Biomime

stent design, clinical data,
Bulgarian experience

Biomime Morph stent

design and concept

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BioMime Stent Architecture

Meril
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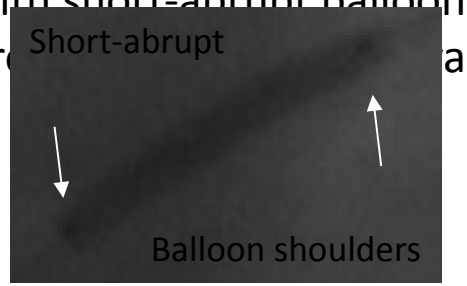
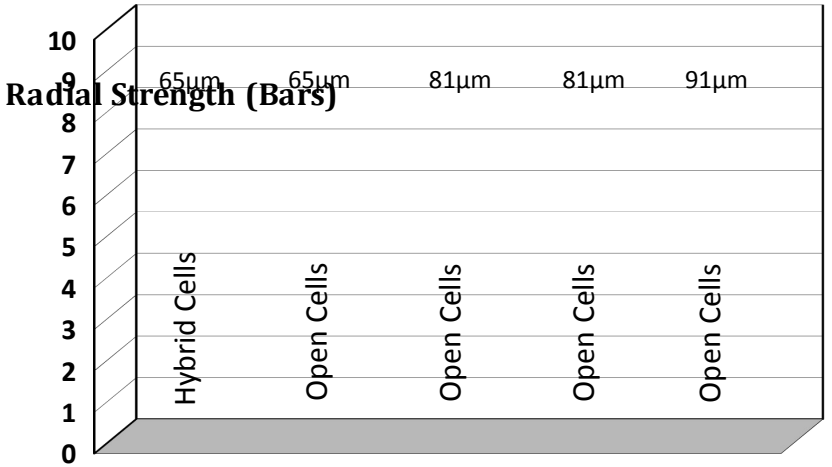
- Cobalt chromium (L605) platform with 65µm strut thickness.
- Hybrid cell design comprising of an intelligent mix of open and close cells resulting in excellent radial strength with a high flexibility.
- Unique strut width variability that ensure a <3% recoil and 0.29% foreshortening.
- Special electro-polishing technique eliminates surface nickel oxides.
- Stent is mounted on a flexible Rx PTCA Balloon catheter with short-abrupt balloon shoulders, having a pr ascular injury



65µm Co-Cr L605 stent struts

Open cells in mid segment Close cells at edges

Uncompromised Radial Strength



Data on file with Meril Life Sciences.

BioMime – Morphology Mediated Expansion

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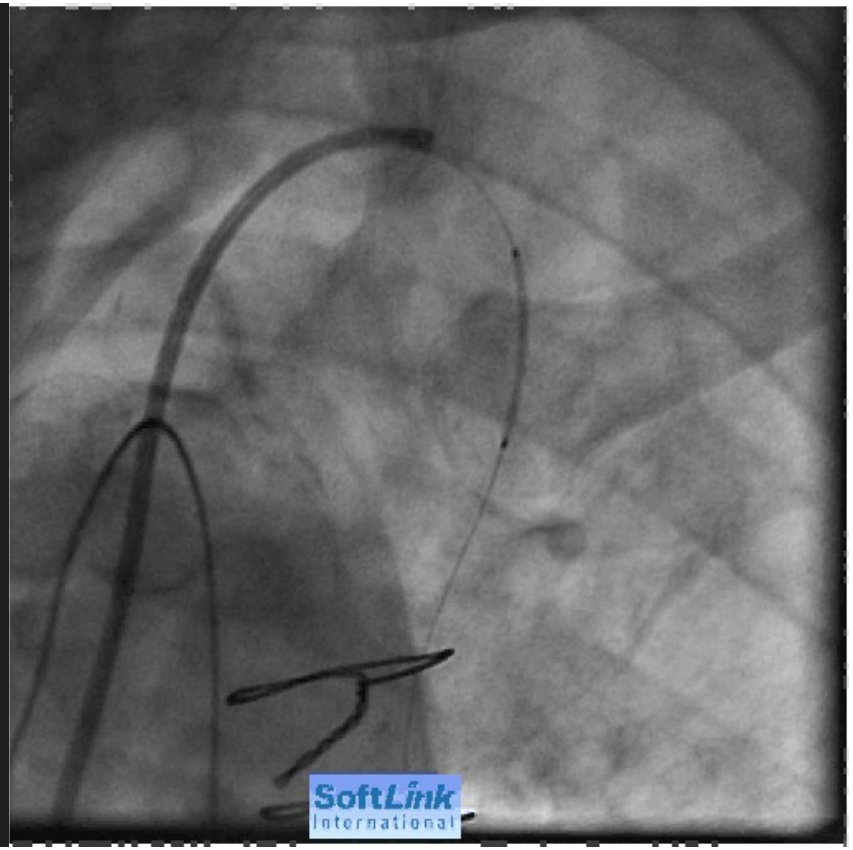
Morphology Mediated Expansion

Conventional Stent Dog-bone Expansion

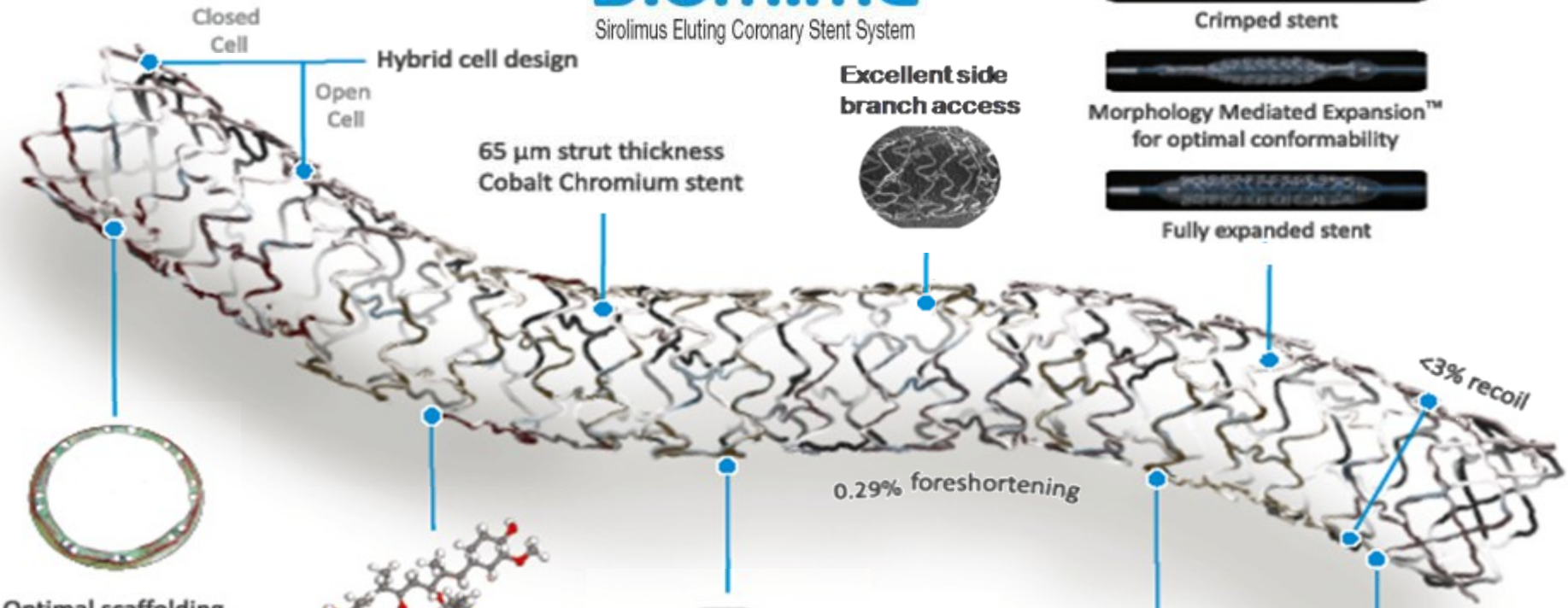


Propensity to minimize edge injury

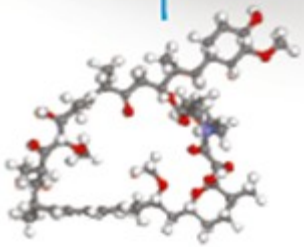
Propensity to cause edge dissections

biomime

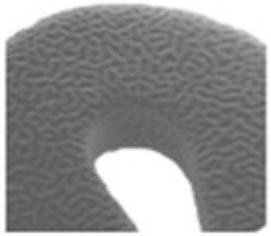
Sirolimus Eluting Coronary Stent System



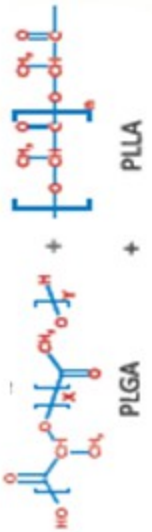
Optimal scaffolding, wall apposition with superior acute gain[1]



Sirolimus 1.25 µg/mm² of stent surface, 30-days elution kinetics



Stable, elastic non - inflammatory BioPoly™- Biodegradabl coating, 2 µm thick.



Highly flexible and deliverable stent system

Low balloon overhang, short, abrupt balloon shoulders for low balloon - related edge injury

CE & ANVISA approved

New 2.00, 2.25 dia & 44, 48 mm Lengths

Available in 54 sizes-
Diameters (mm): 2.50, 2.75, 3.00, 3.50, 4.00, 4.50
Lengths (mm) : 8, 13, 16, 19, 24, 29, 32, 37, 40

BioMime Clinical Trial Program

Meril
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>5,800 Patients

meriT-China* (n=1,000)
RCT 200:200 SES Vs EES
+ 600 SES. 1 year MACE, ST

meriT-5* (n=260)
RCT SES Vs EES
Europe & Brazil
Non-inferiority 8m LL

MILES Global* (n=2,500)
Real World Registry
1 year MACE, ST

meriT-3 (n=1,110)
Real world registry
1 yr MACE 2.2%, ST 0.1%

meriT-4* (n=660)
RCT SES Vs EES
Japan, Europe & Brazil
Non-inferiority TVF

meriT-1# (n=30)
Single, denovo lesions.
2 yr MACE 0%, ST 0%
8m LL 0.15mm

meriT-2 (n=250)
Complex, MVD lesions.
1 yr MACE 6%, ST 0.8%
8m LL 0.12mm

S. Dani et.al. EuroInterventions 2013; 9:493-500

* To be initiated. Under preparation.

meriT-1, 2, 3 Study Designs

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Study Design	meriT-1*	meriT-2#	meriT-3$
Principal Investigator	Dr. Sameer Dani, Ahmedabad, India	Dr. Ashok Seth, New Delhi India	Dr. R. K. Jain, Hyderabad, India
Study design	Prospective, phase IV, single center, non-randomized	Prospective, phase IV, multi-centric, non-randomized	Prospective, phase IV, multi-centric, non-randomized
N	30	250	1,110
Inclusion criteria	Single, discrete, de novo lesions, Mean vessel lumen diameter 2.5, 3.0 and 3.5 mm. Stent lengths 19 to 24mm	Most lesions (+CTO's). Vessel Dia. >2.5 and <3.5mm Lesion lengths upto 37mm treated with max. stent length of 40mm	Real world. All patients eligible for angioplasty and stenting with Sirolimus Eluting Coronary Stent system
Exclusion criteria	CTO's, Bifurcations, SVG's, AMI's, LM disease, LVEF <30 %	SVG's, AMI's, LM disease, LVEF <30%	None. Classical DES Tx exclusion criteria.
Clinical follow-up	30d, 6m, 8m, 1y, 2y	30d, 6m, 8m, 1y, 2y, 3, 5y	30d, 6m, 1y
Angiographic follow-up	All patients 8 months	All patients 8 months	None

* S. Dani et.al. EuroInterventions 2013; 9:493-500. # Presented by Dr. Ashok Seth at EuroPCR 2013. $ Presented during IndiaLIVE 2013

meriT-1, 2, 3 Study Designs & Key Demographics

Meril
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Study Design	meriT-1	meriT-2	meriT-3
Primary End points	30-days MACE and late loss at 8 months angio follow-up	30-days MACE and late loss at 8 months angio follow-up	30-day and 6m MACE
Secondary End points	MACE, ST upto 12months. Late loss at 8m angio follow-up	MACE, ST upto 12months. Late loss at 8m angio follow-up	1 year MACE, ST
Study status	2 years completed.	8months completed.	1 year completed.

Key Demographics	meriT-1 N=30	meriT-2 N=250	meriT-3 N=1,110
Mean age, years	50.5 ± 8	56.72 ± 10.55	56.3± 10.3
Gender, males	25 (83%)	208 (83%)	883 (79.5%)
Diabetics	9 (30%)	91 (36%)	454 (40.9%)
Hypertensives	17 (57%)	123 (49%)	589 (53.1%)
Smokers	7 (23%)	66 (28%)	178 (16.0%)
Hyperlipidimia	3 (10%)	26 (11%)	64 (5.8%)
Previous MI	13 (43%)	80 (32%)	156 (14.1%)

* S. Dani et.al. EuroInterventions 2013; 9:493-500. # Presented by Dr. Ashok Seth at EuroPCR 2013. $ Presented during IndiaLIVE 2013

meriT-1, 2, 3 Results

Meril
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Results	meriT-1 2-years f/up N = 28	meriT-2 3-years f/up N=249	meriT-3 1-year f/up N=1,110
MACE	0 (0%)	14 (6.82%)	24 (2.20%)
Cardiac deaths	0 (0%)	2 (0.97%)	10 (0.90%)
Non-fatal MI	0 (0%)	0 (0.00%)	2 (0.20%)
Clinical TLR	0 (0%)	10 (4.87%)	7 (0.63%)
Stent Thrombosis			
Acute (<24hrs)	0 (0%)	1 (0.4%)	1 (0.1%)
Sub-acute (2-30d)	0 (0%)	1 (0.4%)	0 (0%)
Late (>30days)	0 (0%)	0 (0.0%)	0 (0%)
Late Loss (8m QCA)	N = 26	N = 218, 309 lesions	
In-segment	0.17	0.11	
In-stent	0.15	0.13	Only Clinical Follow-up
Binary Restenosis	0 (0%)	19 (6.2%)	

Independent Core Lab – CRC – Cardiovascular Research Center, Brazil
Dr. Ricardo Costa, Dr. Alexandre Abizaid

Median Late Loss Values due to non-normality of data

* S. Dani et.al. EuroInterventions 2013; 9:493-500. # Presented by Dr. Ashok Seth at EuroPCR 2013. $ Presented during IndiaLIVE 2013. **meriT-2 Subset Interim Analysis

Results from a single-centre, all-comer retrospective registry of the use of BioMimeTM coronary stent system.

- The conducted study was a retrospective, non-randomised, single-arm, clinical registry of the performance of the BioMime SES in the treatment of **all-comer patient population** in a single cardiovascular PCI capable institution.
- The objective was to determine the **long-term safety, feasibility and efficacy of this stent system** in patients indicated for percutaneous coronary intervention (PCI). All patients were treated in a single institution (Multiprofile hospital for active treatment MHAT “Blagoevgrad” AD, Blagoevgrad, Bulgaria).
- Coronary native and graft vessels with **reference diameter (RD) 2.25 to 4,5 mm** (by visual estimation); with diameter stenosis (DS) of 50% to 100% were treated. The study had **approval from the local ethics committee** of MHAT “Blagoevgrad” AD.

Design of the registry, follow-up and endpoints

A total number of 262 patients were treated with PCI solely with BioMime stent implantation starting 01/Nov/2011. The end of the Follow-up period was up to 01/Nov/2013. The following variables were analyzed:

- Patients' **baseline characteristics**, including co-morbidities, ejection fraction at admission, type of anti platelet medication.
- Interventional **procedure variables** (indications for PCI, vessels treated, total number of stents per patient, type of stenting technique, total number of stents evaluated, stent length and diameter, mean deployment pressure).
- Details about the **performance of the device** were especially sought, e.g. (shaft breakage, balloon rupture, stent fracture, stent loss, stent thrombosis, in-stent restenosis).
- The clinical follow-up included assessment of major adverse cardiovascular events (MACE) based on patient **survival**; **target lesion revascularization**. The time points at which events were assessed were at the end of the PCI, at hospital discharge, every 3 month at year 1 and then every 6 months.

Patient population and baseline characteristics

- Patients included - 262
- Mean age - 65,4 years (38-87). Males - 141 (53.81%); Females - 121 (46.19%).
- The mean ejection fraction (EF) at admission was 54.1%.

Table 1 - Patients' Baseline characteristics-1

	Absolute number of patients	Percentage
Diabetes Mellitus	120	45.80
Hypertension	228	87.02
Dyslipidemia	224	85.49
Ejection fraction (EF) at admission		
EF<40%	14	5.34
EF-41-49%	48	18.32
EF>50%	200	76.33

PCI procedure

- PCI appropriateness was based on ESC guidelines
- Radial approach 5-7 F was preferred, although switch to femoral was done in isolated cases.
- The target lesions could be pretreated with a regular balloon angioplasty. Direct stenting was allowed. Postdilation was left on operator's discretion.
- BioMime SES device was available in the

Clinical scenario and lesions

- Stable forms of coronary artery disease (SCAD) - in 70 patients (26.72%);
- Unstable angina (UA) / non ST-elevation myocardial infarction (NSTEMI) - in 128 patients (48.85%);
- ST-elevation myocardial infarction (STEMI) - in 64 patients (24.43%).
- Total number of PCI procedures analyzed - 294, of which 262 as a first (index) one and 32 - staged due to multi-vessel coronary disease

Vessels treated and lesion subtypes

	Number of lesions	Percentage
Vessels treated		
Left main (LM)	9	2.82
Left Anterior descending (LAD)	160	50.16
Left circumflex (LCx)	92	28.84
Right coronary artery (RCA)	57	17.87
Sapheous venous graft (SVG)	1	0.31
Lesion types		
Chronic total occlusions (CTO)	11	4.62
Bifurcation (provisional 1 stent)	61	25.63
Direct stenting	125	52.52
PCI due to restenosis of BMS	41	17.23

Biomime stent parameters

399 BioMime stents were implanted in 319 arteries. Mean deployment pressure - 17,98 Bar.

Table 2 - Parameters of stents used

	Absolute number of stent implanted	Percent
Stent diameter (mm)		
2.5	77	19.3
2.75	110	27.57
3	110	27.57
3.5	73	18.3
4	22	5.51
4.5	7	1.75
Stent length (mm)		
8	26	6.52
13	49	12.28
16	58	14.54
19	67	16.79
24	63	15.79
29	61	15.28
32	32	8.02
37	31	7.77
40	12	3.01

Diagram 1 - Distribution of stent diameters

Stent and patient follow-up

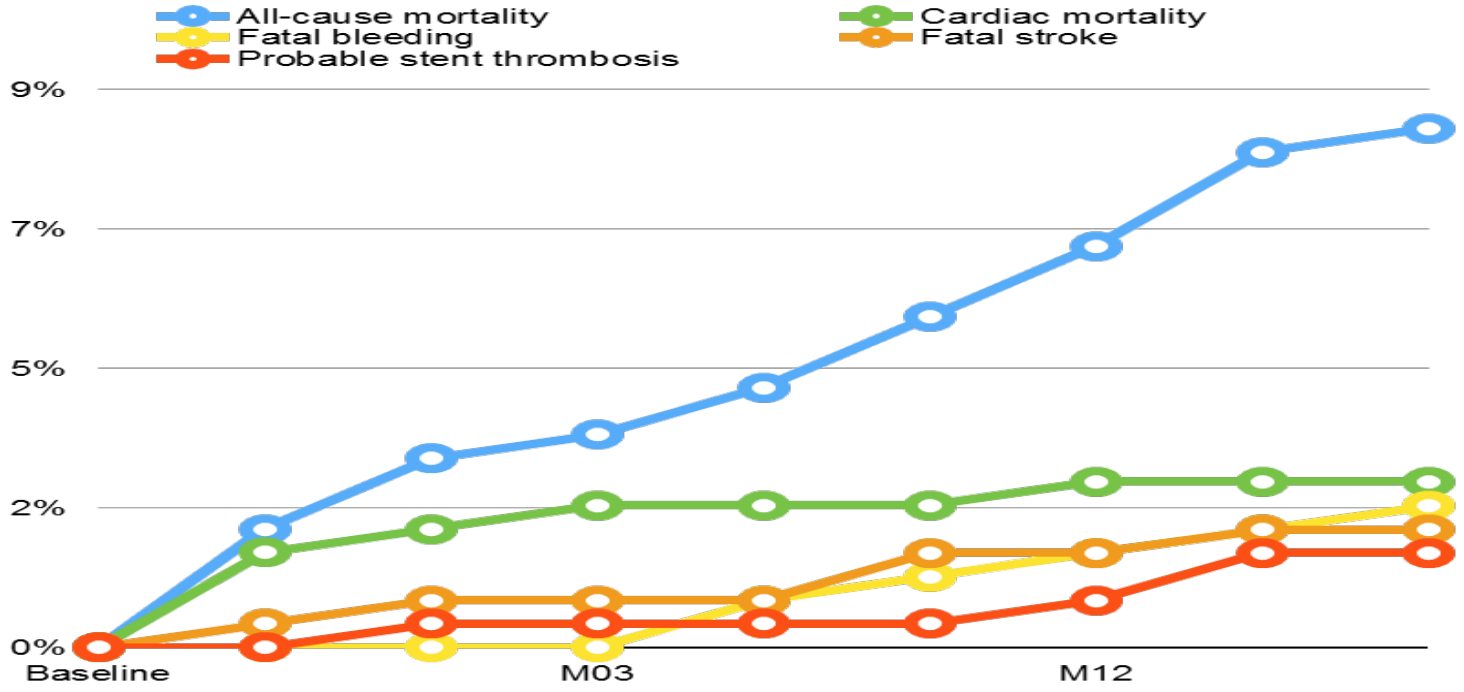
Stent performance: One case of shaft breakage. No cases of balloon rupture, stent fracture, stent migration or loss.

Six patients underwent target vessel revascularization (TLR) - 5 by PCI and 1 by CABG.

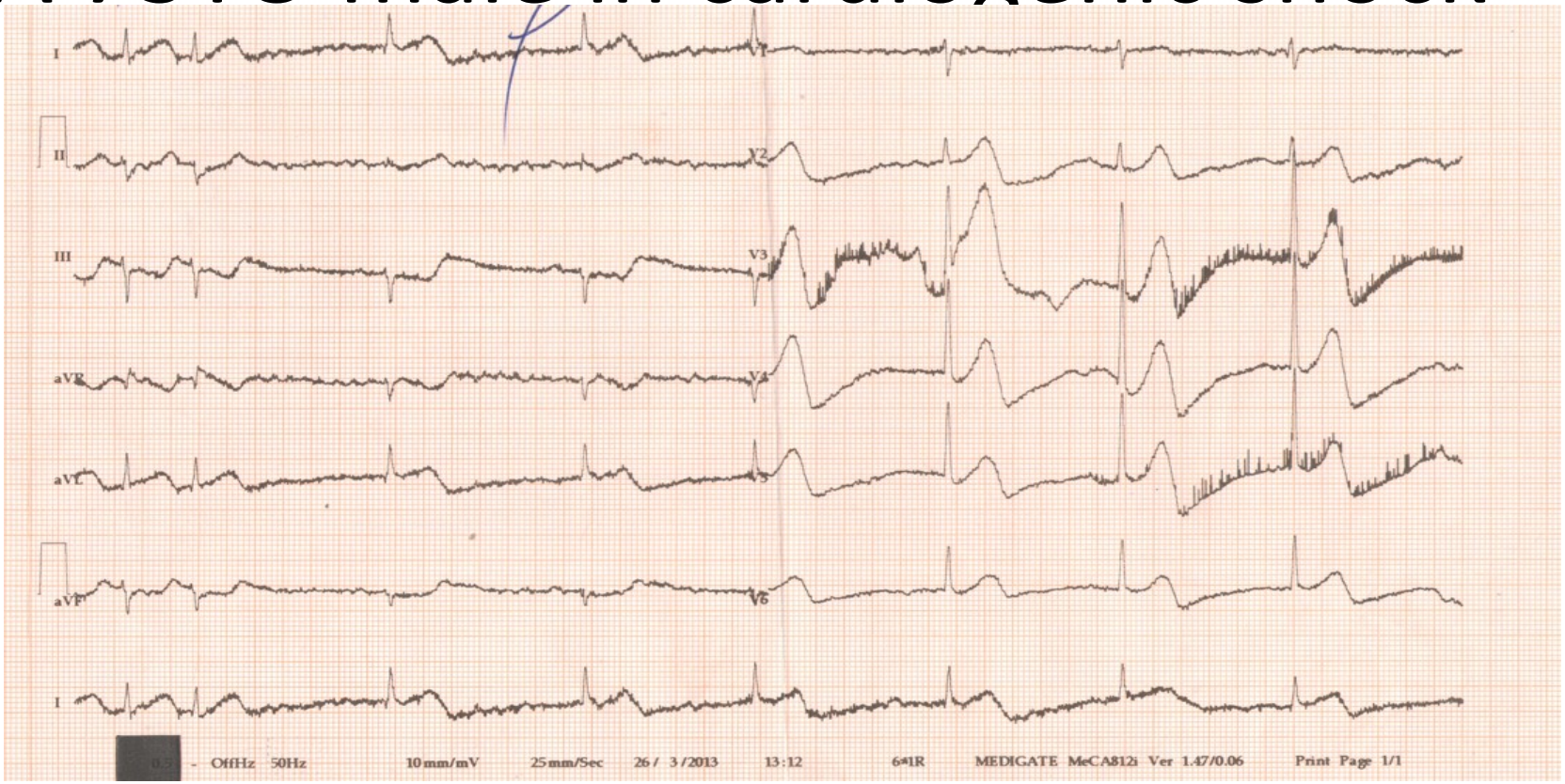
- 2 cases presented with definitive stent thrombosis and underwent urgent re-PCI.
- 4 cases presented with in-stent restenosis treated by PCI (balloon angioplasty, paclitaxel-eluting stent) in 3 cases and 1 had successful CABG. The restenosis cases were detected by a recurrence of angina.

The hard endpoints – survival

	Baseline	In hospital/Periprocedure	M01	M03	M06	M09	M12	M18	M24
All-cause mortality									
Cardiac mortality	#cases	4	1	1	0	0	1	0	0
Fatal bleeding	#cases	0	0	0	2	1	1	1	1
Fatal stroke	#cases	1	1	0	0	2	0	1	0
Probable stent thrombosis	#cases	0	1	0	0	0	1	2	0
All-cause mortality	0%	2%	3%	3%	4%	5%	6%	8%	8%
Cardiac mortality	0%	2%	2%	2%	2%	2%	3%	3%	3%
Fatal bleeding	0%	0%	0%	0%	1%	1%	2%	2%	2%
Fatal stroke	0%	0%	1%	1%	1%	2%	2%	2%	2%
Probable stent thrombosis	0%	0%	0%	0%	0%	0%	1%	2%	2%



Case presentation
A 73YO male in cardiogenic shock



Diagnosis, noninvasive evaluation and therapeutic strategy

Diagnosis

- CAD. STEMI – anterior. Cardiogenic shock.

Initial lab evaluation

- eGFR – 59,9ml/min/1,73m2; Hb – 124g/l; CK, CK-MB – still negative

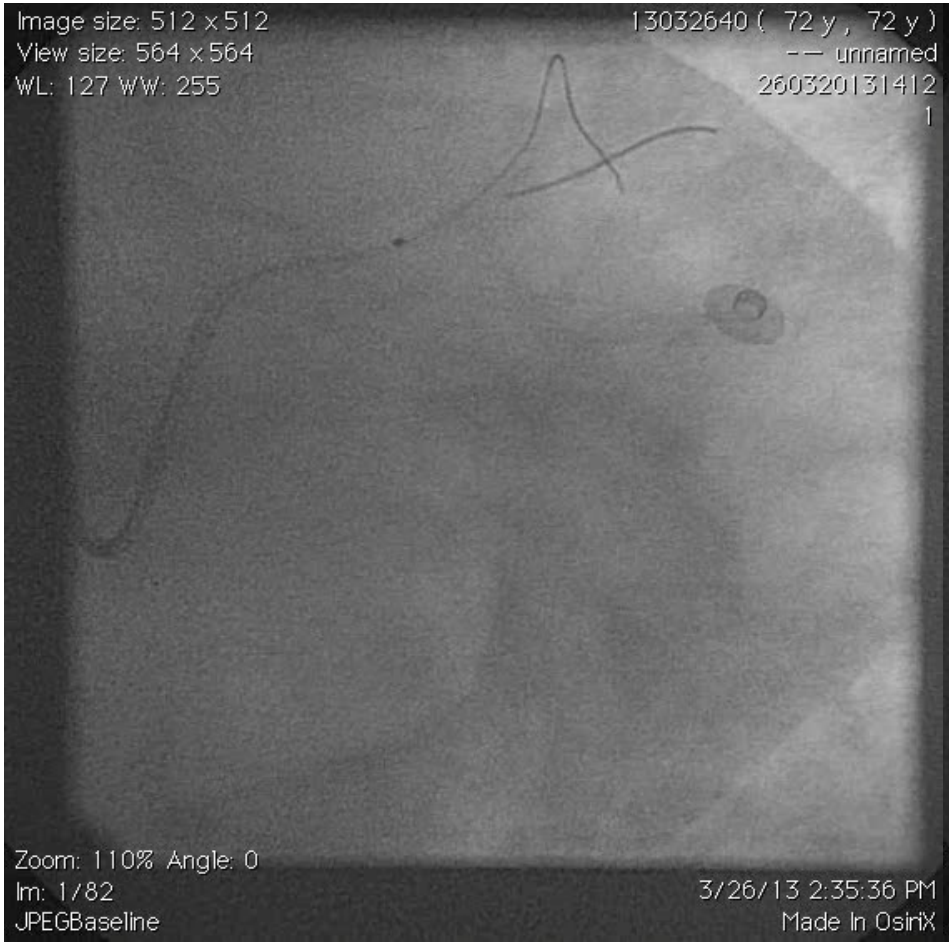
Therapeutic strategy

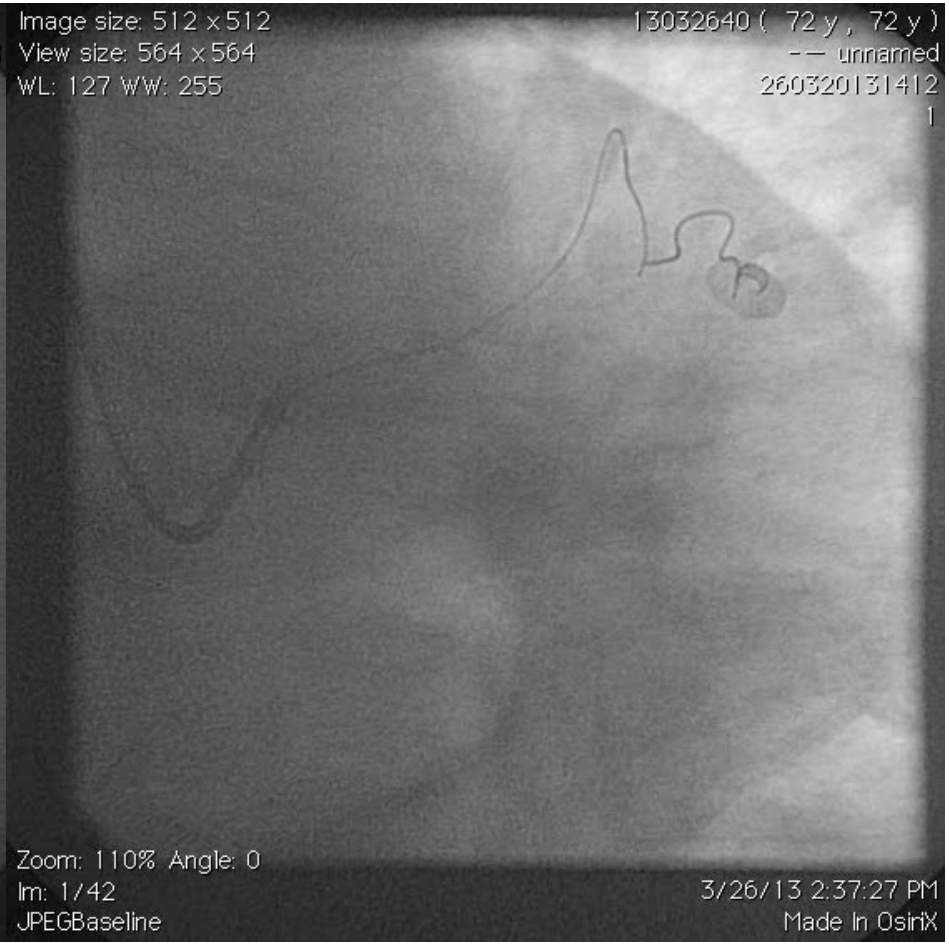
- Immediate loading with antiplatelets and anticoagulants - Brilique – 180mg, ASA – 250mg, Heparin 5000 IU bolus
- Hemodynamic stabilization – Dopamin 5mcg/kg/min, Furosemide – 60mg iv.

CAG – Proximal thrombosis of LAD, no significant stenoses of Cx and RCA

Invasive strategy

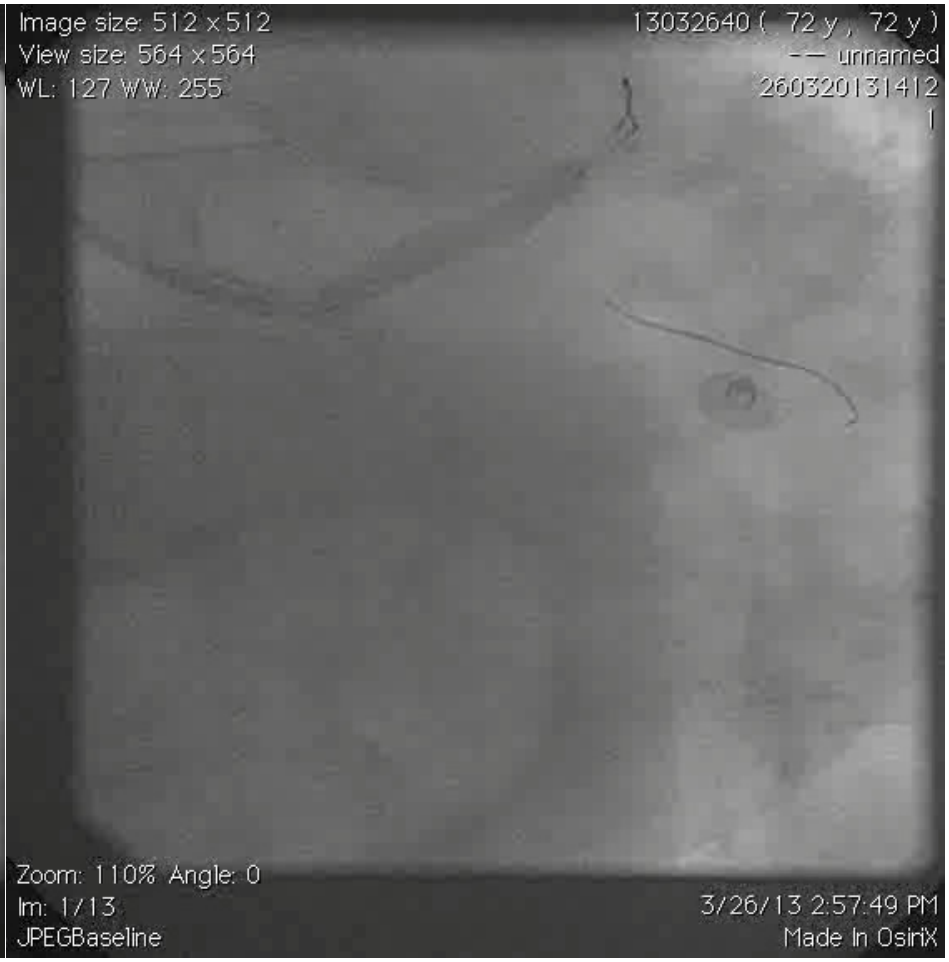
TA of LAD and D1. Decision for stenting of LM





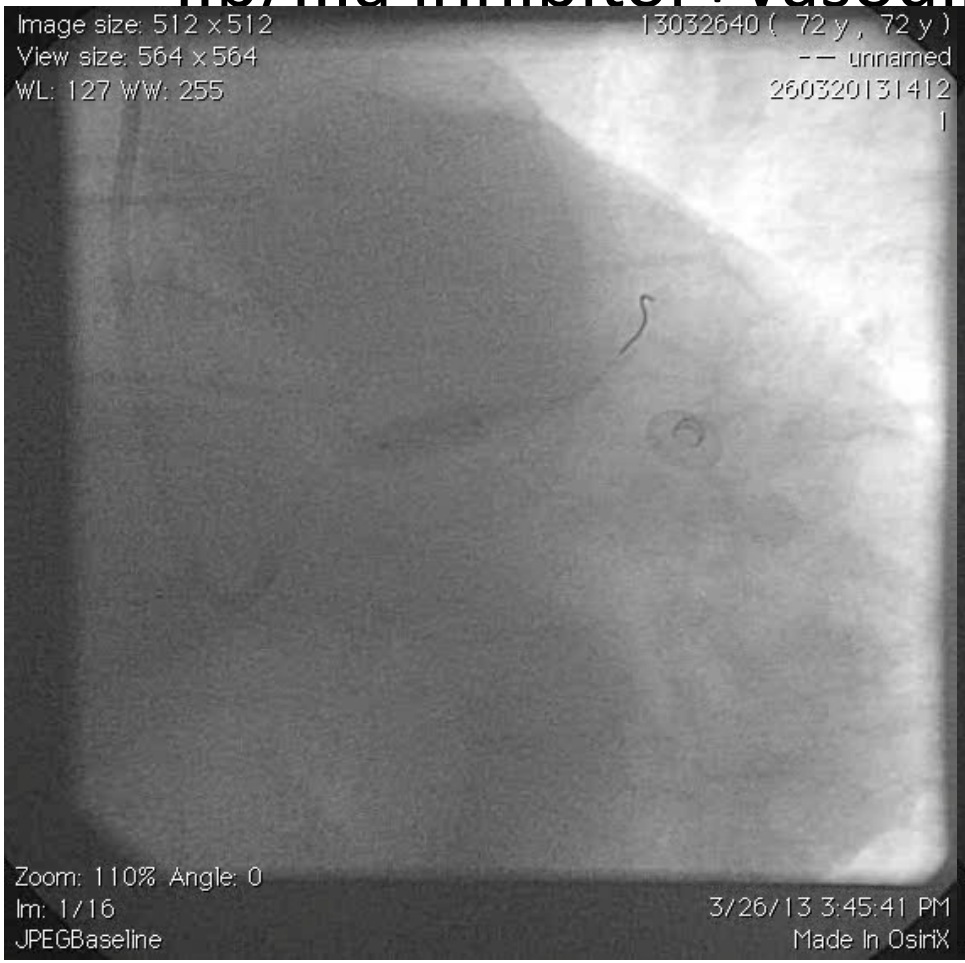
Invasive strategy (2)

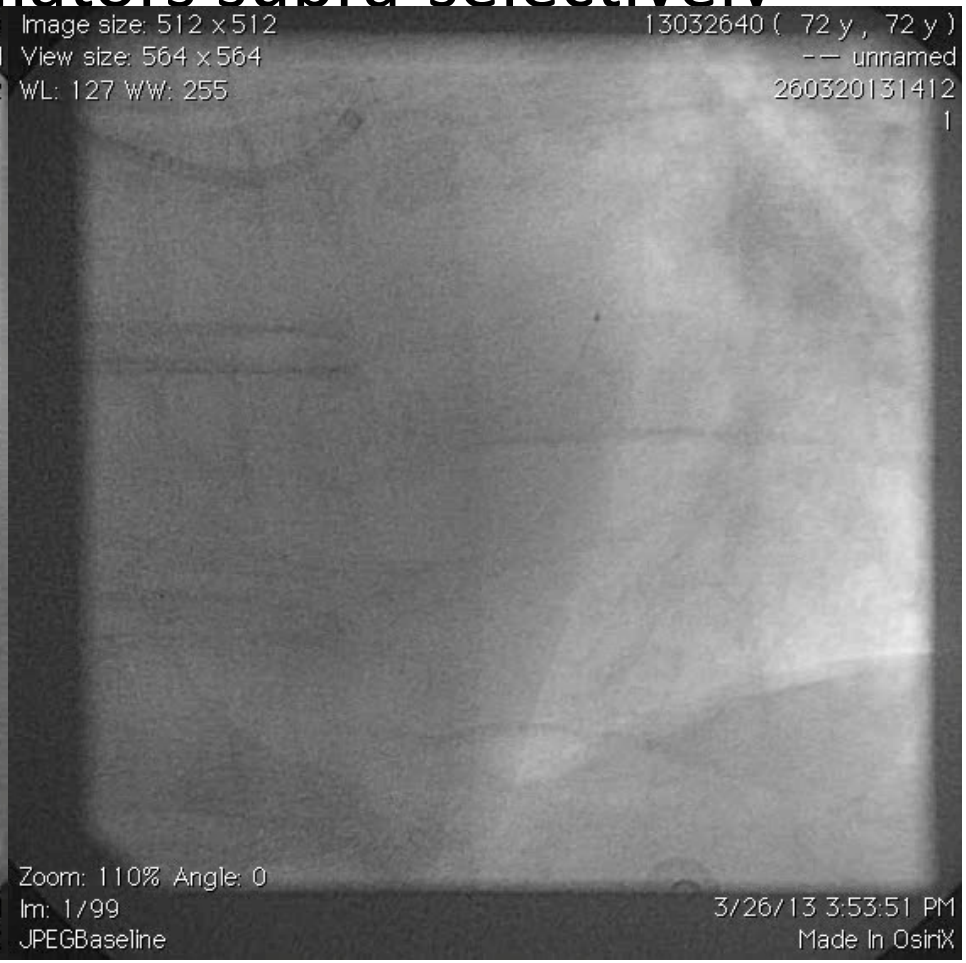
Implantation of Biomime 4,0x29mm in LM



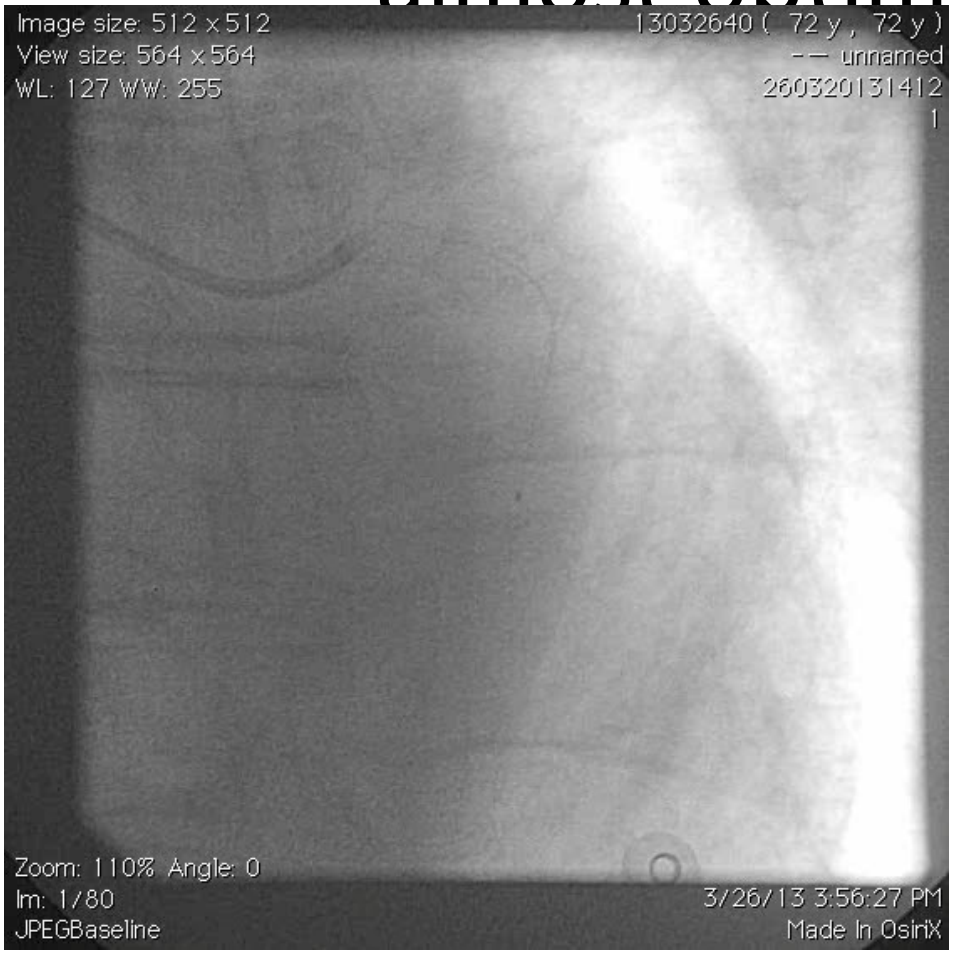
POT in LM

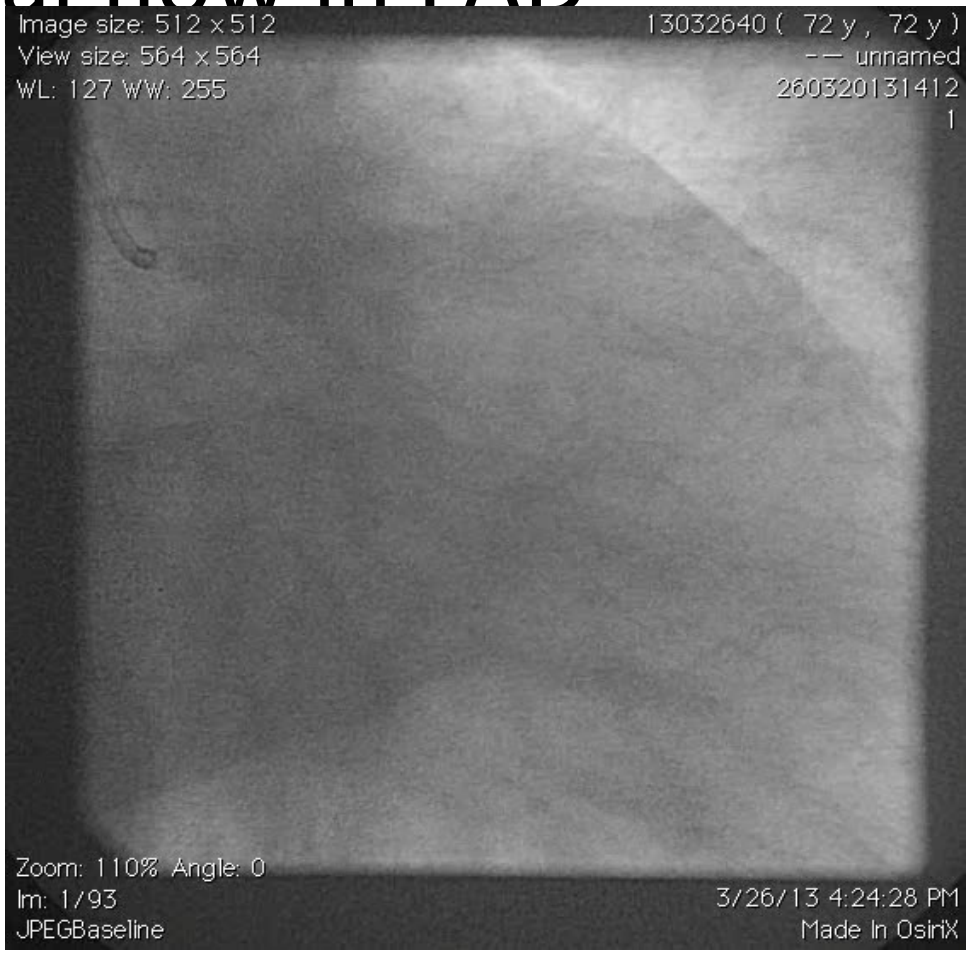
after which No-Reflow in LAD – treated with local IIb/IIIa inhibitor+Vasodilators supra-selectively





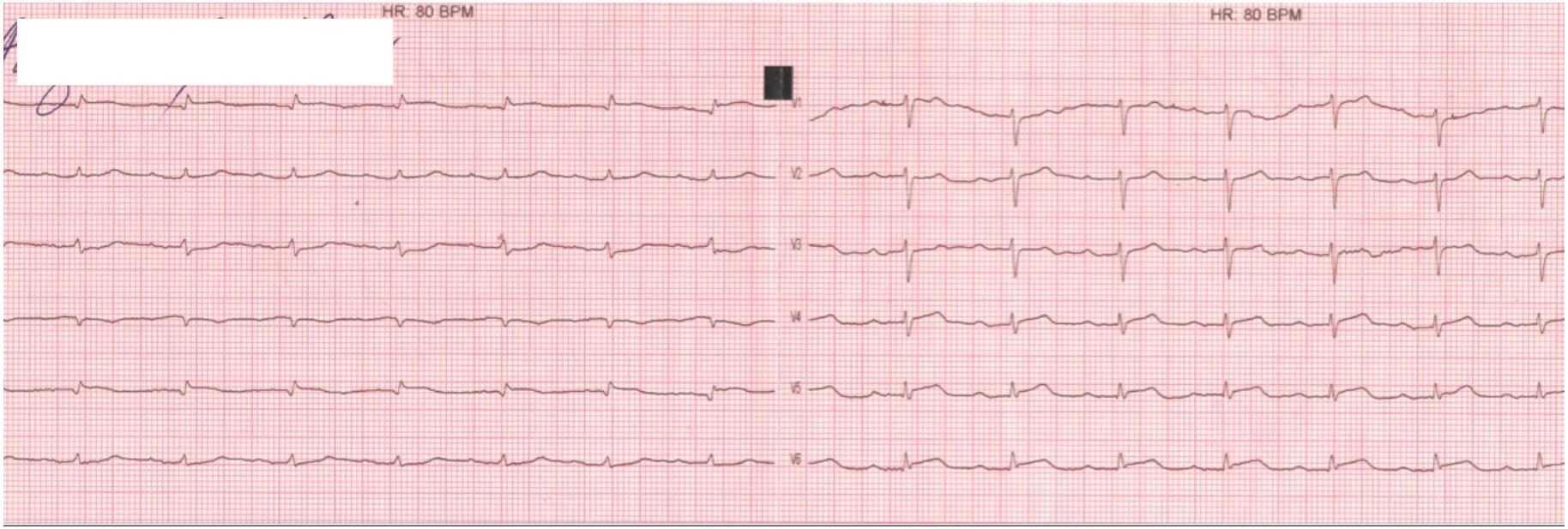
Optimal final angiografic result with almost optimal flow in LAD



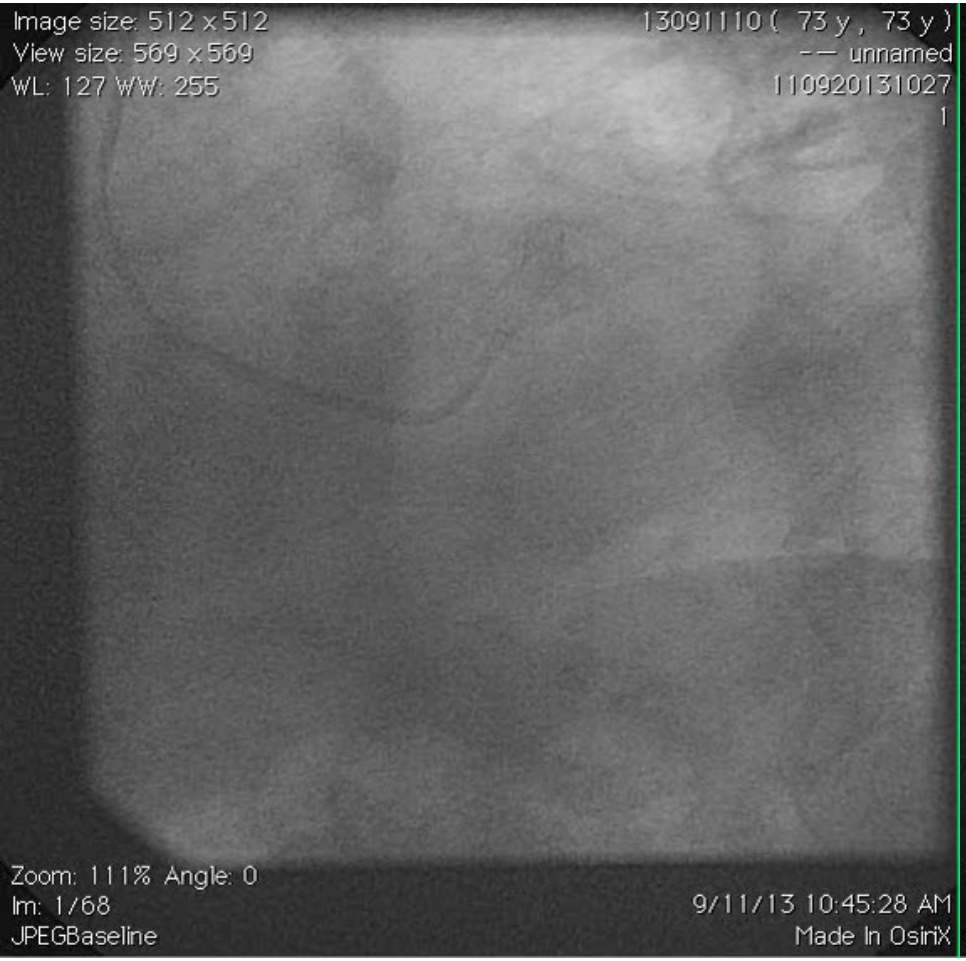


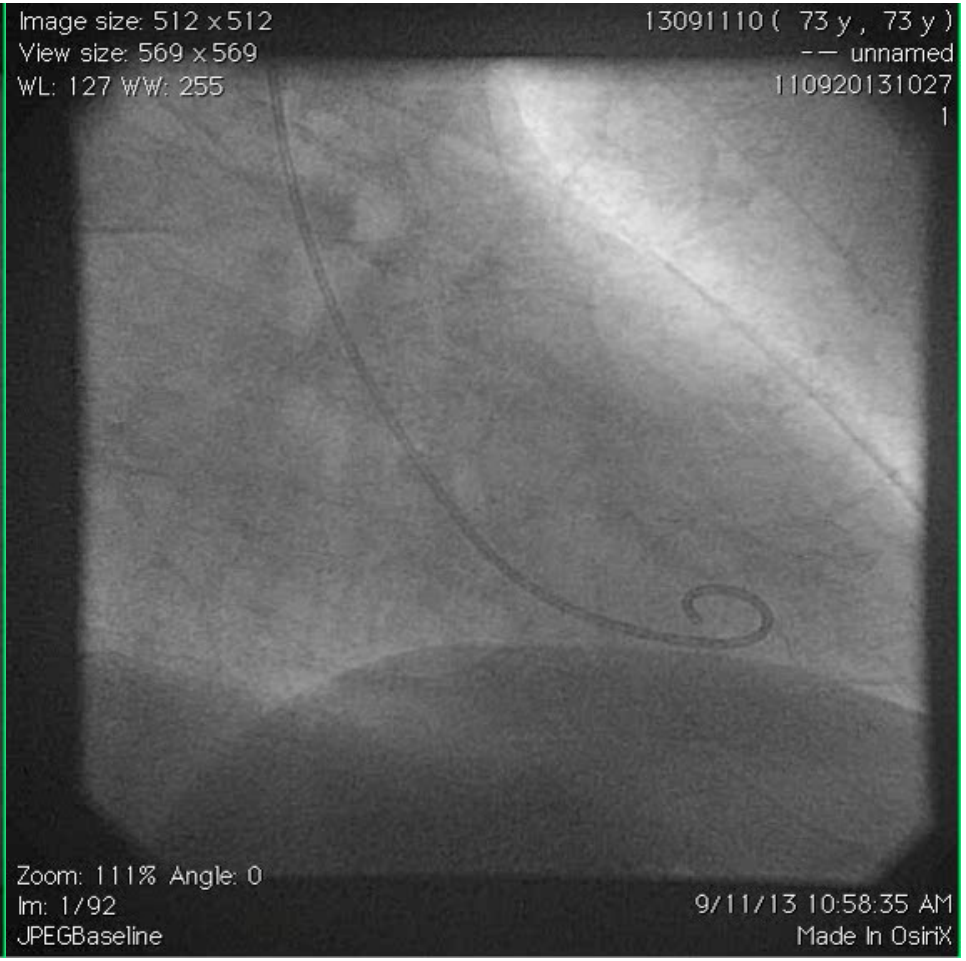
Postprocedure period

- Impressive ECG resolution after PPCI.
- Cardiac echo with LVEF – 35%.
- Peak of CK/MB – 3920/176 IU/L.



6Month angiographic follow-up
Optimal result of PCI. LVEF-56%



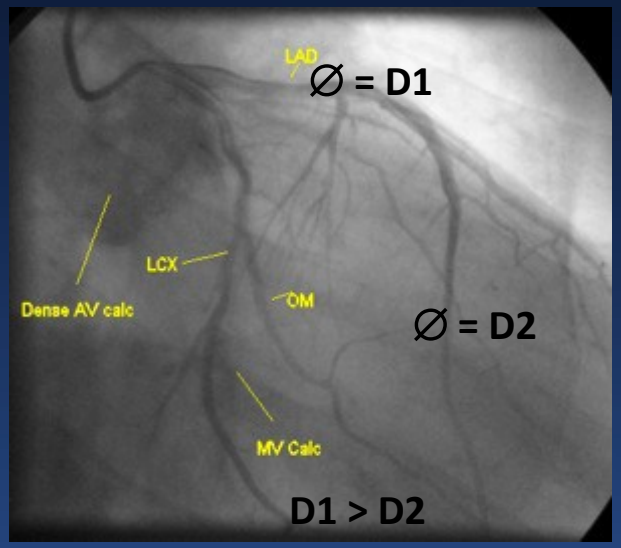


Biomime Morph stent

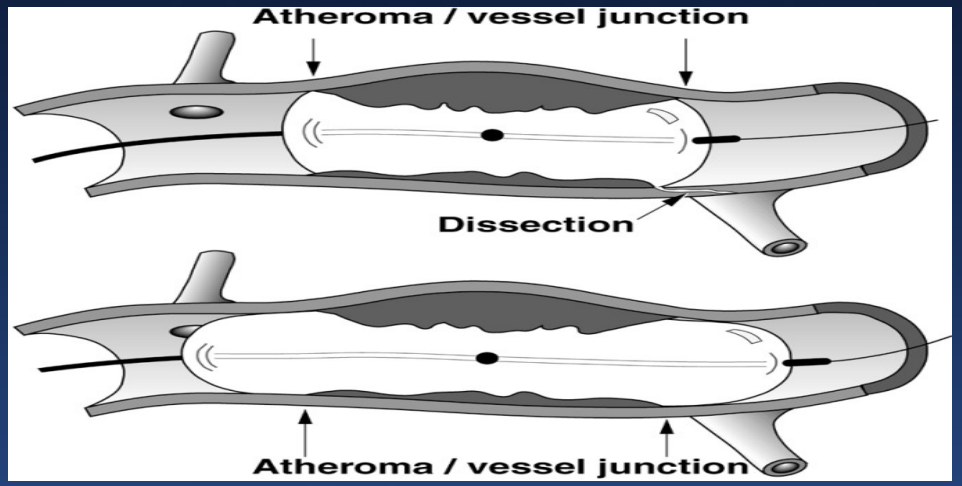
design and concept

Natural Taper of Coronary Arteries

- Most branching coronary arteries taper in diameter by at least 0.5 mm over 20 mm of vessel length.
- Significant tapering often poses a problem for optimal balloon sizing, especially for long lesions.

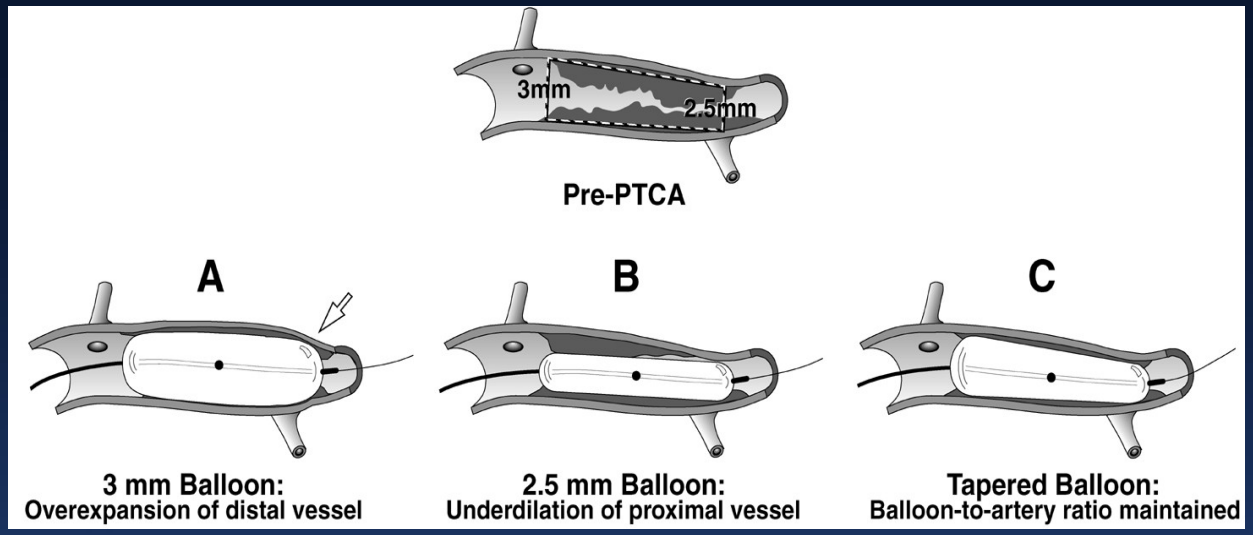


Long Lesion & small Vessel



Natural Taper of Coronary Arteries

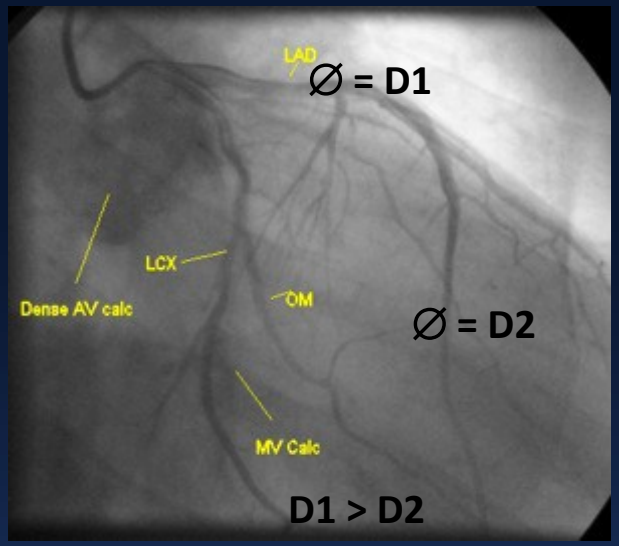
- In addition, natural shape of coronary arteries tapers from proximal to distal and this becomes more pronounced as the artery throws up branches. While conventional stents are available only in cylindrical shapes and these alter the vessel anatomy rendering the vessel less flexible.



A. Sizing to match the proximal segment results in overdilating the distal segment, increasing the risk of dissection.
B. Sizing to match the distal segment results in underdilating the proximal segment.
C. A tapered stenting theoretically ensures better matching of balloon/stent and vessel size.

Current Clinical Practice

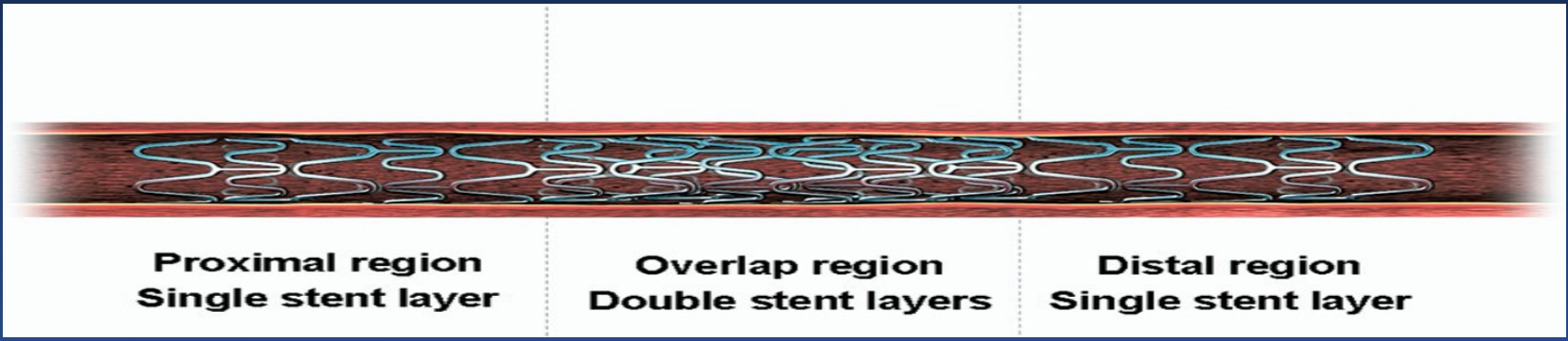
- In the present scenario, there is a compulsion to use two stents to treat lesions having length > 48 mm
- Stents of length >48 mm are not commercially available
- Additionally, long and diffuse lesions with frequent side branches often taper proximal to distally



- Overlapping DES are associated with increased risk of inflammation and delayed healing response

Limitations of Overlap Stenting

- Interestingly overlapping of stents required to treat long lesions is known to be a potential site for restenosis and stent thrombosis (due to malapposed struts) and also potentially jail important side branches.
- Overlapped stented lesion divides into 3 regions - proximal single stent layer, middle overlapping double stent layers, and distal single stent layer. There is a potential for delayed healing in such overlapping segments.



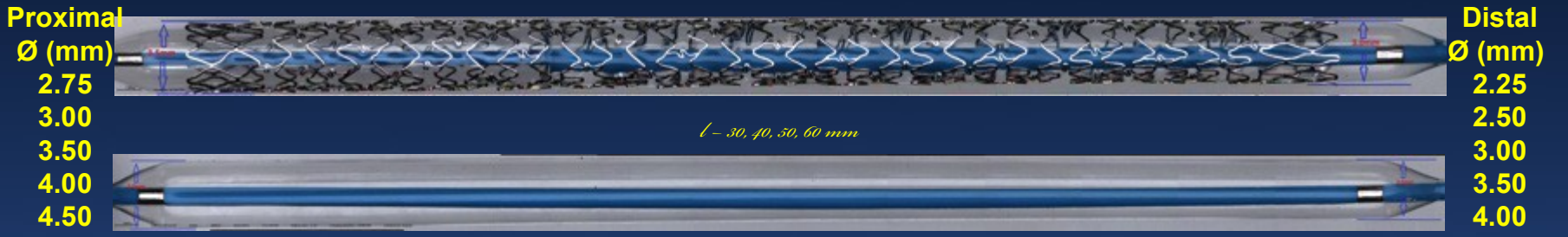
BioMime Morph – The Concept

- These long and tapered stents are designed to deploy across the **single long length stenosed lesion** to cover multiple blockages of the **tapered coronary artery.**
- The purpose of tapered stent system is for stenting the de novo lesions having length ≤ 56 mm in coronary arteries like LAD, LCx.
- These stents are used to position in the proximal, mid & distal segment of the diseased coronary artery with adaptability to artery anatomy i.e.,
  - Vessel conformability
  - Homogenous radial force
  - Mechanical stress
  - Stent-arterial wall ratio along the stented segment.

BioMime Morph –

Sirolimus Eluting Tapered Coronary Stent System

- Provide anatomically correct treatment.
- Avoid overlapping – thus fracture & restenosis.
- Treat long diffused lesions with a single stent – one and done.
- Reduce procedural time.
- Avoid over radiation and contrast.
- Save costs – less $ than multiple tandem stents.

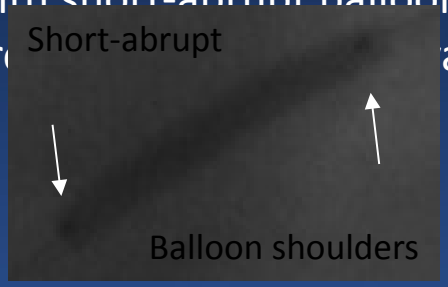


- Hybrid cell design structure - open cells in the mid and close cells at the edges.
- Maintains high radial strength and uncompromised flexibility.
- 1.25 µg/mm2 of Sirolimus formulated with biodegradable polymer mix of PLLA+PLGA.
- Mounted on a newly created extra support Rx balloon catheter with ½ size tapered diameters.

BioMime Morph

Stent Architecture

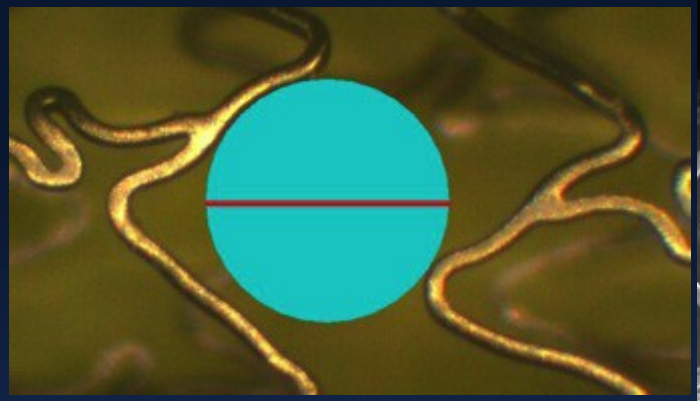
- Cobalt chromium (L605) platform with 65µm strut thickness.
- Hybrid cell design comprising of an intelligent mix of open and close cells resulting in excellent radial strength with a high flexibility.
- Unique strut width variability that ensure a <3% recoil and 0.29% foreshortening.
- Special electro-polishing technique eliminates surface nickel oxides.
- Stent is mounted on a flexible Rx PTCA Balloon catheter with short-abrupt balloon shoulders, having a pr ascular injury



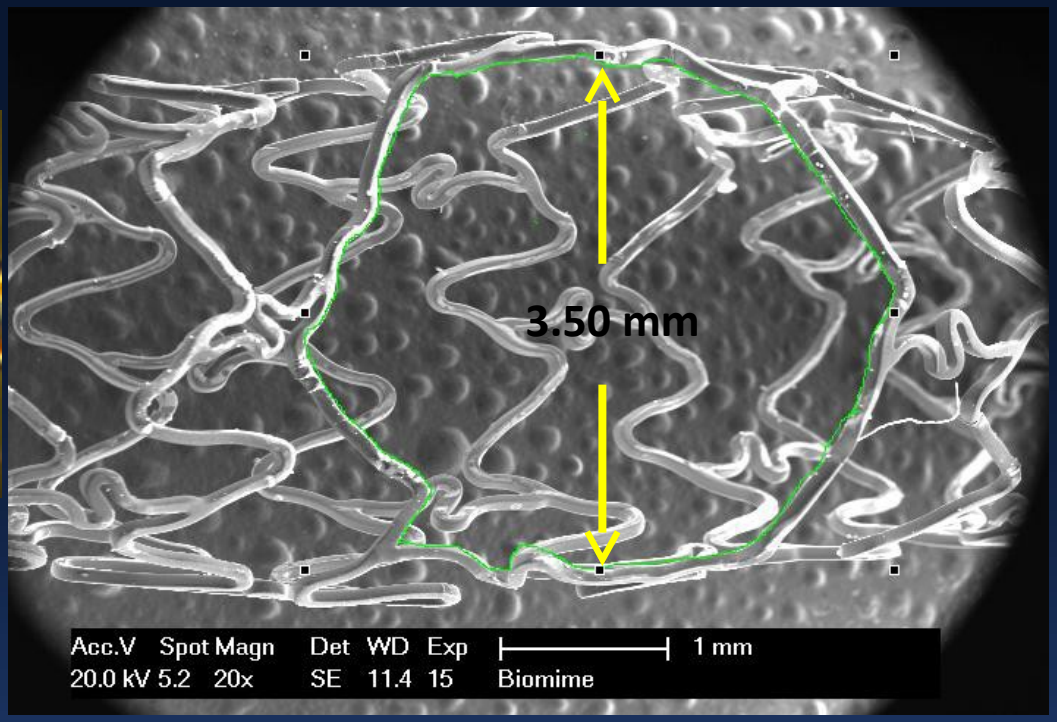
65µm Co-Cr L605 stent struts

Open cells in mid segment Close cells at edges

BioMime Morph –
Side Branch Access/Retention



The area of the largest circle circumscribable in the cell of the stent expanded to the nominal diameter:
Tc = 0.71 mm2



The expanded BIOMIME 3.0 x 16 mm stent after side branch expansion

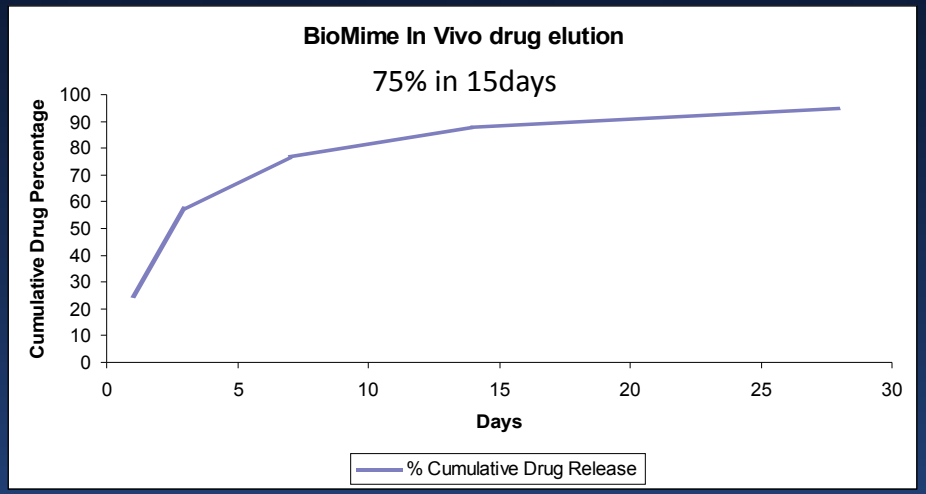
Expanded cell perimeter that ensures side branch access: KSBA = 11.29 mm

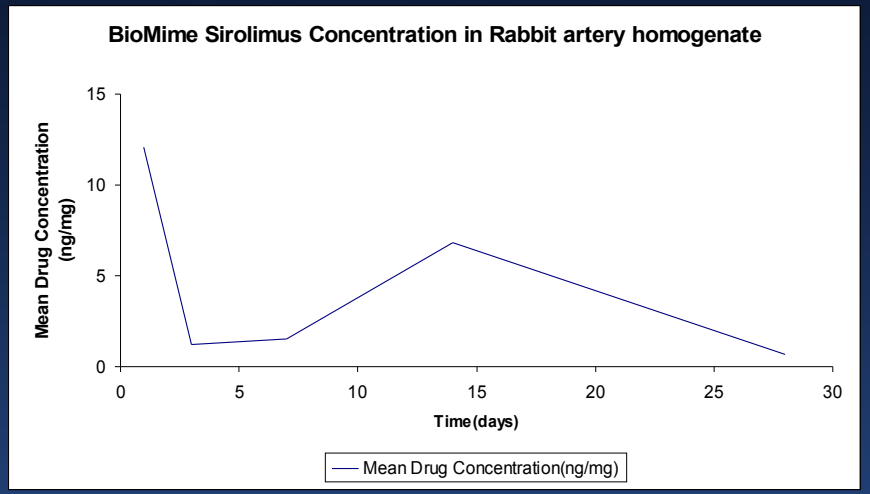
Expanded cell area that ensures side branch access: TSBA = 8.00 mm2

BioMime Morph –
Drug (Sirolimus)

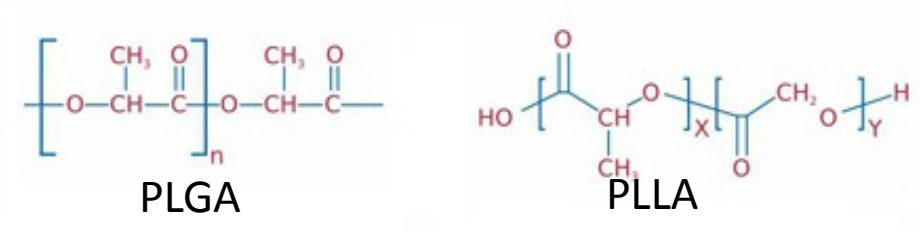
- Sirolimus is an ideal choice considering that it acts on the common final pathway of cell division cycle without exceptional risk of necrosis induction

1.25µgm/mm2 of Sirolimus loading





BioMime Morph –
Biodegradable Polymer BioPolyTM



- BioPoly is Meril's propriety bio-degradable co-polymer formulation.
- The principle mode of BioPolyTM degradation is hydrolysis via mass loss & by products are excreted as CO2and H2O via Kreb's cycle
- The material offers uniformity in stent coating & thin coating of <2µm is possible
- Does-not web, crack, lump or on stent or balloon surface

Conclusion

- Long diffused lesions can be better treated with single long stents to minimize the risk of fracture, binary restenosis and associated adverse events
- Long single stents are also convenience from procedural perspective and allow for reduction of costs
- Simultaneously branching Coronary arteries tend to taper and anatomically designed tapered stents may proved to be better in

Thank you for your attention