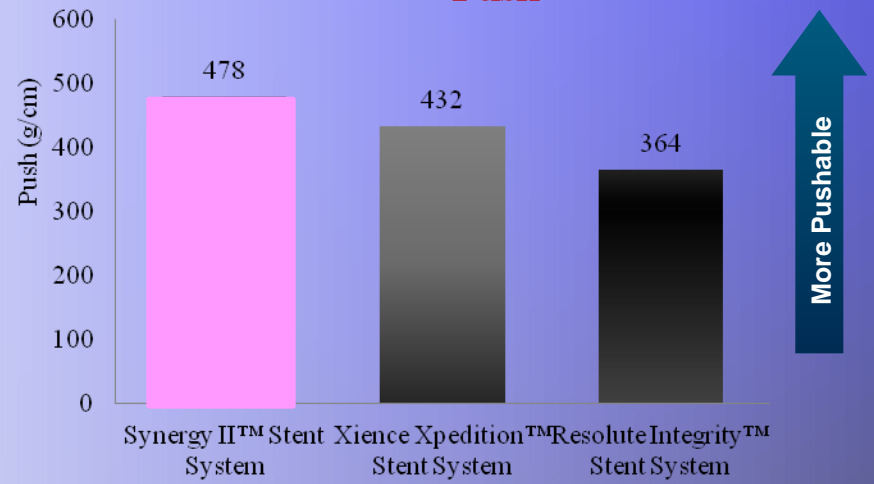
Average Stent Profile



System Flex

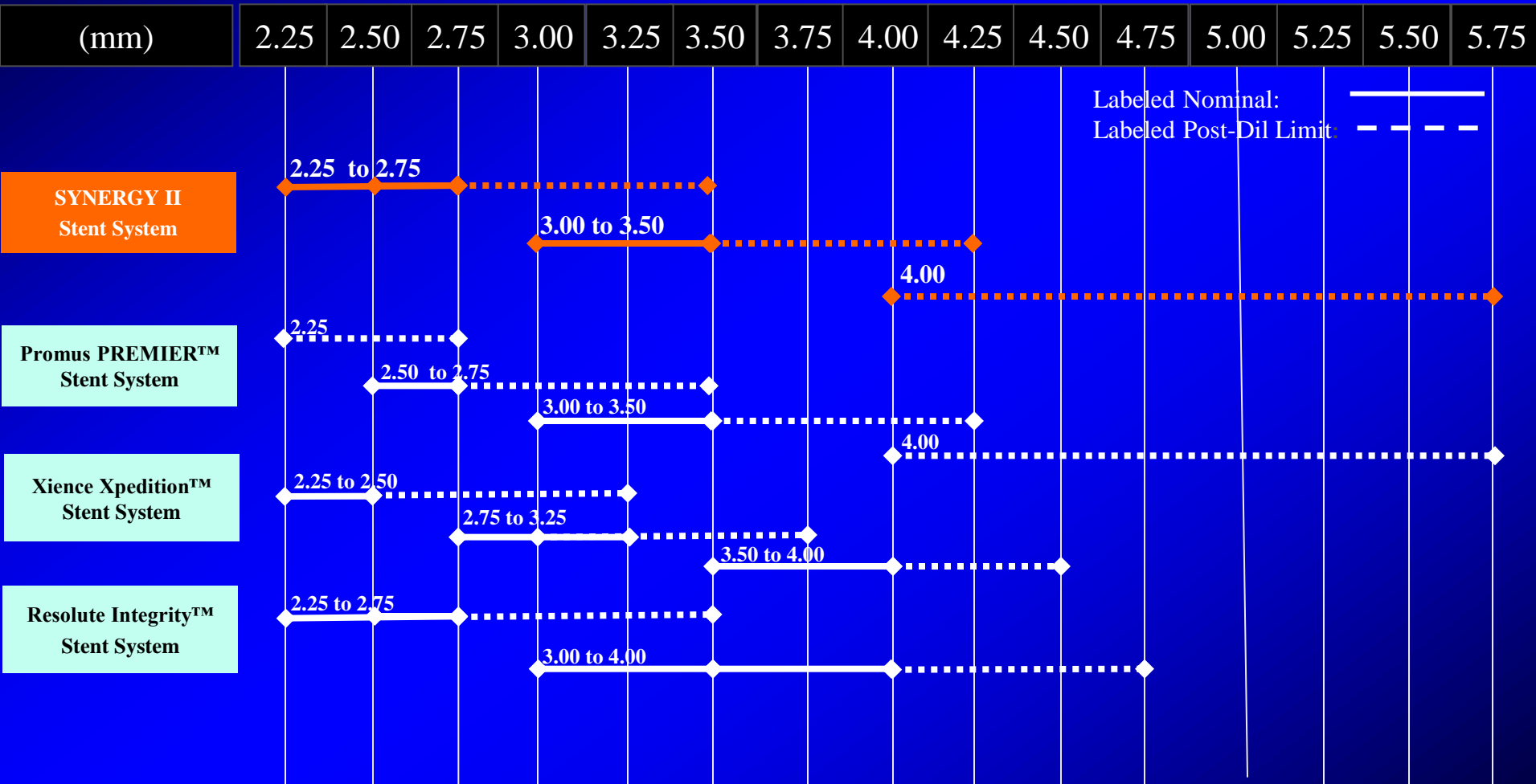


Push

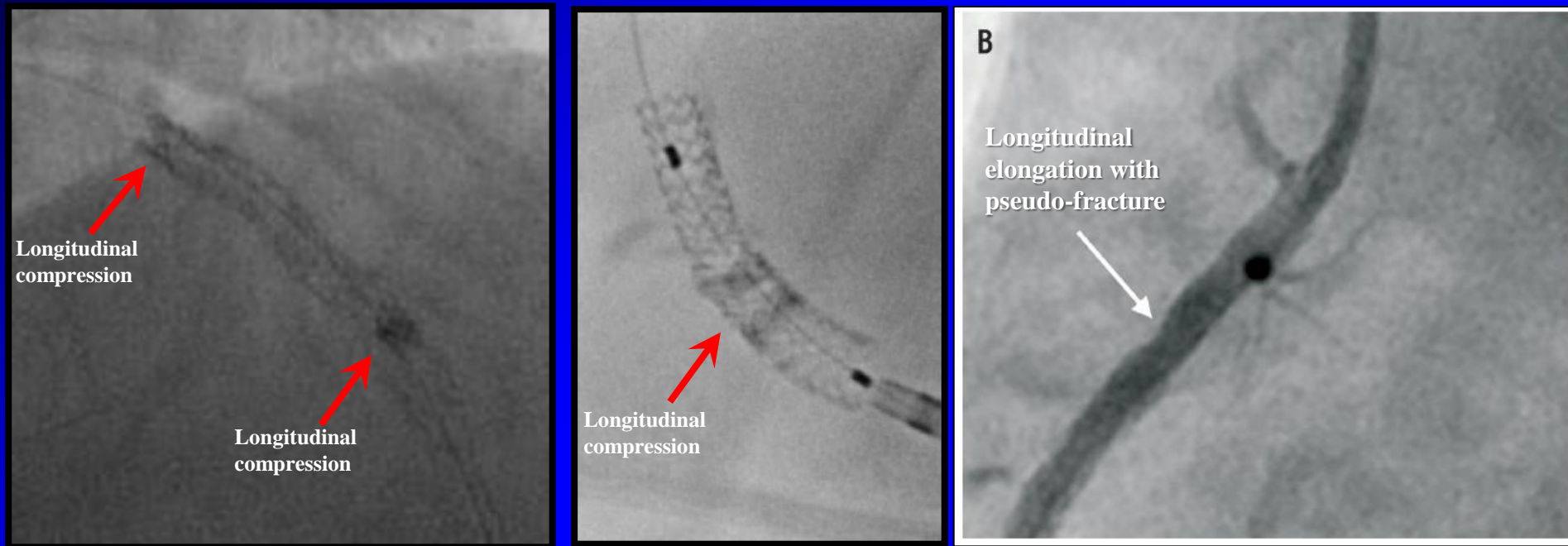


SYNERGY™ II Stent System

Labeled Post-Dilatation Limits*



Longitudinal Stent Deformation: Angiographic Patterns

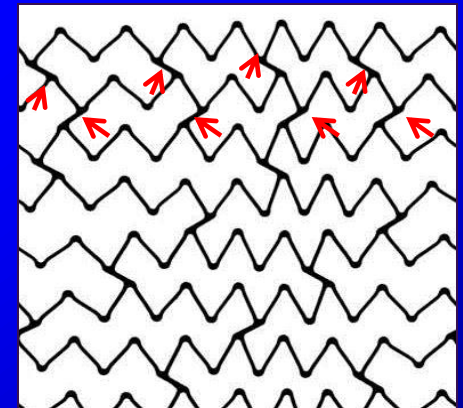
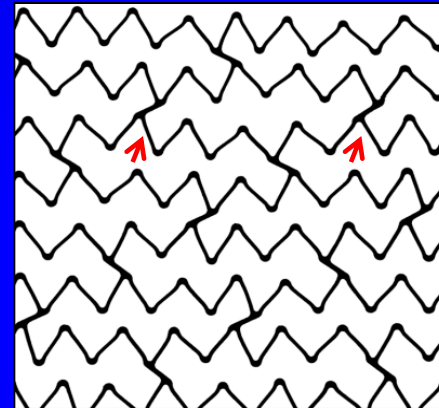
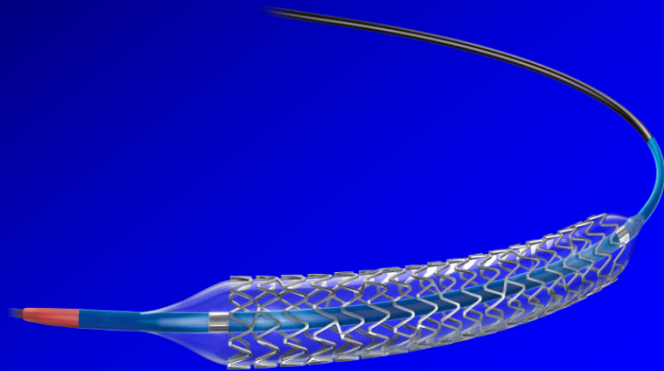


- Longitudinal stent compression: Manifests itself as a dark band in the region of compression (also called stent “accordion”, “concertina”, “wrinkling”, etc.)
- Longitudinal stent elongation: Appears like a fracture in the stent (pseudo-fracture)

SYNERGY™ Stent

- Utilises the same platinum chromium alloy, stent geometry, drug and polymer as the PROMUS Element Stent

- Increased resistance to longitudinal compression: Connectors added to the 2 most proximal stent segments of the small workhorse (2.50-2.75mm), workhorse (3.0-3.5 mm) and large vessel (4.0 mm) stent

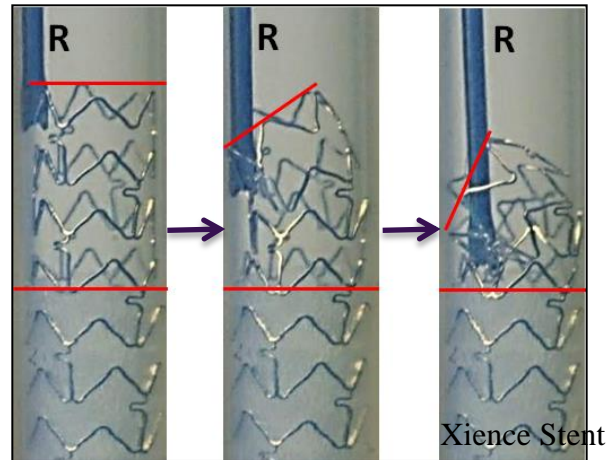


- Delivery system includes a shorter catheter tip to improve tip flexibility, PTFE hypotube coating to reduce friction and a red tip to improve visibility when loading the SDS on a guidewire

Element/OMEGA/ION design	SYNERGY design
The 2.5, 2.75, 3.0, 3.5 and 4.0 mm stents have 2 connectors between segments at the proximal end	The 2.5, 2.75, 3.0 and 3.5 mm stents have 4 connectors between segments at the proximal end; the 4.0 mm stent has 5 connectors

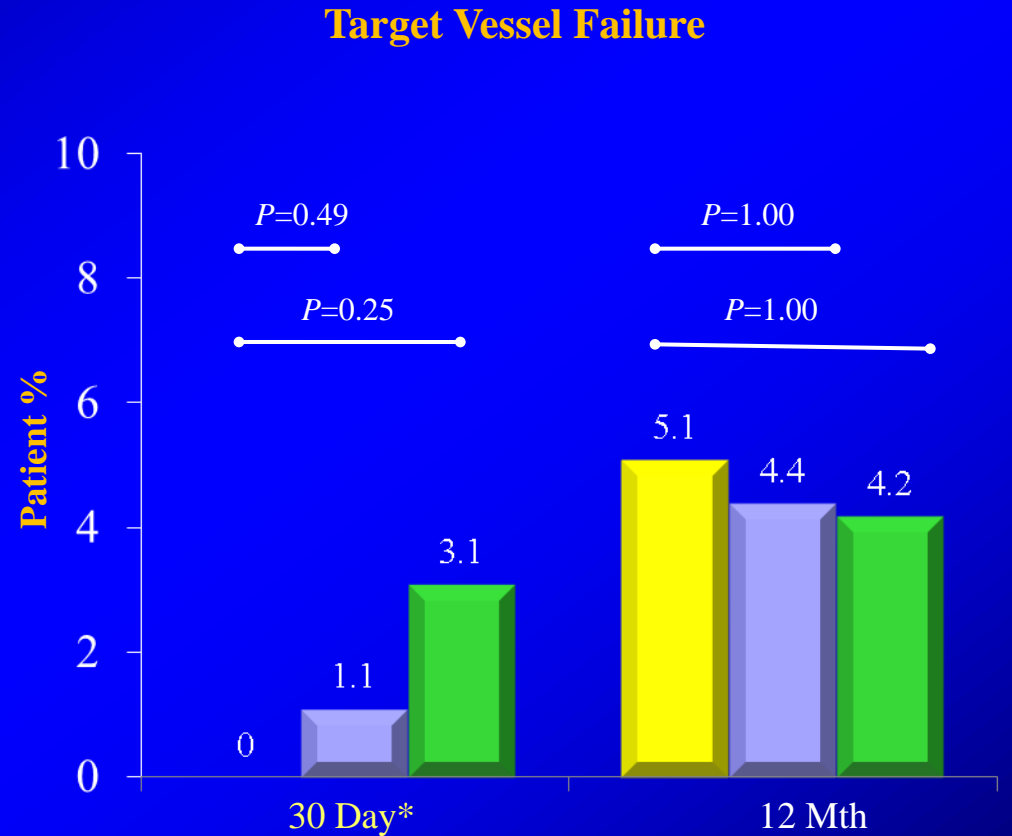
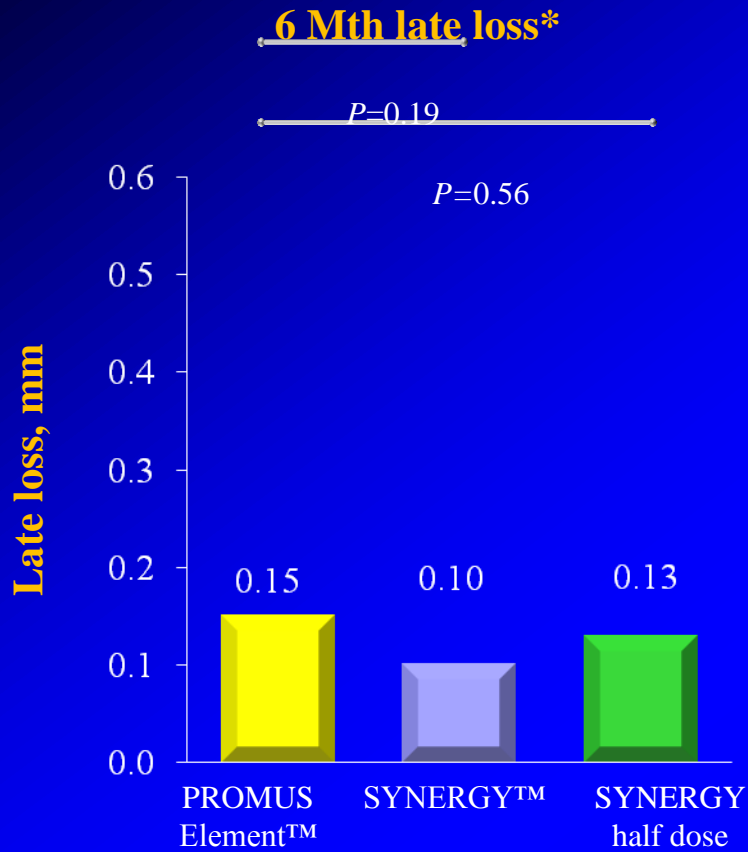
SYNERGY™ Resistance to Compression Similar to Resolute™ and Xience™

Tested in a second generation bench test designed to mimic clinical longitudinal stent distortion (point compression with 0.5N force)



Stent is fixed distally (below red line) and malapposed proximally → Instron applies 0.5N force via a rod → Stent is compressed on side of force and displaced → Instron measures force and distance compressed

EVOLVE Trial Primary Endpoint*



■ PROMUS Element™ (n=98)
 ■ SYNERGY™ (n=94)
 ■ SYNERGY™ ½ Dose (n=99)

No instances of stent thrombosis in any group through 12 month follow up

Meredith et al J Am Coll Cardiol 2012; 59:1362

EVOLVE II Study Design

(SYNERGY Stent Pivotal Trial - RCT Enrollment Complete)

**1,954-2,006 patients with
atherosclerotic native coronary lesions**
≤ 34 mm in length, RVD ≥ 2.25 mm ≤ 4.0, %DS ≥ 50
Up to 3 lesions in 2 vessels
(excludes LM disease, CTO, ISR, STEMI)

Randomized Cohort (RCT)

Up to 160 global sites

PROMUS Element
N=842

SYNERGY
N=842

PK Substudy

SYNERGY
N=20-30

Diabetes Substudy

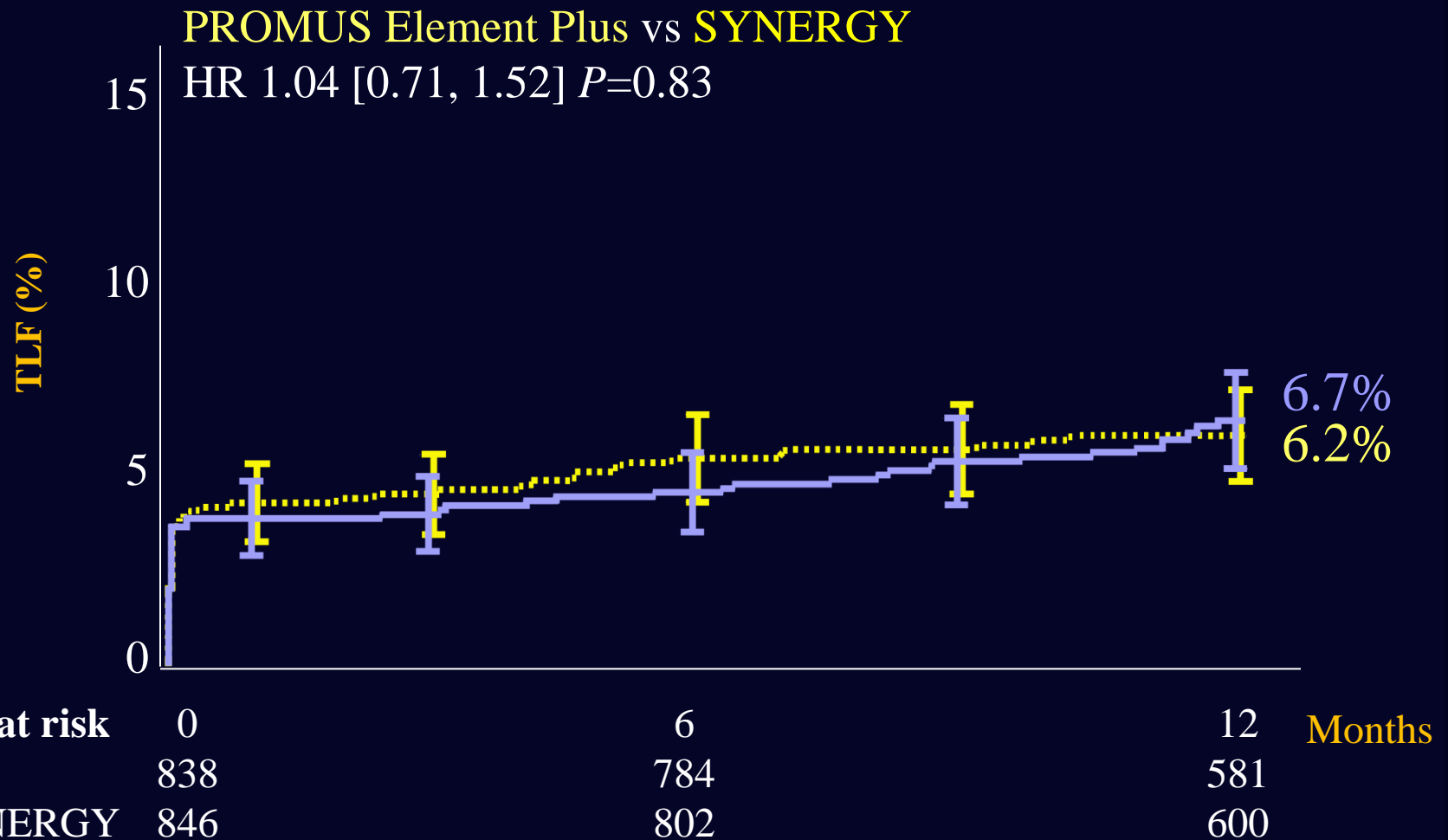
SYNERGY
N=250-292

RCT Design

Multicenter noninferiority trial
Single-blind, 1:1 randomization

Primary Endpoint: TLF (CD, TV-MI, or TLR) at 12 mo
Follow-up: 30d, 6m, 12m, 18m and annual 2-5 yrs

EVOLVE II Primary Endpoint: 12-Month Target Lesion Failure (Intention-To-Treat)



Kereiakes D et al AHA 2014

SYNERGY™ : BSC Clinical Trials



EVOLVE

First Human Use Trial. 291 patients. PROMUS Element vs. SYNERGY vs. SYNERGY Half-Dose (1:1:1). Primary Endpoint: 6 month Late Loss + Composite Safety @ 30 days



EVOLVE II

Global IDE Trial. 1684 patients, 150 sites, 19 countries . PROMUS Element Plus vs. SYNERGY (1:1) single-blind trial. Primary Endpoint: 12 month TLF

Enrollment Complete

EVOLVE II QCA

Quantitative Angiography. 100 Patient Registry, 10-15 sites (Australia, Japan, New Zealand, Singapore). Primary Endpoint: 9 month in-stent Late Loss

Enrolling

EVOLVE China

China regulatory approval trial (SFDA). 400 patients, up to 15 sites. PROMUS Element Plus vs. SYNERGY (1:1) Primary Endpoint: 9 month Late Loss

EVOLVE DAPT

3/12 DAPT.
Prospective, Multi-center, Global, 4000 patients. Primary Endpoint: Cardiac Death/ MI

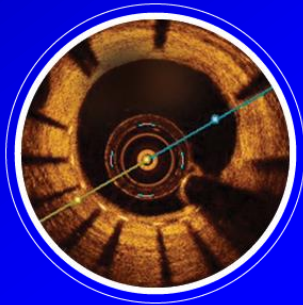
HORIZONS II

AMI Indication. 7000-1000 patients with STEMI, SYNERGY vs. Promus Element vs. Resolute Integrity vs. Omega BMS. Primary Endpoint: 1 year TLF

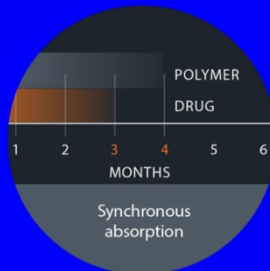
SYNERGY™ Stent System: Healing With Confidence



Designed to Heal



Early Healing

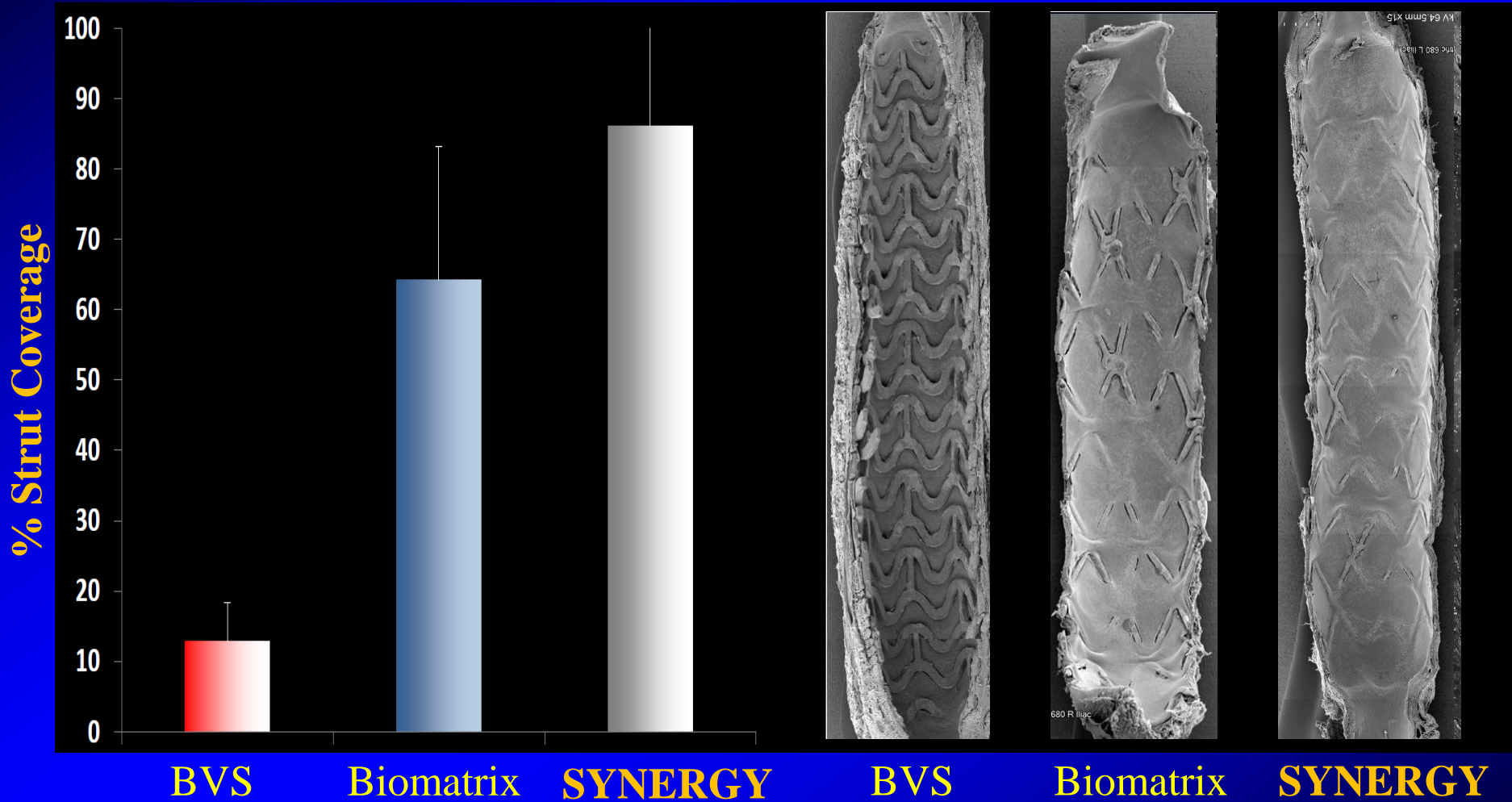


Freedom from Long-term Polymer Exposure

Thick vs Thin Strut DES

Healing and Endothelialization in SYNERGY, Biomatrix, and ABSORB BVS

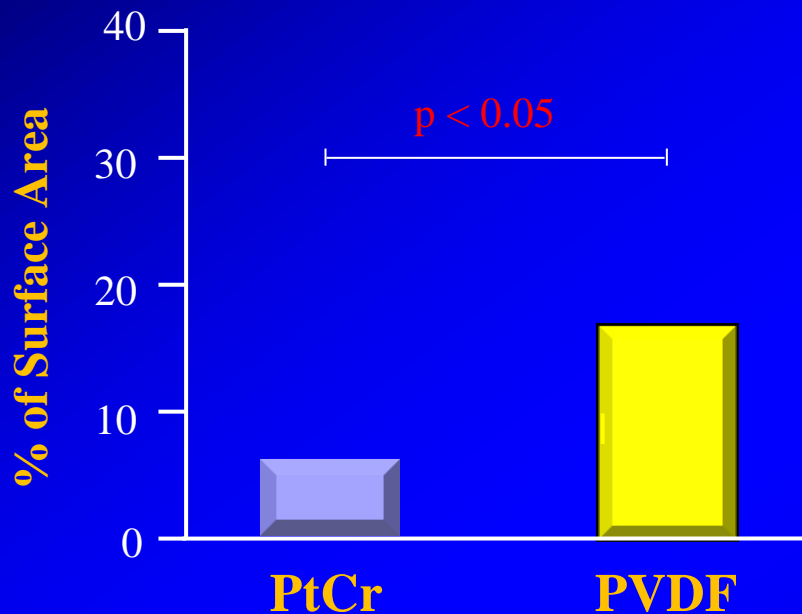
Endothelialization in Rabbit at 28 Days



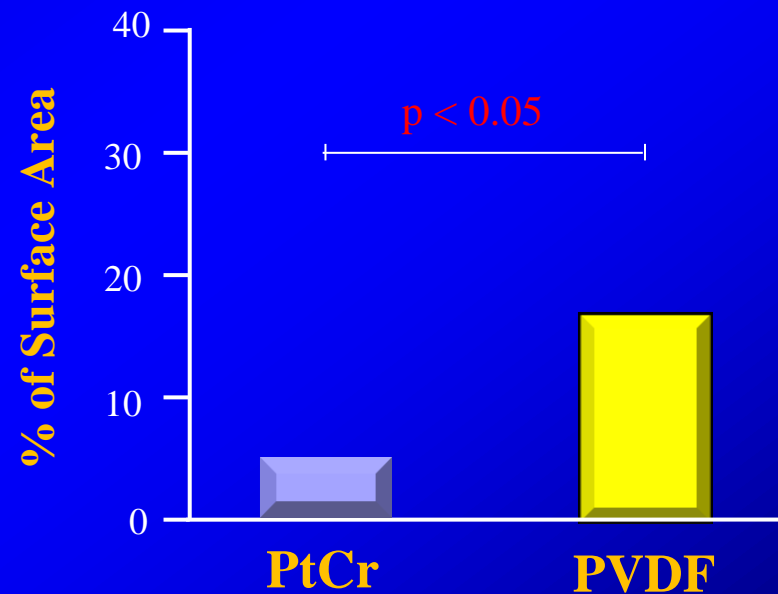
Renu Virmani, at TCTAP 2014

Improved Thromboresistance with Bare PtCr vs “Best in Class” Durable PVDF Polymer

Platelet Adhesion



Platelet Activation



PVDF-HFP exhibits higher degrees of platelet activation-adhesion and thrombus accumulation in vivo compared with PtCr

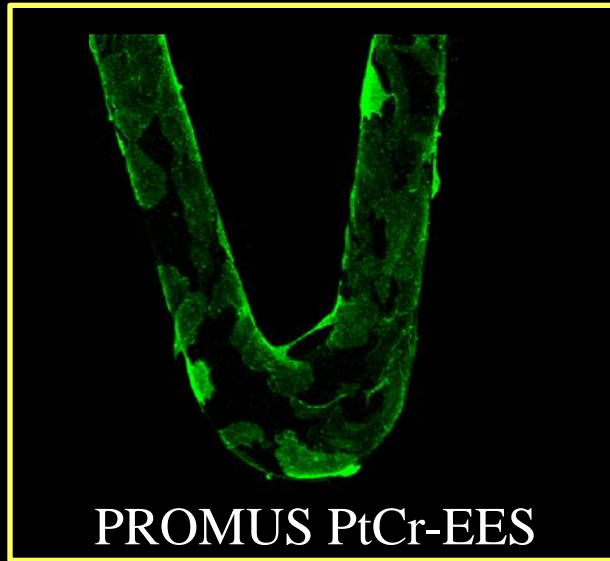
PVDF-HFP: Polyvinylidene fluoride-co-hexafluoropropene

Eppihimer et al *Circ Cardiovasc Interv.* 2013; 6: 370-377

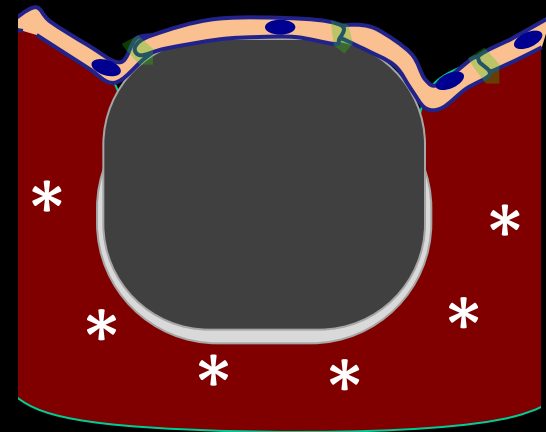
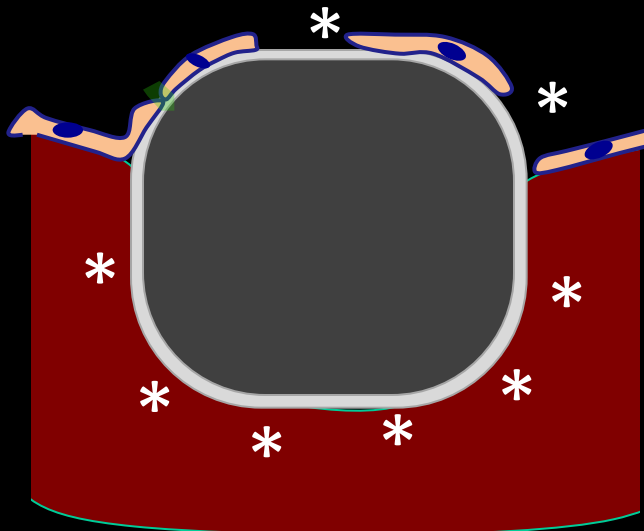
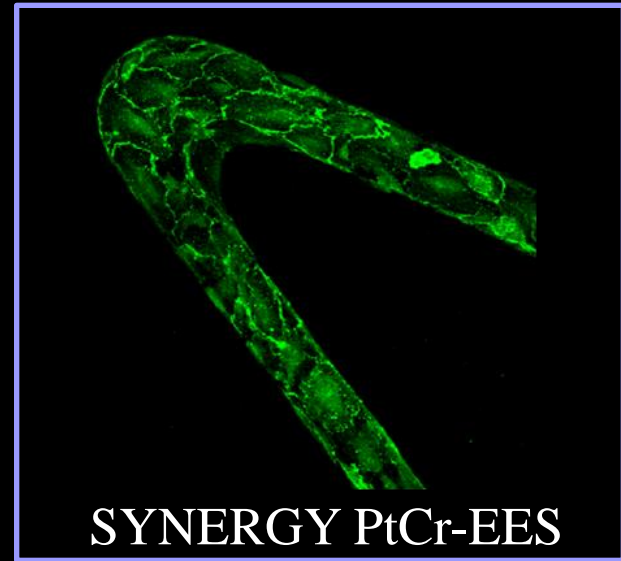


Abluminal vs Conformal Polymer

Abluminal coating improves EC barrier formation compared to conformal coating



● Greater localization of VE-cadherin at cell junctions
↓
Improved EC function



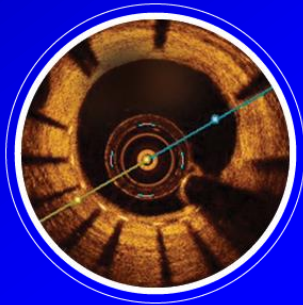
From data presented by Mike Eppihimer, PhD at EuroPCR 2013



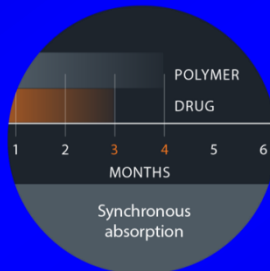
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Designed to Heal



Early Healing



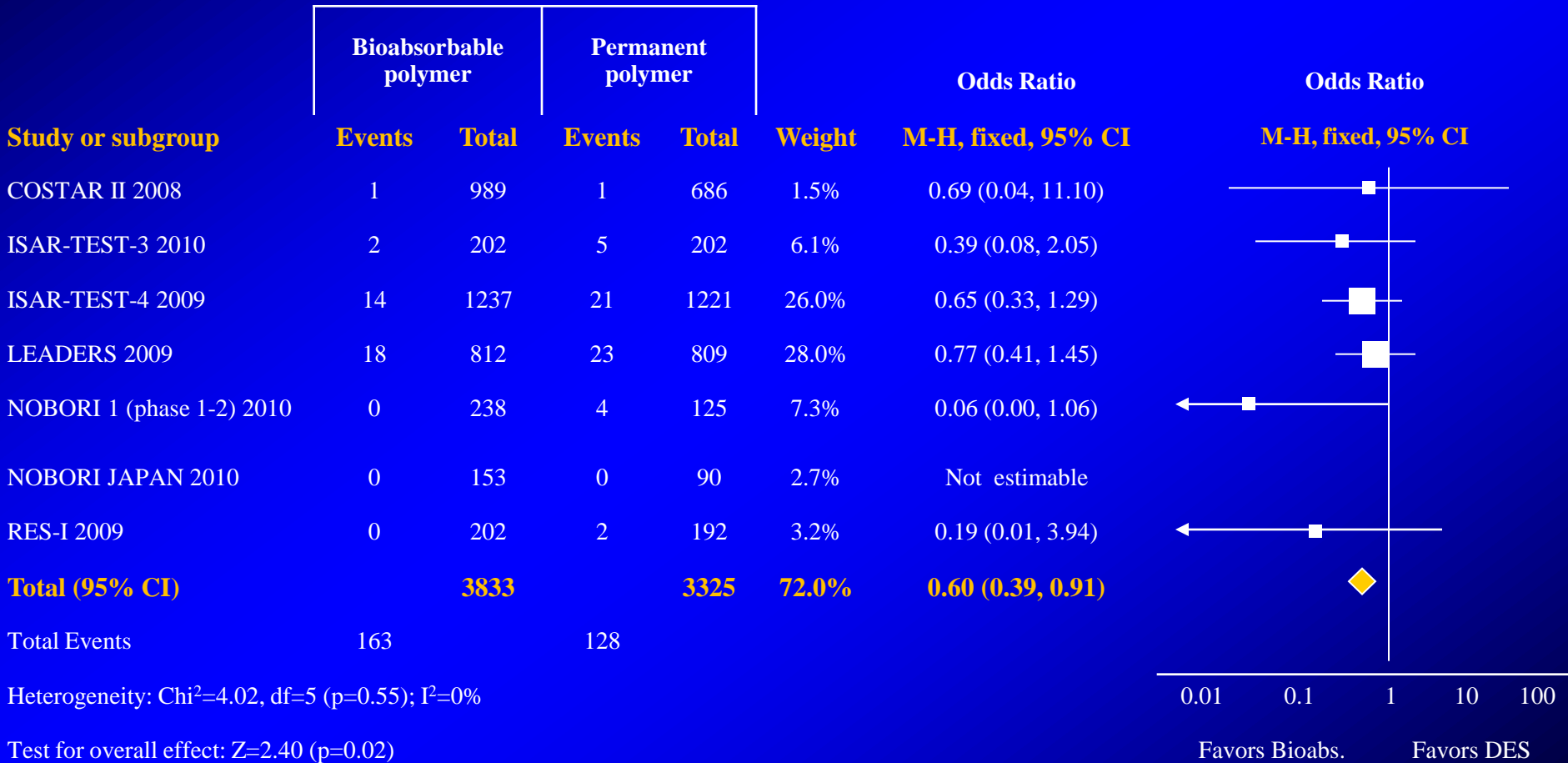
Freedom from Long-term Polymer Exposure

Bioabsorbable vs Durable Polymer DES: Meta-Analysis of 8 Trials Involving 7481 Patients

Bioabsorbable Polymers More Effective at Reducing Late Stent Thrombosis

Stent Thrombosis: Stratified Analysis

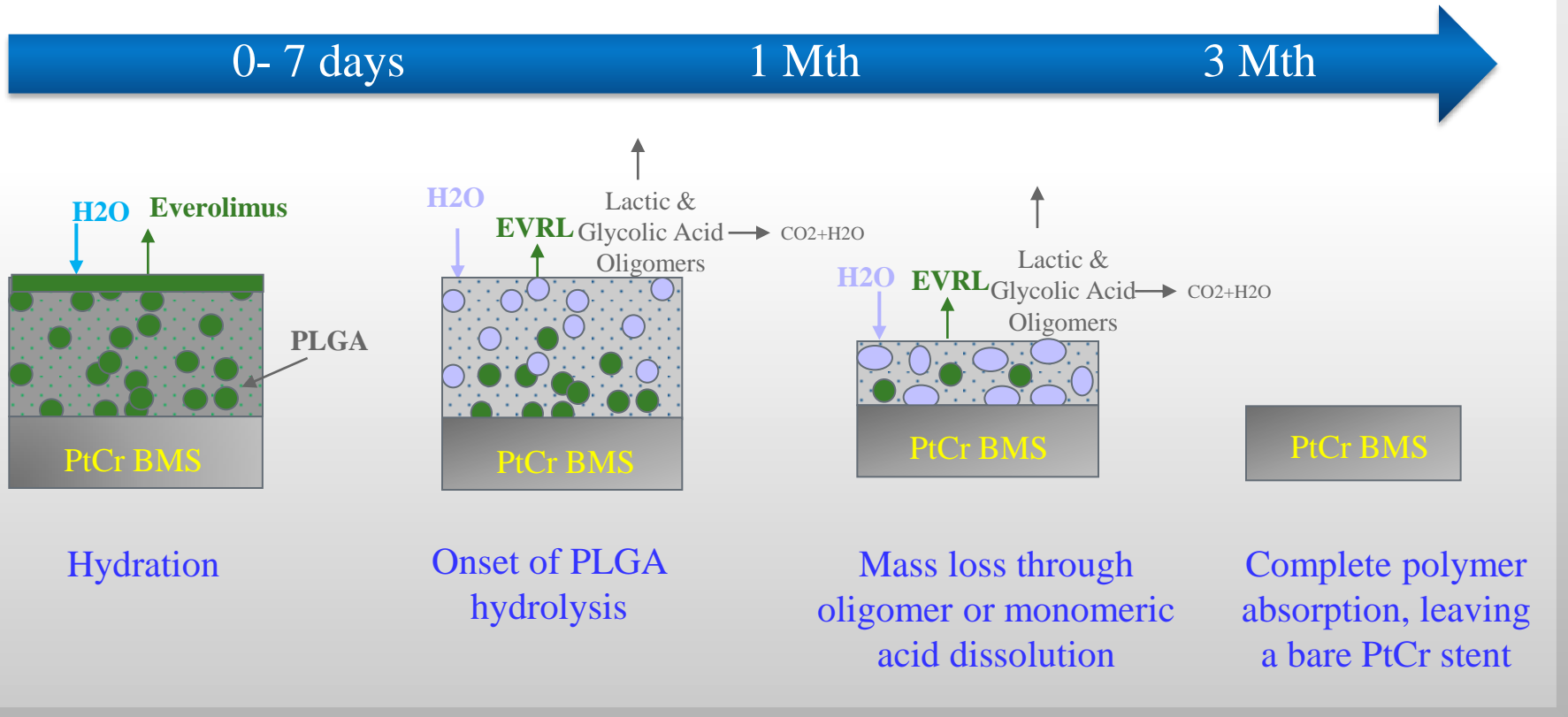
Late/Very Late ST



Navarese et al EuroIntervention 2011; 7: 985-94



SYNERGY™ Stent: Synchronous Drug Release and Polymer Absorption



PLGA polymer is fully absorbed shortly after everolimus delivery is complete, returning SYNERGY to a bare PtCr stent

Bioabsorbable Coatings in Perspective

Relative Polymer and Drug Absorption Profiles

Bioabsorbable Polymer-Coated Stents

Bioabsorbable Scaffold

SYNERGY™

Polymer: PLGA
Absorption Time:
3-4 mo

**Nobori™ and
BioMatrix Flex™**

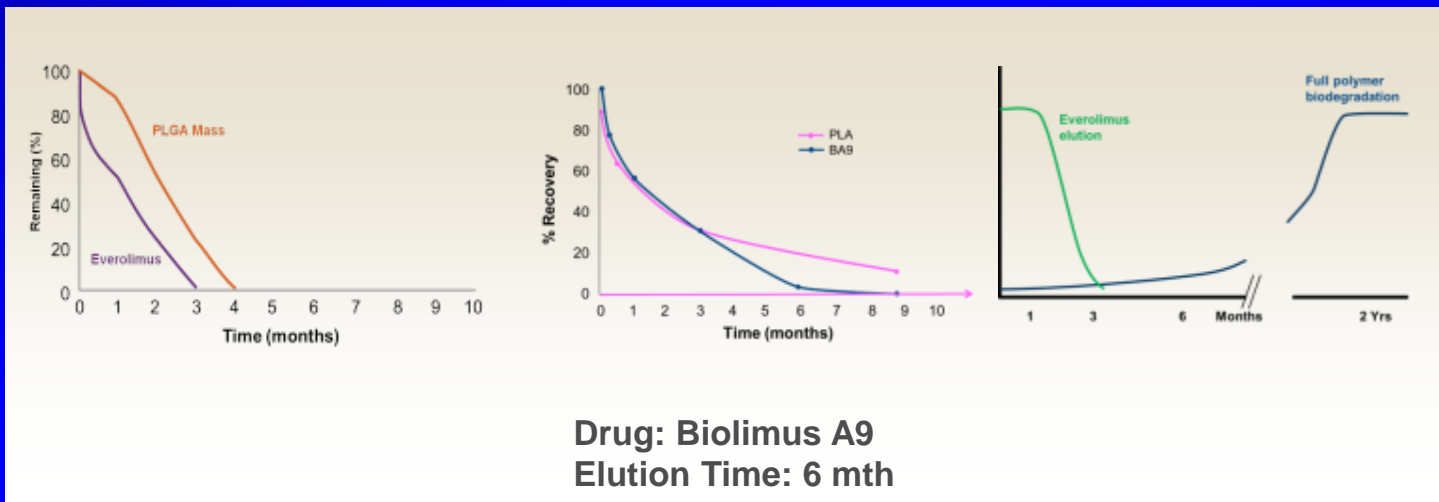
Polymer: PLA
Absorption Time:
>9 mo

Orsiro™

Polymer: PLLA
Absorption Time:
>12 mo

**Absorb™
BVS**

Scaffold: PLLA
Polymer: PDLLA
Absorption Time: >2 yrs



*SYNERGY has the Only Polymer to Absorb Shortly After
Drug Elution Ends at 3 Months*

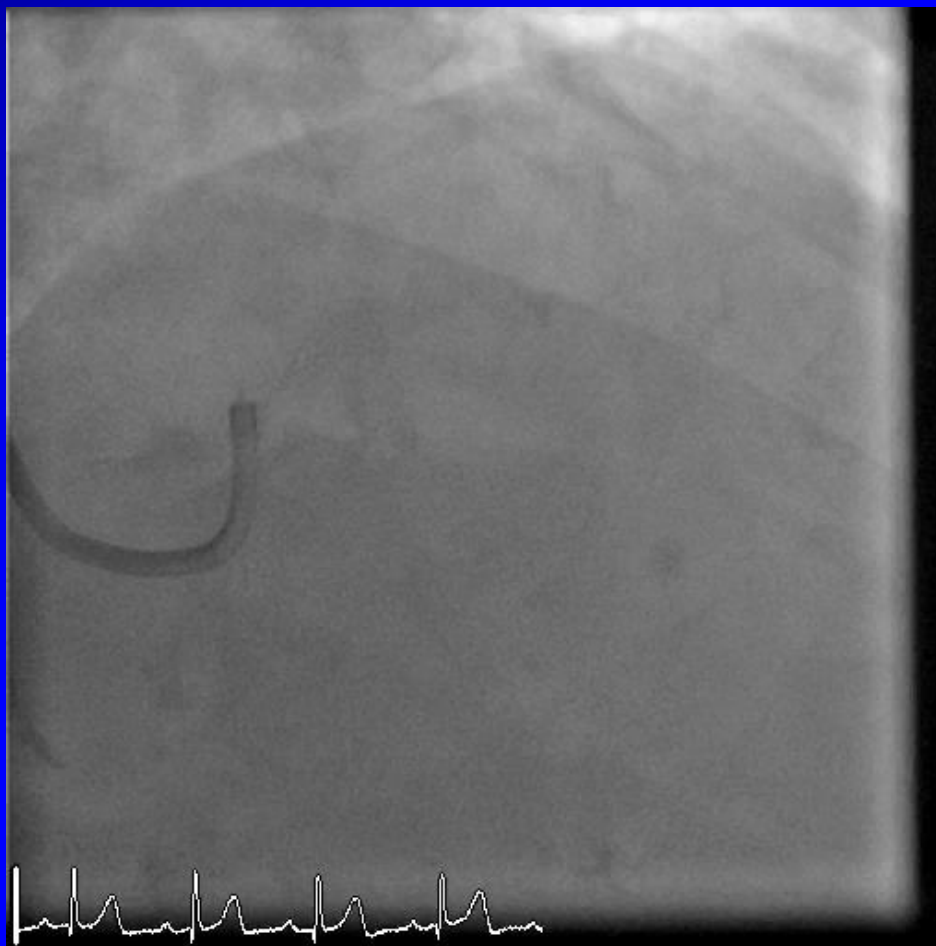


SYNERGY™ Case Examples

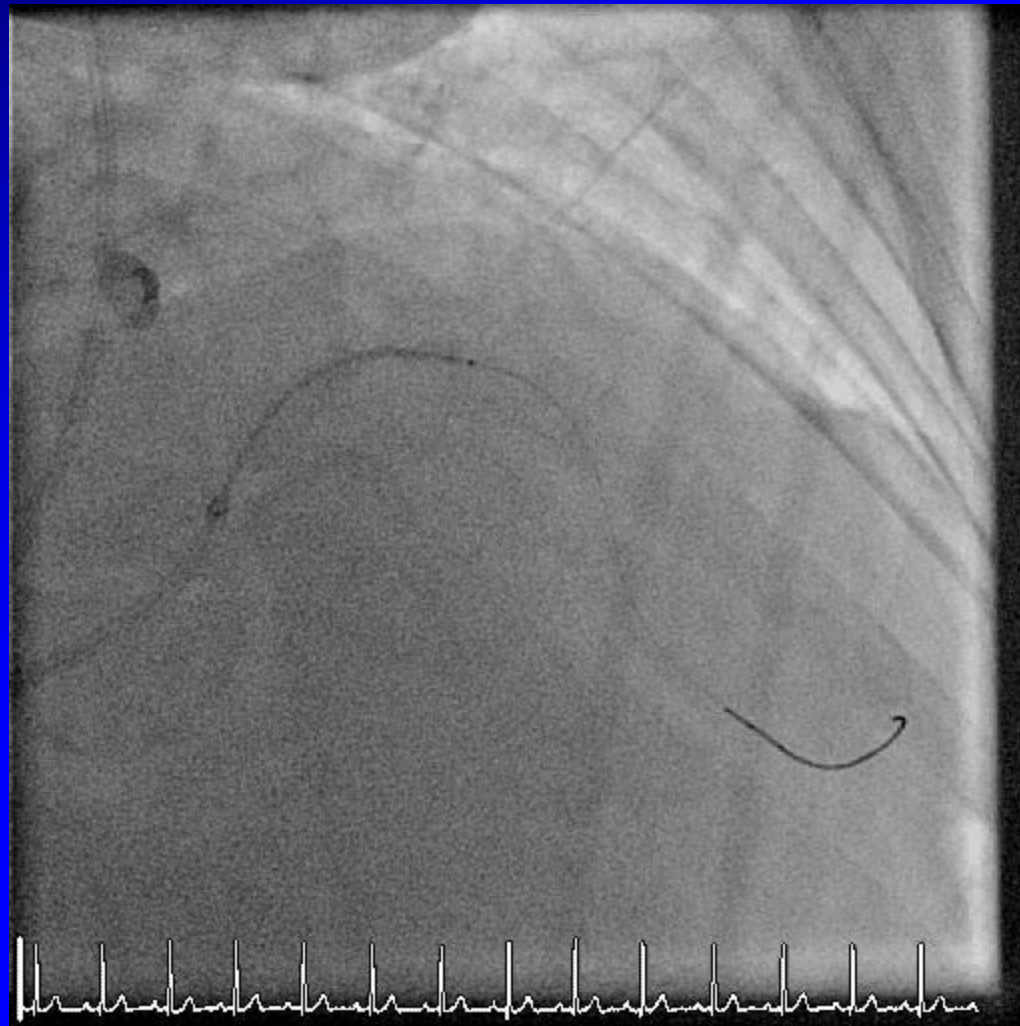


Case Example

- F/72 CVRF hypertension, hyperlipidemia
- Angina pectoris. MPI showed mid LAD ischemia

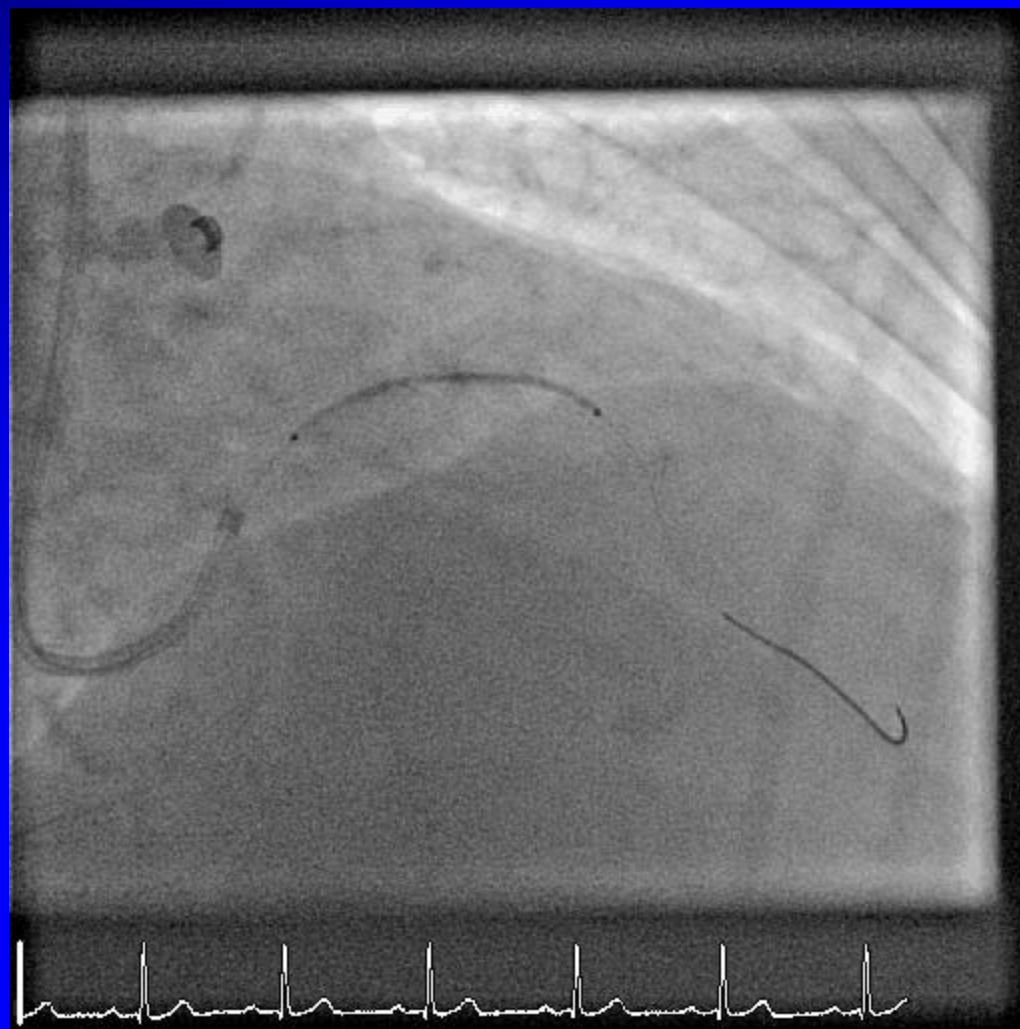


SYNERGY™ Case Study

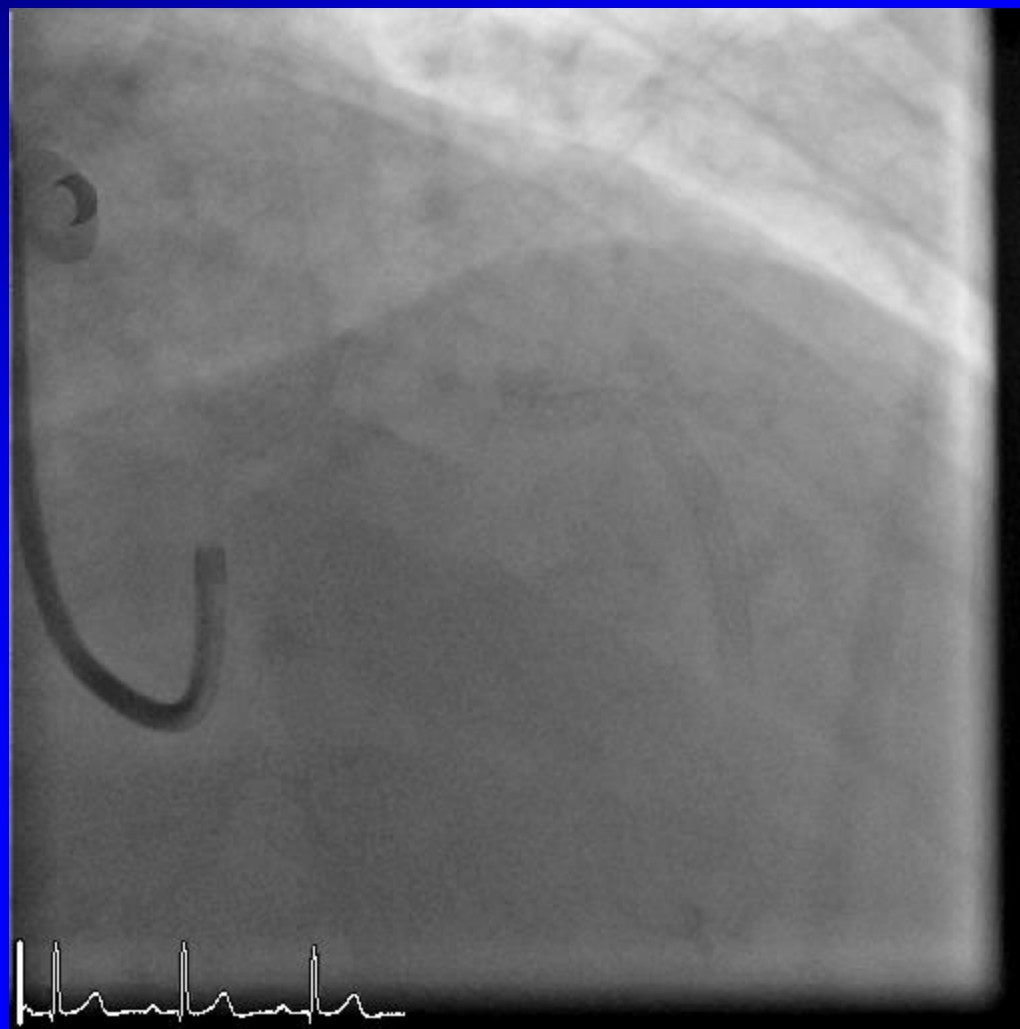


Synergy 2.25x32mm Stent

SYNERGY™ Case Study



SYNERGY™ Case Study

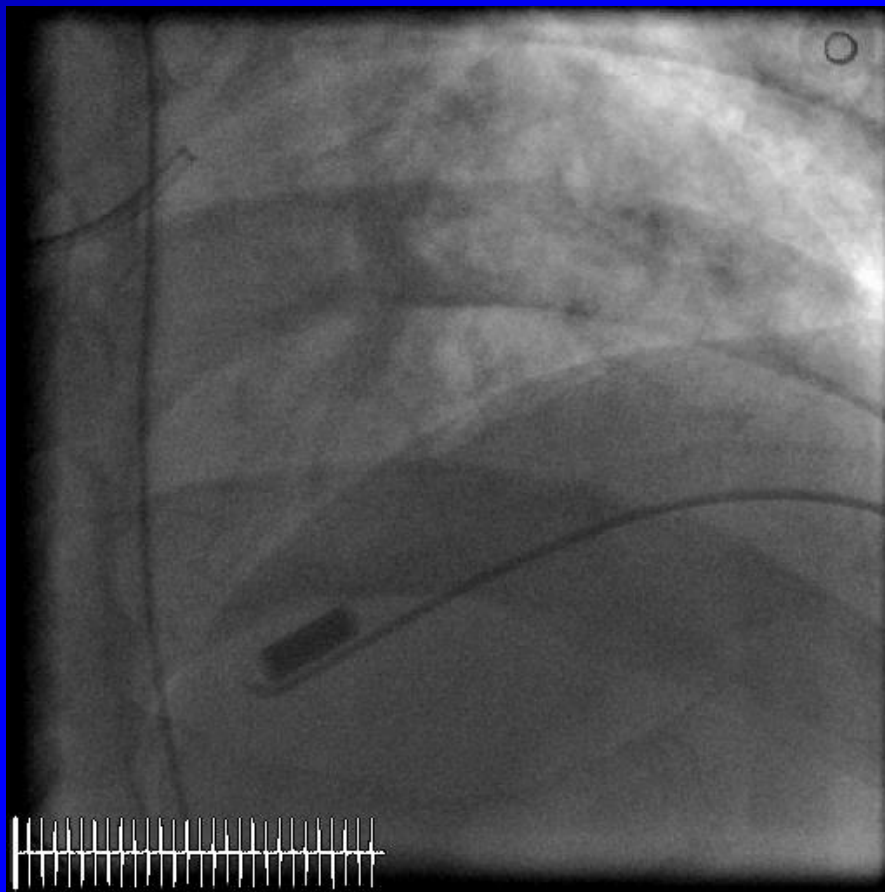




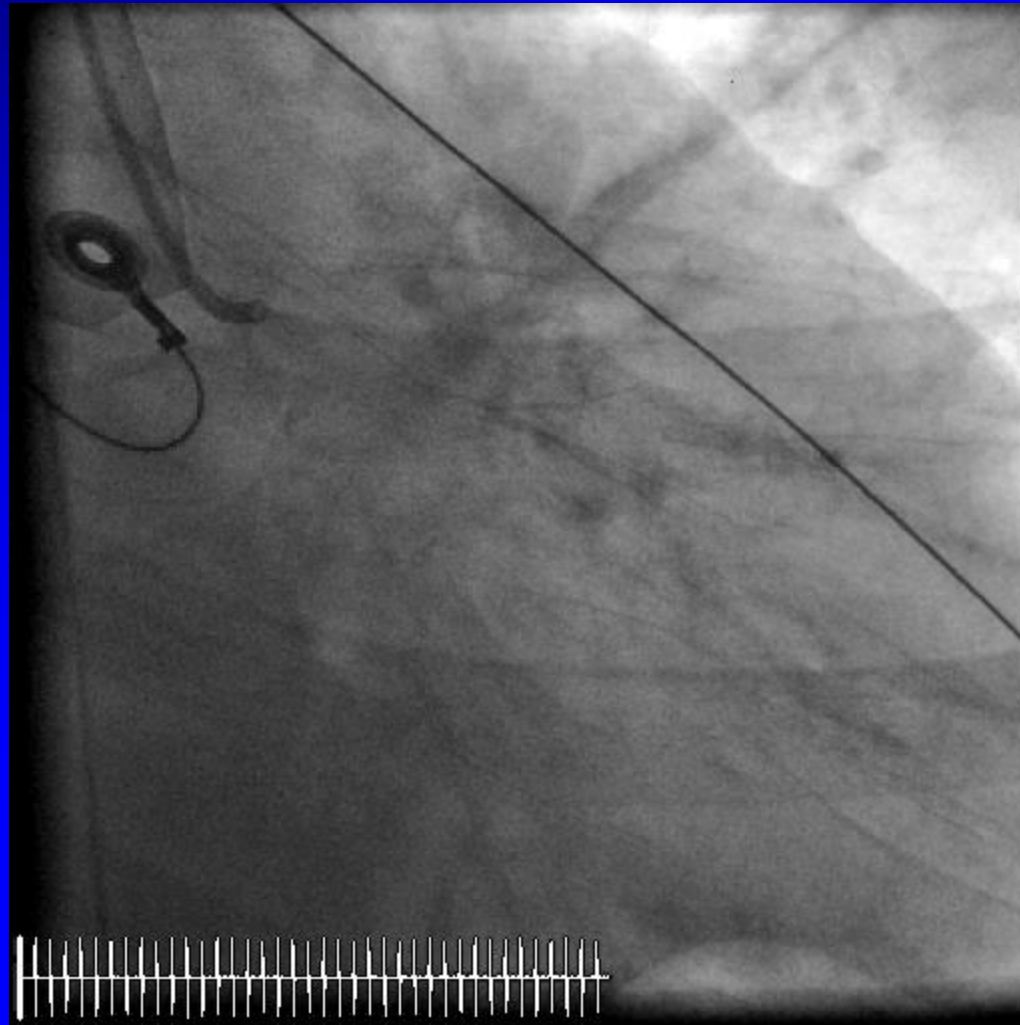
Case Example



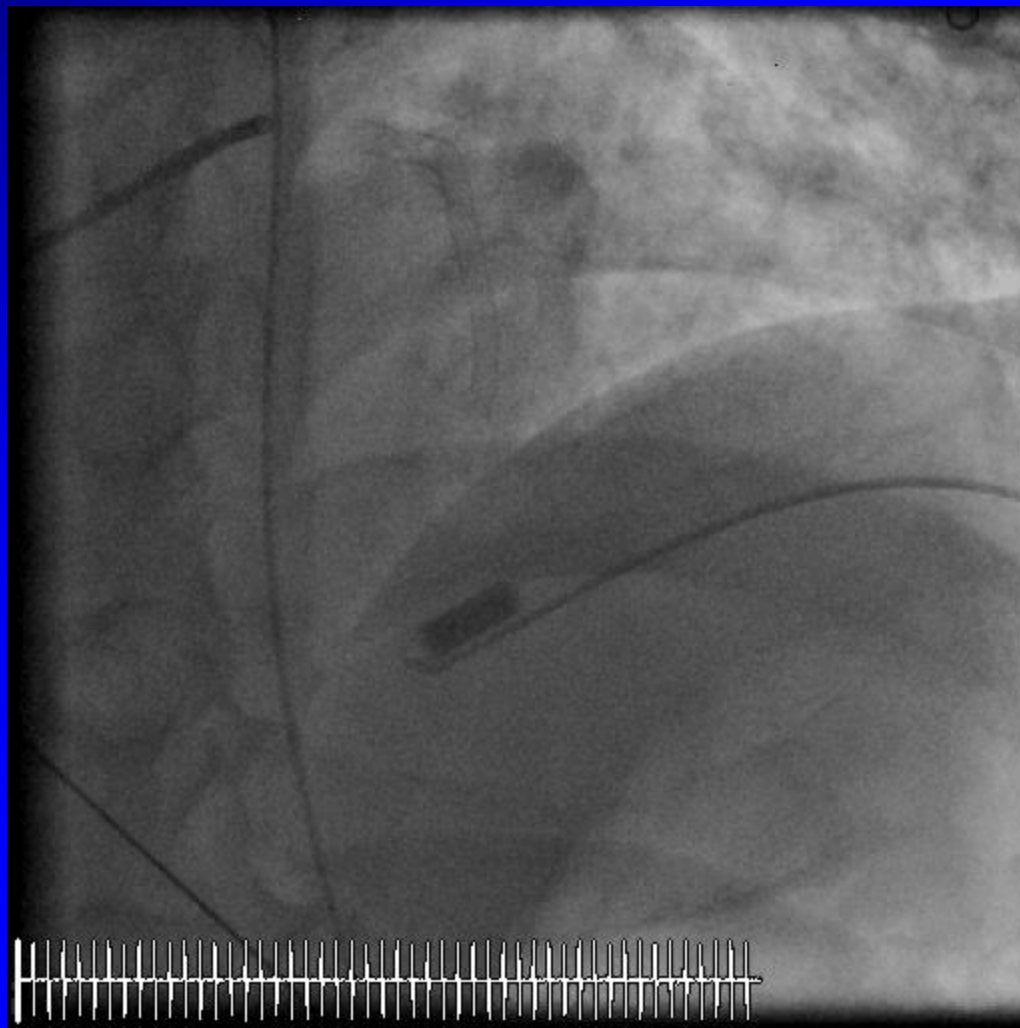
- 47-yr-old man. VF collapse from anterior MI while playing badminton.
- CPR and DC shock enroute to hospital in ambulance
- In cardiogenic shock



Two CoCR Stents Implanted in LAD Artery



Final Angiography Results



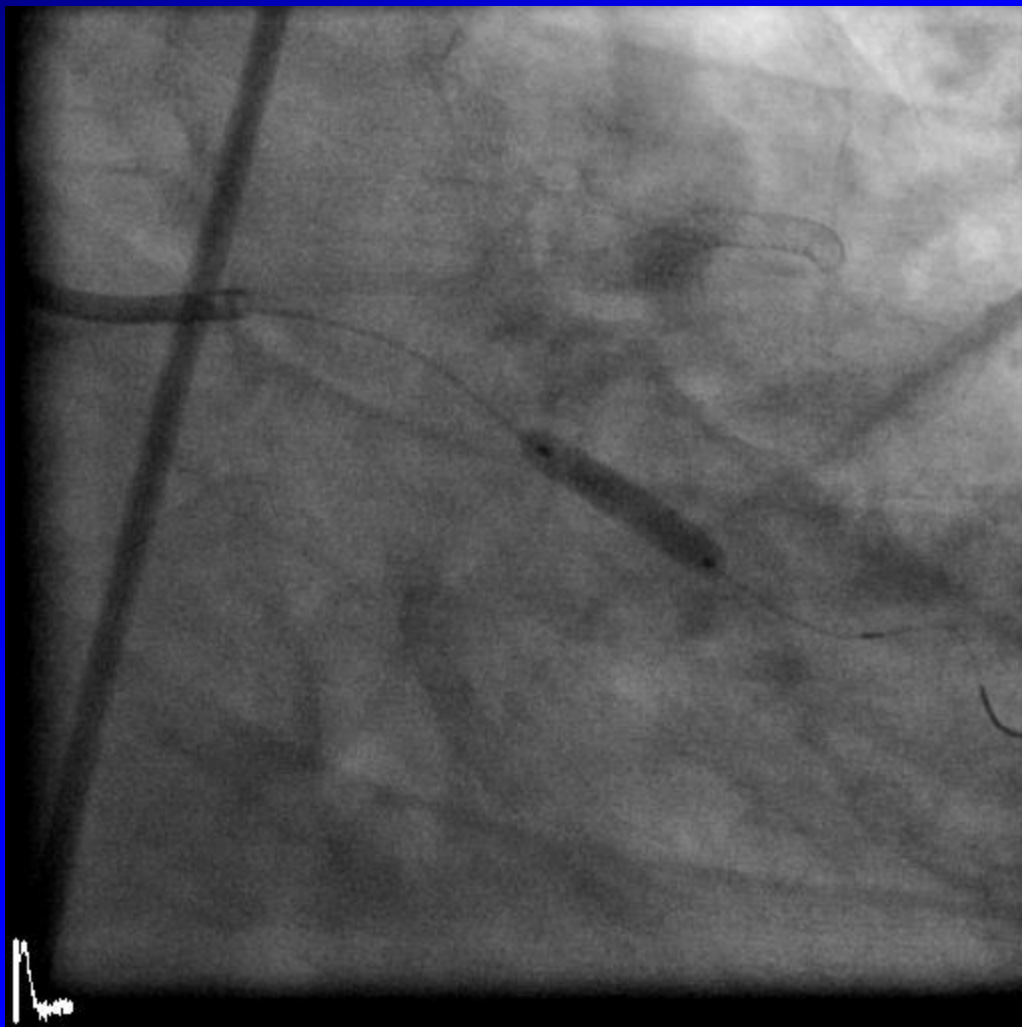
Clinical Course

- Intra-aortic balloon pump
- Hypothermia therapy
- Stayed in CCU for a week
- Discharged on Day 13. Full neurological recovery
- Two-dimensional echocardiogram showed mild left ventricular systolic dysfunction. LVEF 42%

Elective Staged PCI to LCx



SYNERGY™ Case Study



Synergy™ 2.75x16mm Stent

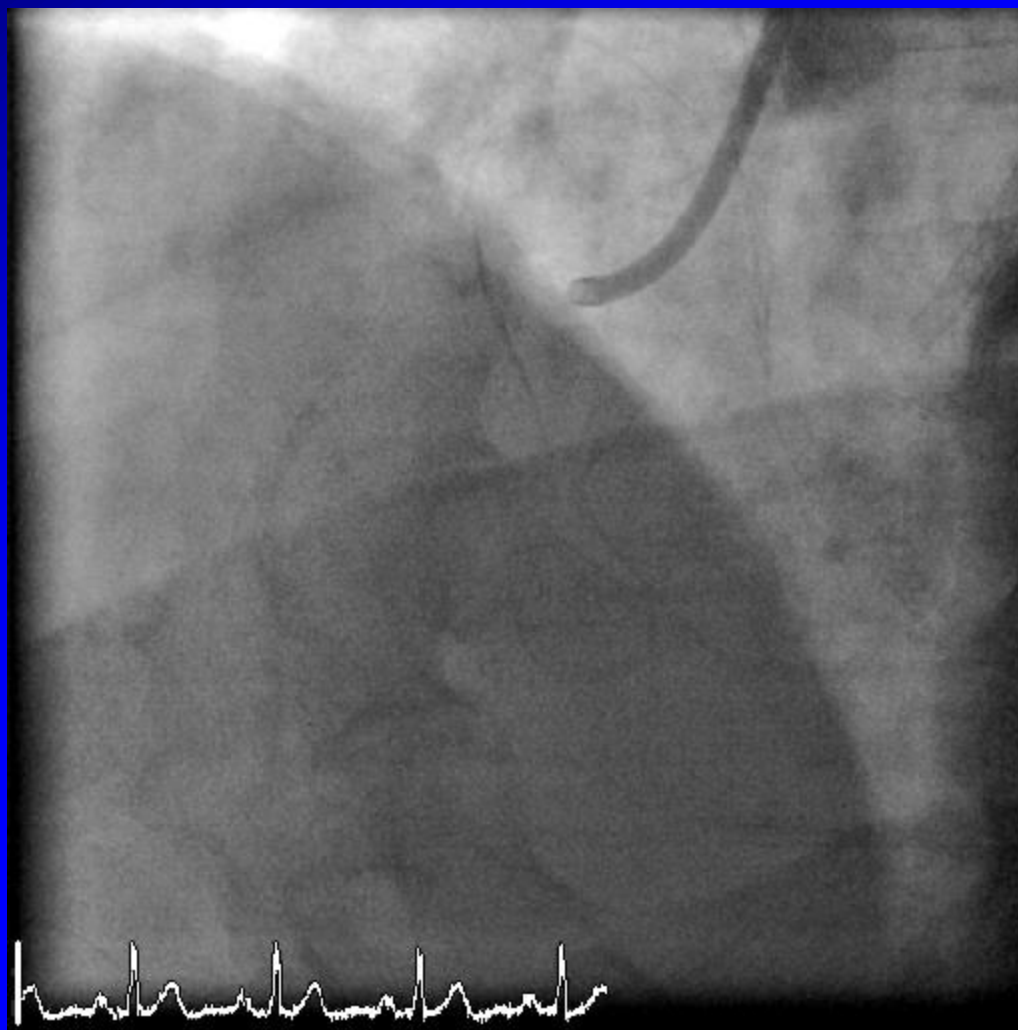
SYNERGY™ Case Study



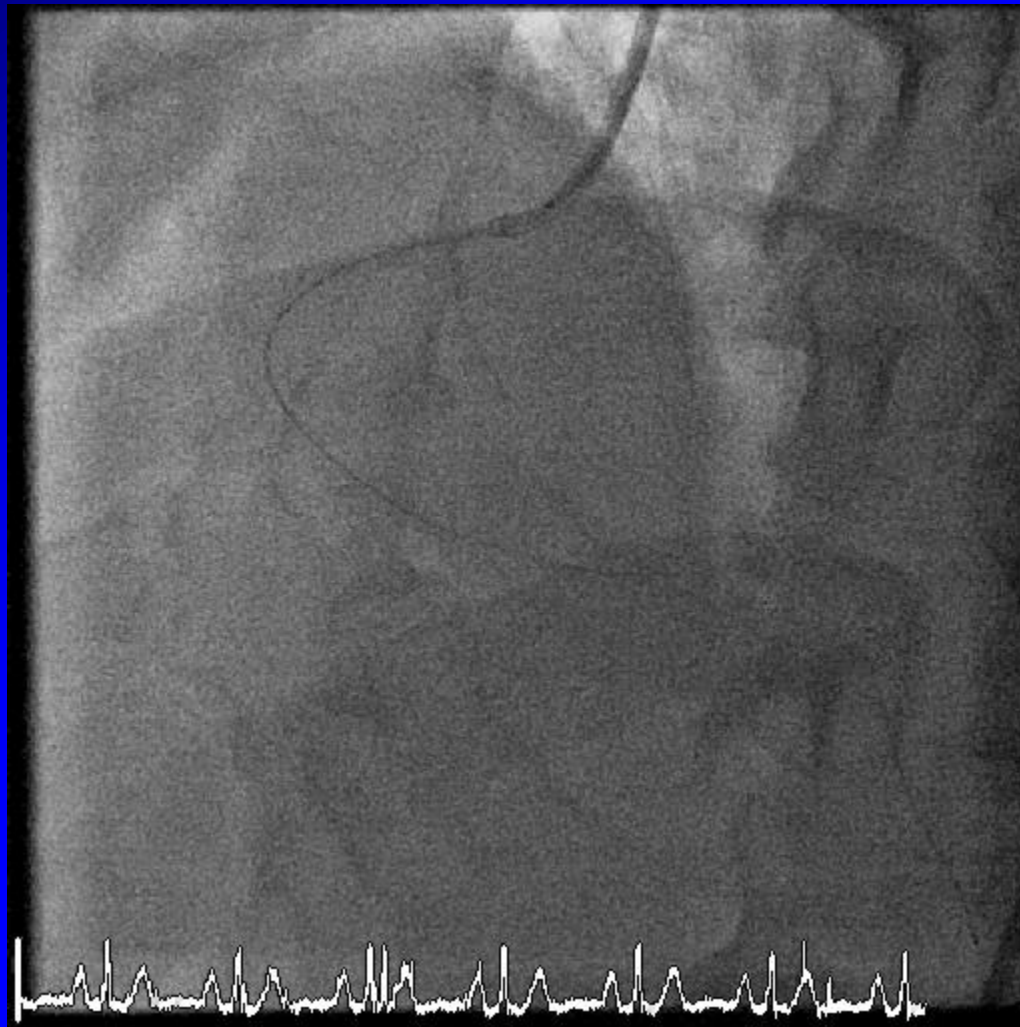
SYNERGY™ Case Study



SYNERGY™ Case Study

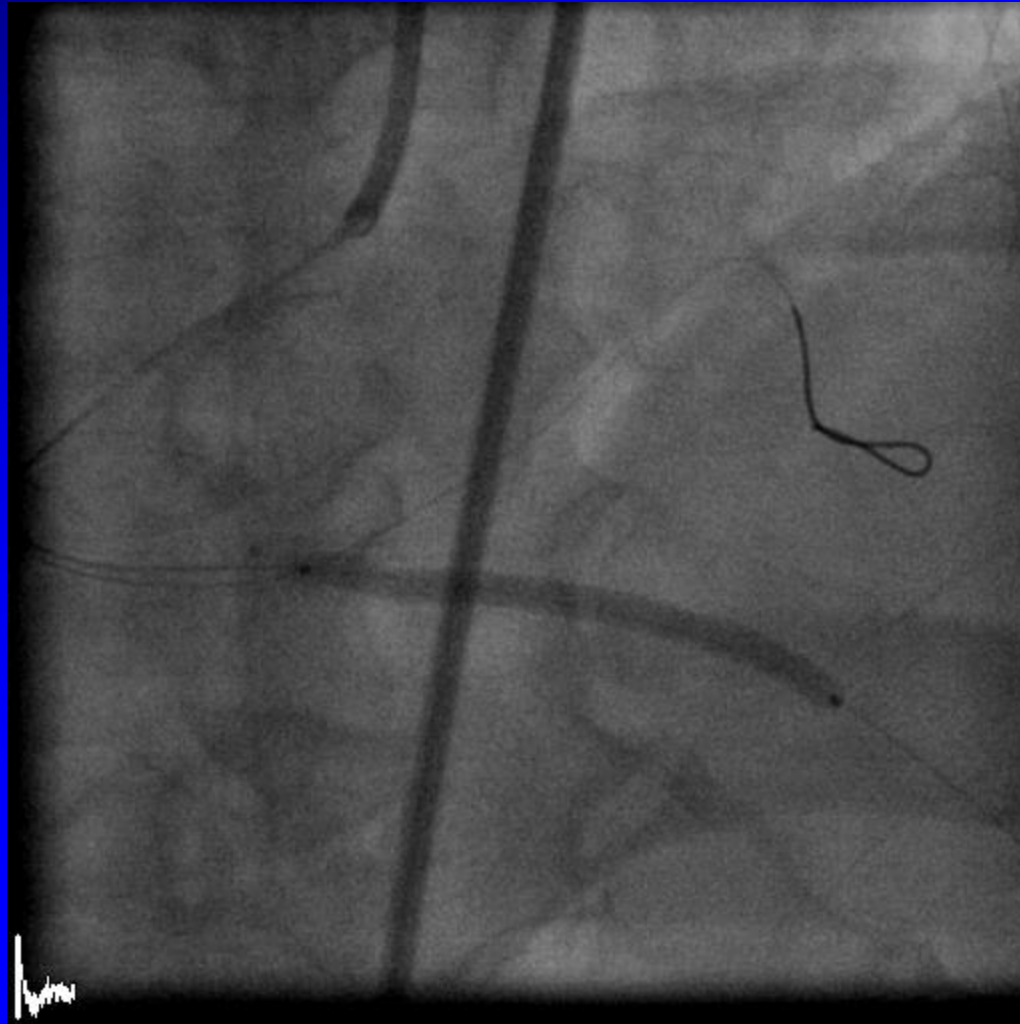


SYNERGY™ Case Study



SYNERGY™ 2.25x38mm stent

SYNERGY™ Case Study

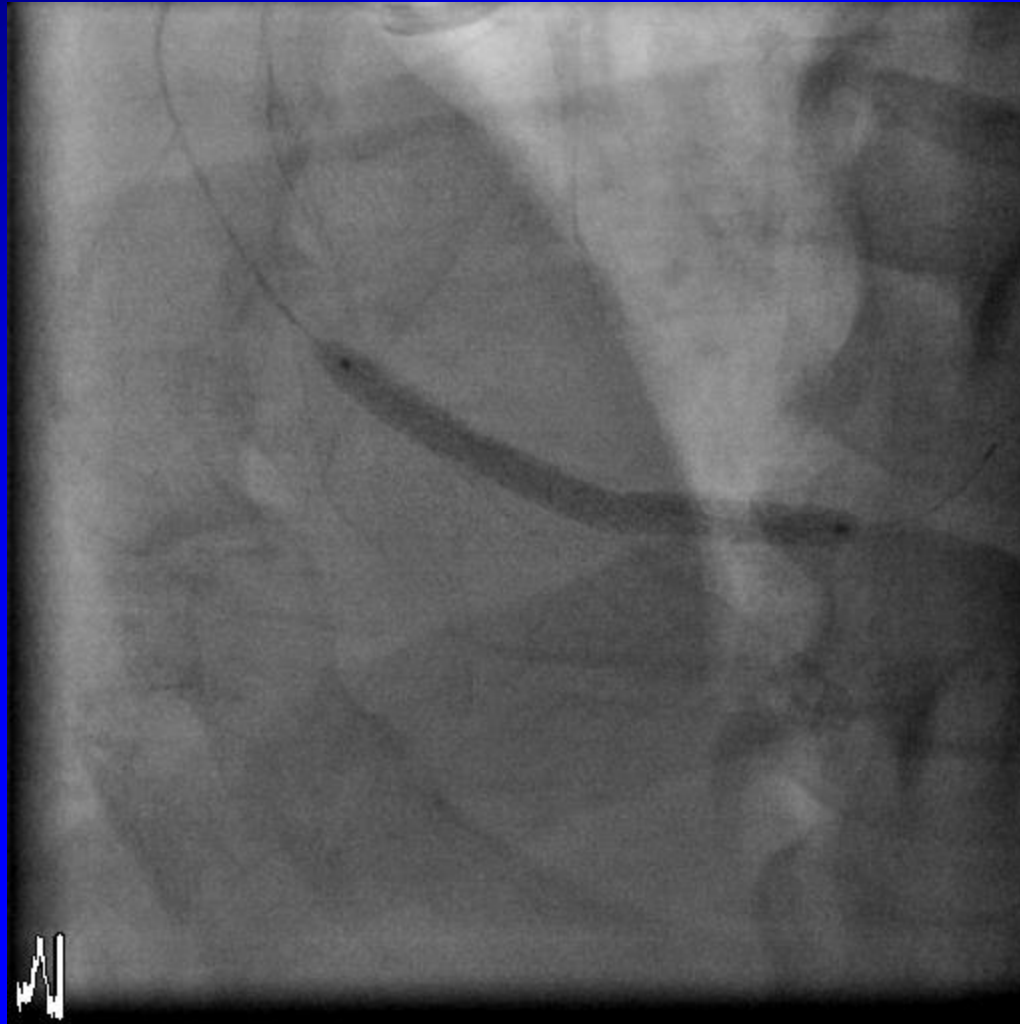


SYNERGY™ Case Study



SYNERGY™ 3.0x38mm stent

SYNERGY™ Case Study



SYNERGY™ Case Study

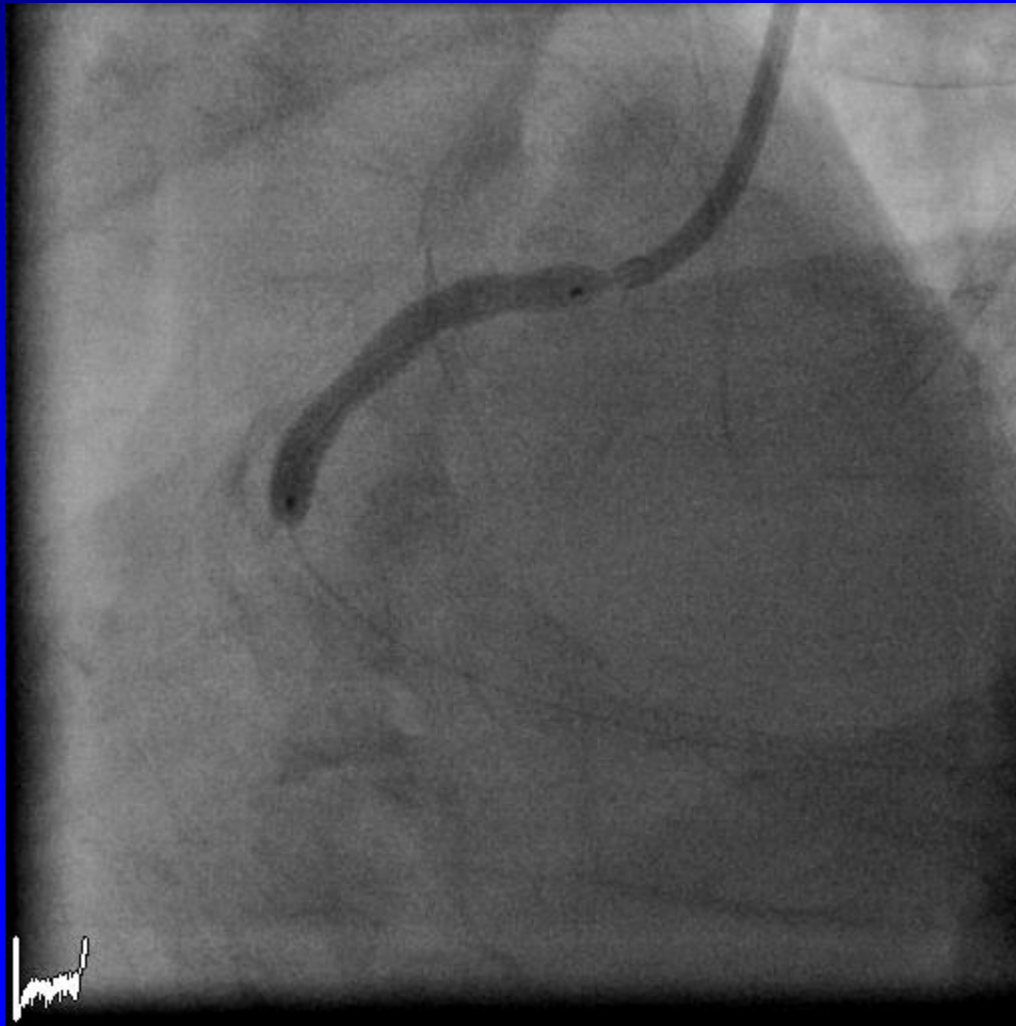


SYNERGY™ Case Study



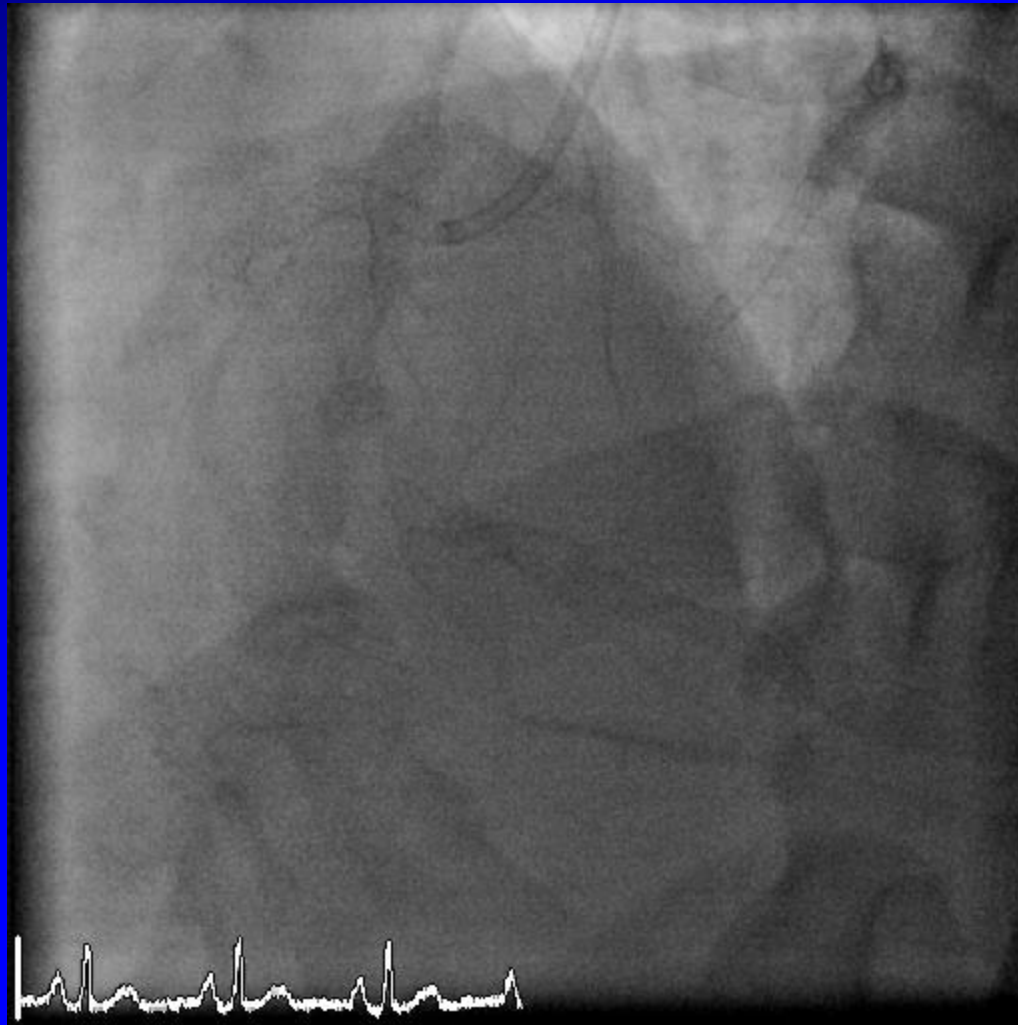
SYNERGY™ 3.5x38mm stent

SYNERGY™ Case Study

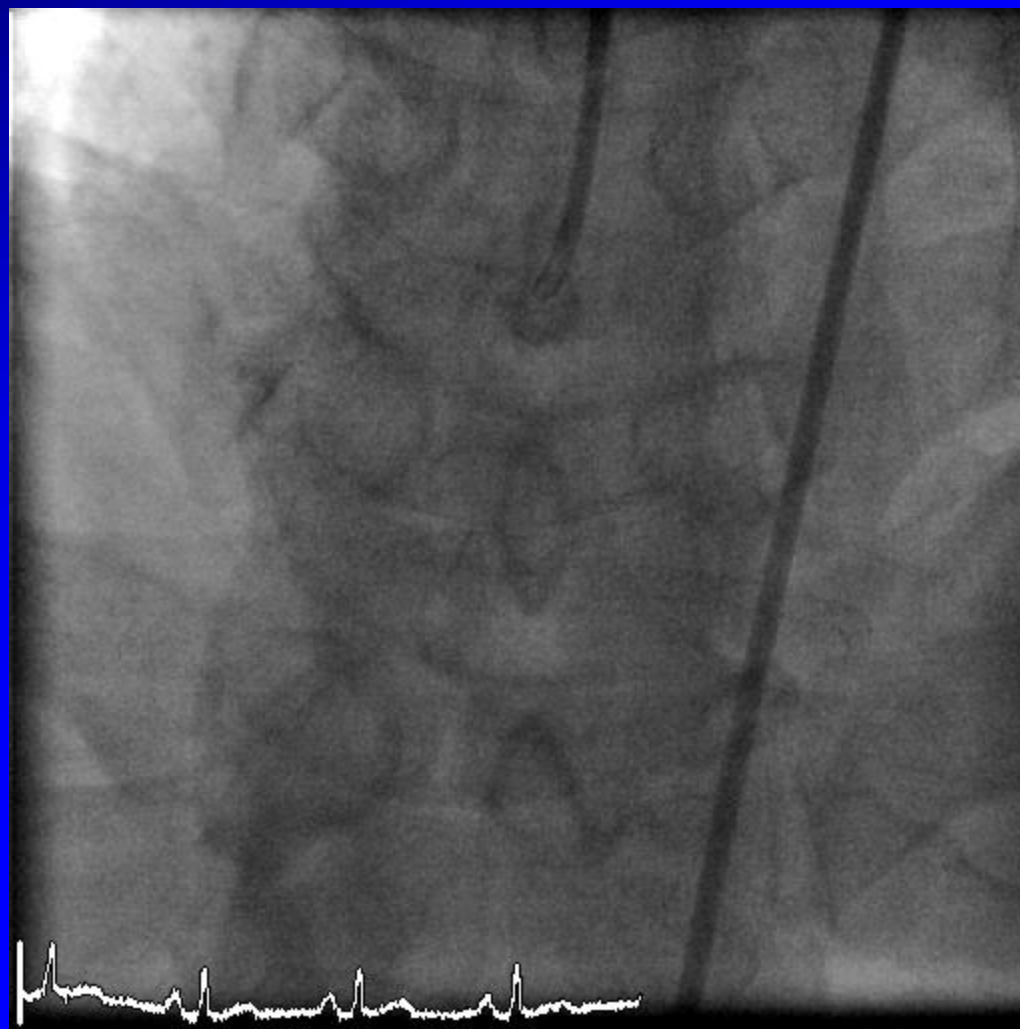


Post-dilation Sapphire NC 3.5x18mm balloon

SYNERGY™ Case Study



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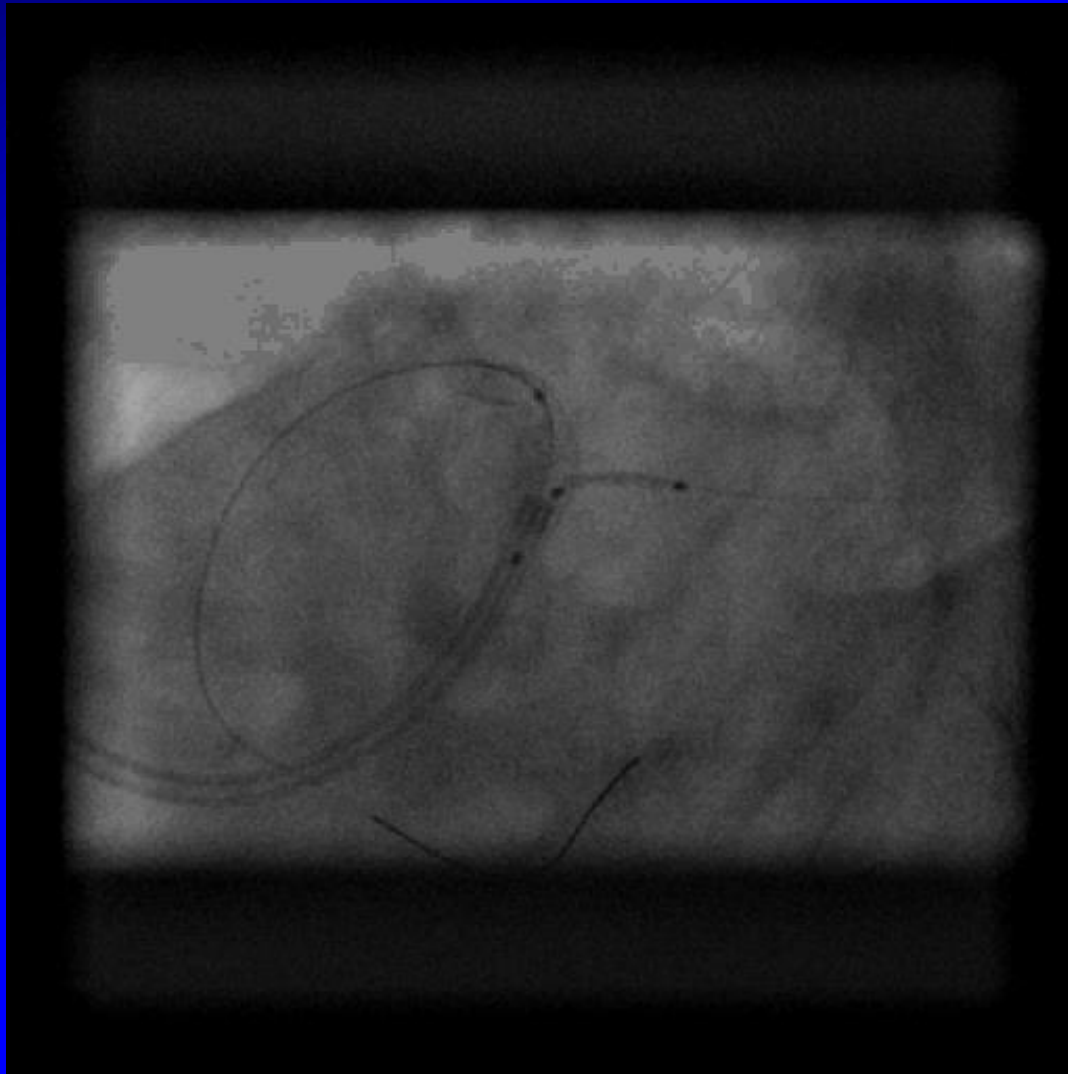


Case Example

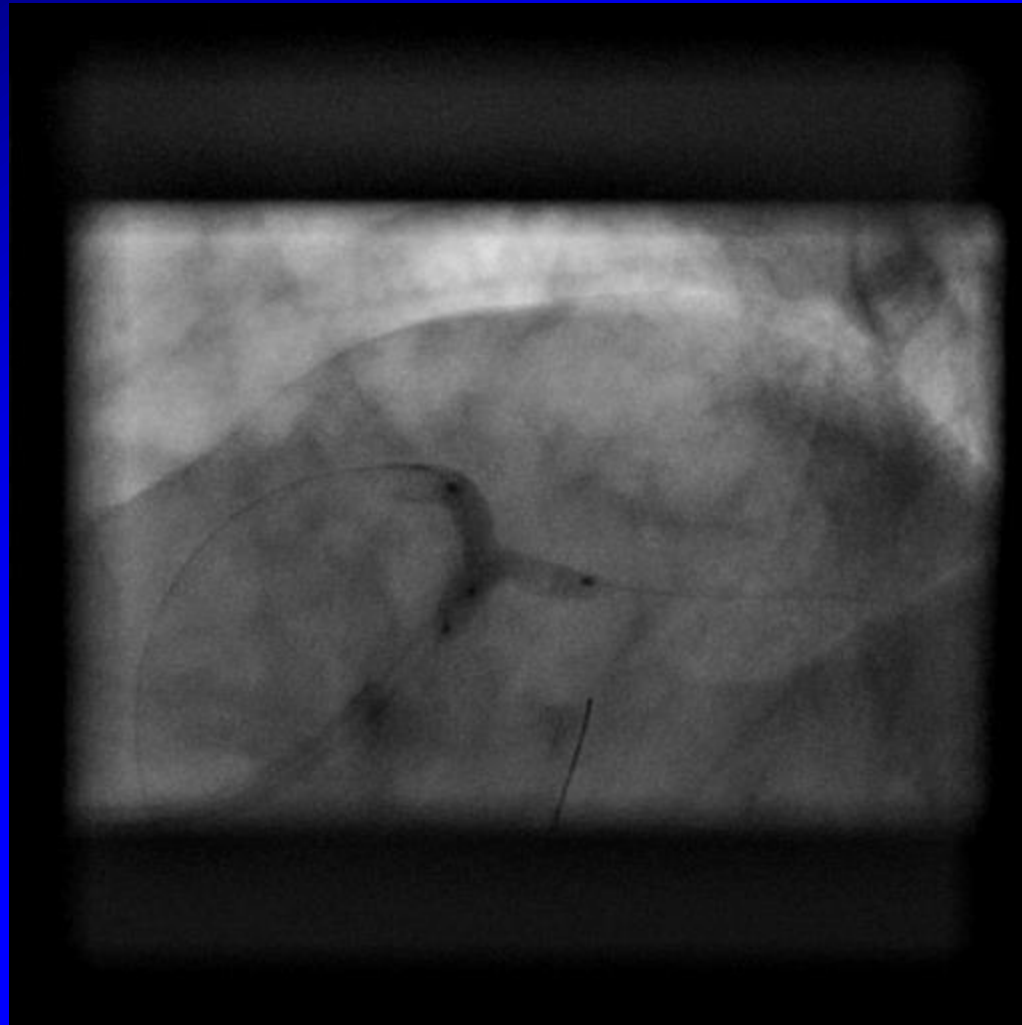
- M/70 CVRF diabetes mellitus, hyperlipidemia
- Status post PCI left main 1 year ago.
- Has unstable angina pectoris



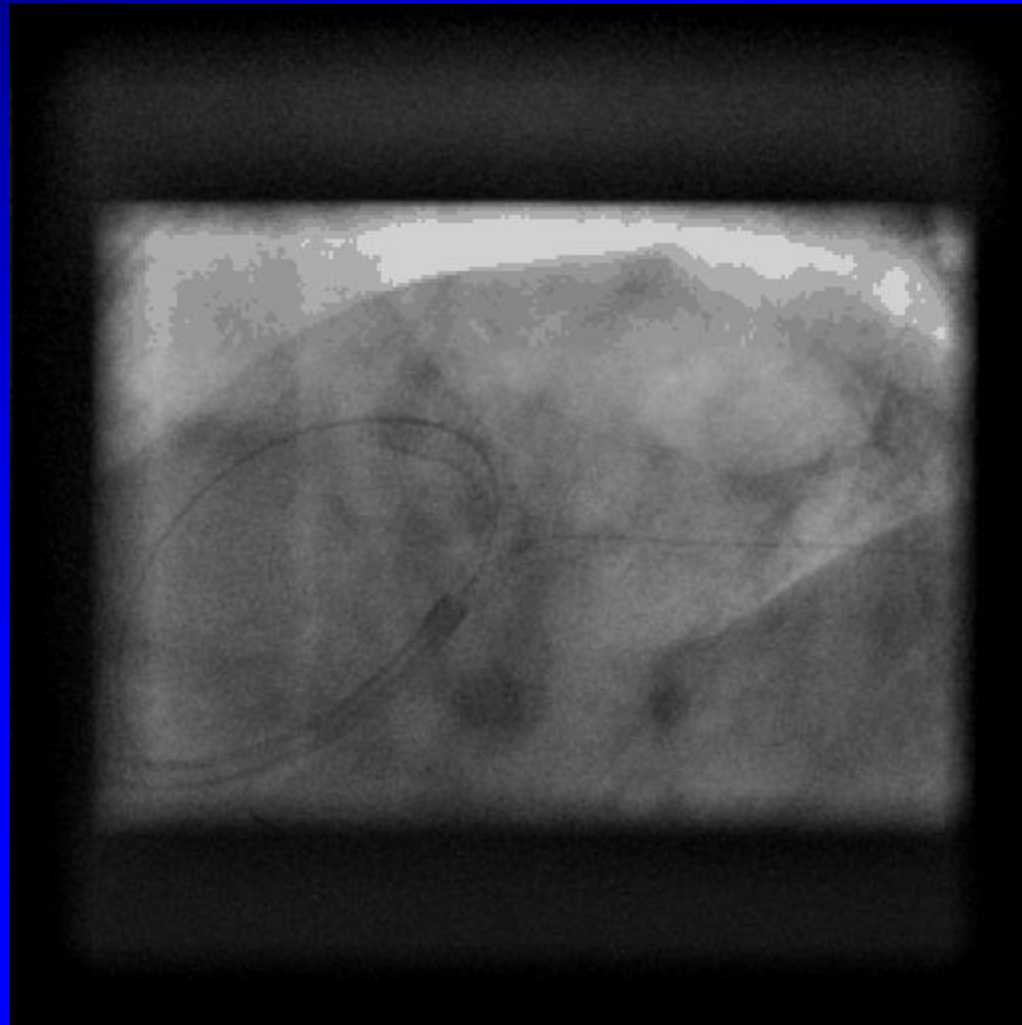
Case Example



Case Example



Case Example



Conclusions

- Modification of stent geometry and design answers clinical needs for improved longitudinal strength and reduced risk of stent deformation. Thinner stent struts and stent delivery system enhances deliverability and flexibility but with ? reduced radiopacity
- Bioabsorbable polymer design potentially enhances the safety of SYNERGY™ DES with no risk of chronic inflammation and late stent thrombosis. Allows for shortened duration of dual antiplatelet therapy but this needs to be validated in clinical studies
- Early evidence with SYNERGY™ suggests comparable efficacy to other DES with no safety concerns related to the novel stent design and biodegradable polymer



ASIAN INTERVENTIONAL CARDIOVASCULAR THERAPEUTICS

THE OFFICIAL CONGRESS OF APSIC



NOVEMBER 13-14, 2015

Pan Pacific Sonargaon Hotel
Dhaka, Bangladesh



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