



BEGIN: Randomized trial of DP-EES vs. BD-BES for true bifurcation lesion

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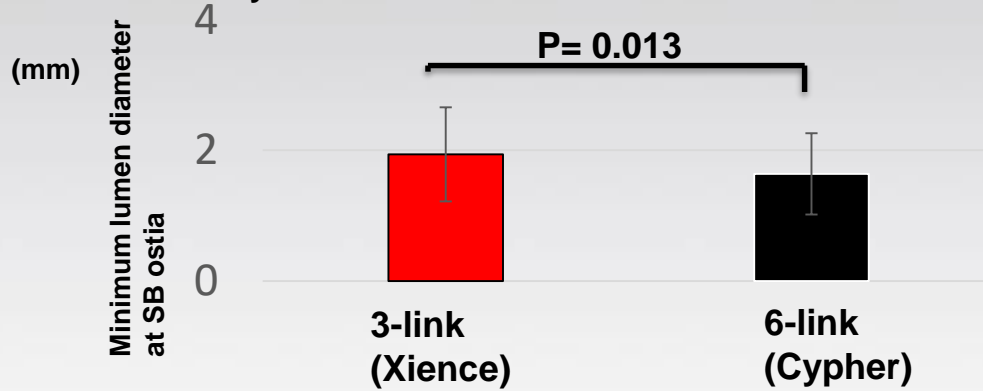
(10)Department of cardiology, Kurashiki Central Hospital, Kurashiki, Japan

Dr. Kazuaki Mitsudo deceased on 18. Oct. 2015



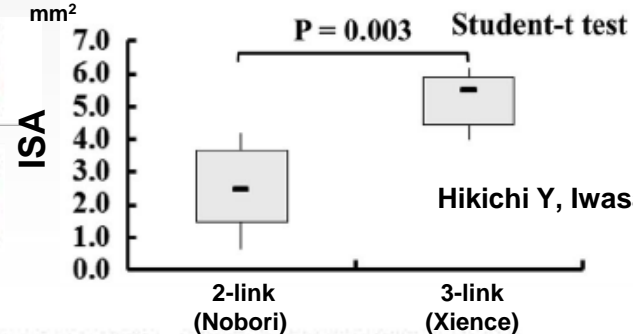
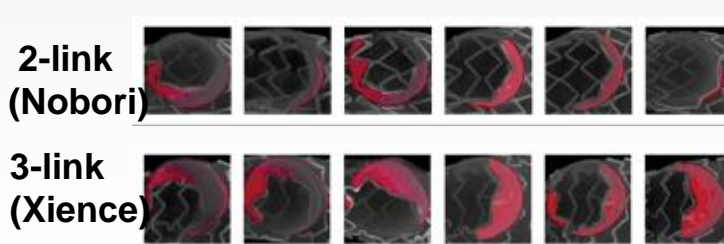
Smaller number of links connecting metal hoops has been reported to be associated with better SB results after bifurcation PCI

☑ SEA-SIDE trial (SES vs. EES) ; 3-link system is better than 6-link in regard of MLD at SB ostium immediately after bifurcation PCI



Burzotta F JACC CVI 2011

☑ Bent test showed 2 link Nobori compared to 3-link Xience reduced in-stent apposition rate at SB ostium



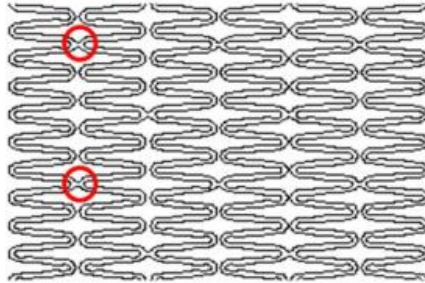
Hikichi Y, Iwasaki K, CVIT2016



Nobori (Terumo, Tokyo, Japan), a biolimus-eluting stent (BES) made of stainless steel with an abluminal biodegradable polymer, is a 2-link DES. Different from global design (3.5 mm 3-link with 9 crowns, Biomatrix), inter-strut dilation diameter in the Japanese design (3.5 mm 2-link with 10 crowns) is the maximum at 4.2 mm

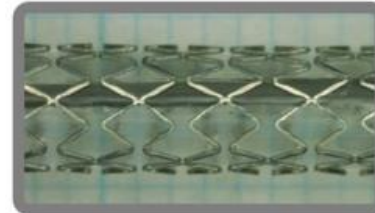
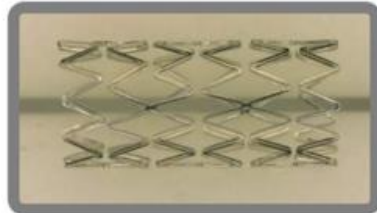
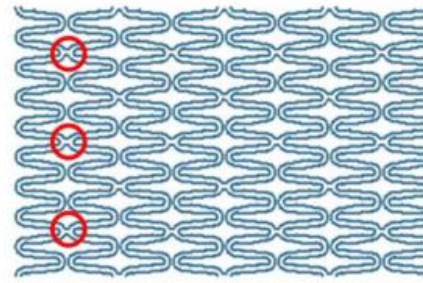
Japanese design

2-link 10 crowns



Global design

3-link 9 crowns



Nakao F, Heart and Vessel 2016



Hypothesis

We hypothesized that the design of the 2-link BES (Nobori) platform, because of its higher possibility of dilating and device access in the SB than that of the 3-link EES(Xience), could improve the angiographic results at the SB orifice.



BEGIN trial (enrollment from 34 centers in Japan)

P.I Toshiya Muramatsu. M.D
(Saiseikai Yokohama City Eastern Hospital)

Adviser: Kazuaki Mitsudo M.D
(Kurashiki Central Hospital)

Steering committee, clinical research organization ; Kurashiki Central Hospital
Clinical Research Center, (Kurashiki, Japan),

Angiographic core laboratory ; Japan
Cardiovascular Imaging Core Laboratory
[JCICL], (Tokyo, Japan)

Statisticians ;AC Medical Inc., (Tokyo, Japan)

Sponsor ; TERUMO Japan, Tokyo



Participating center (>3 cases enrolled)	Enrolled case number
Saiseikai Yokohama City Eastern Hospital	32
Yokohama Shintoshi Neurosurgery Hospital	31
Kurashiki Central Hospital	30
Tokushima Red Cross Hospital	16
Iwate Medical University Hospital	15
Toyohashi Heart Center	14
Ako City Hospital	10
Tsukuba Medical Center	10
Kochi Medical Center	8
Chikamori Hospital	8
Yokohama City University Medical Center.	8
Miyazaki Medical Association Hospital	6
Edogawa Hospital	5
Ogaki City Hospital	5
Okamura Memorial Hospital	5
Toho University Oomori Hospital	5
Shiroyama Hospital	4
Tokai University Hospital	4
Tokyo University Hospital	4
Saga University Hospital	3
Fukuoka Wajiro Hospital	3



Inclusion and exclusion criteria

- ✓ **de novo and true coronary bifurcation**, $\geq 50\%$ diameter stenosis (DS) in the MV and SB belonging to **Medina classes (1.1.1), (1.0.1), and (0.1.1)**
- ✓ visually estimated target lesion reference vessel diameter (RVD), 2.5–5.0 mm in the MV, and **≥ 2.25 mm in the SB**
- ✓ target CBLs treatable with one or two stents in both branches (treatable within 4 stents in lesions including CBLs);
- ✓ One target bifurcation per patient treated with the study device was enrolled.



Exclusion criteria

- ✓ Pregnancy
- ✓ Life expectancy < 1 year
- ✓ acute myocardial infarction (MI) within 1 week
- ✓ left ventricular ejection fraction $< 30\%$
- ✓ Scheduled for elective treatment requiring antiplatelet drug withdrawal
- ✓ 3-vessel diseases
- ✓ Serum creatinine level ≥ 2.0 mg/dL.
- ✓ Vascular morphological restriction criteria included lesions proximal to coronary artery bypass graft anastomotic site (visual estimation ≤ 5.0 mm) or including a part of the coronary artery bypass grafting
- ✓ in-stent restenosis
- ✓ severe calcification or usage of debulking device (rotablator or directional coronary atherectomy).

Procedure consensus in study group

- Re-wire at near carina (distal cell) using IVUS guided or double-lumen catheter



- 1 stenting + final kissing is default technique. **Culotte or TAP is recommended** for elective or bail-out 2-stent technique (**× Crush**)

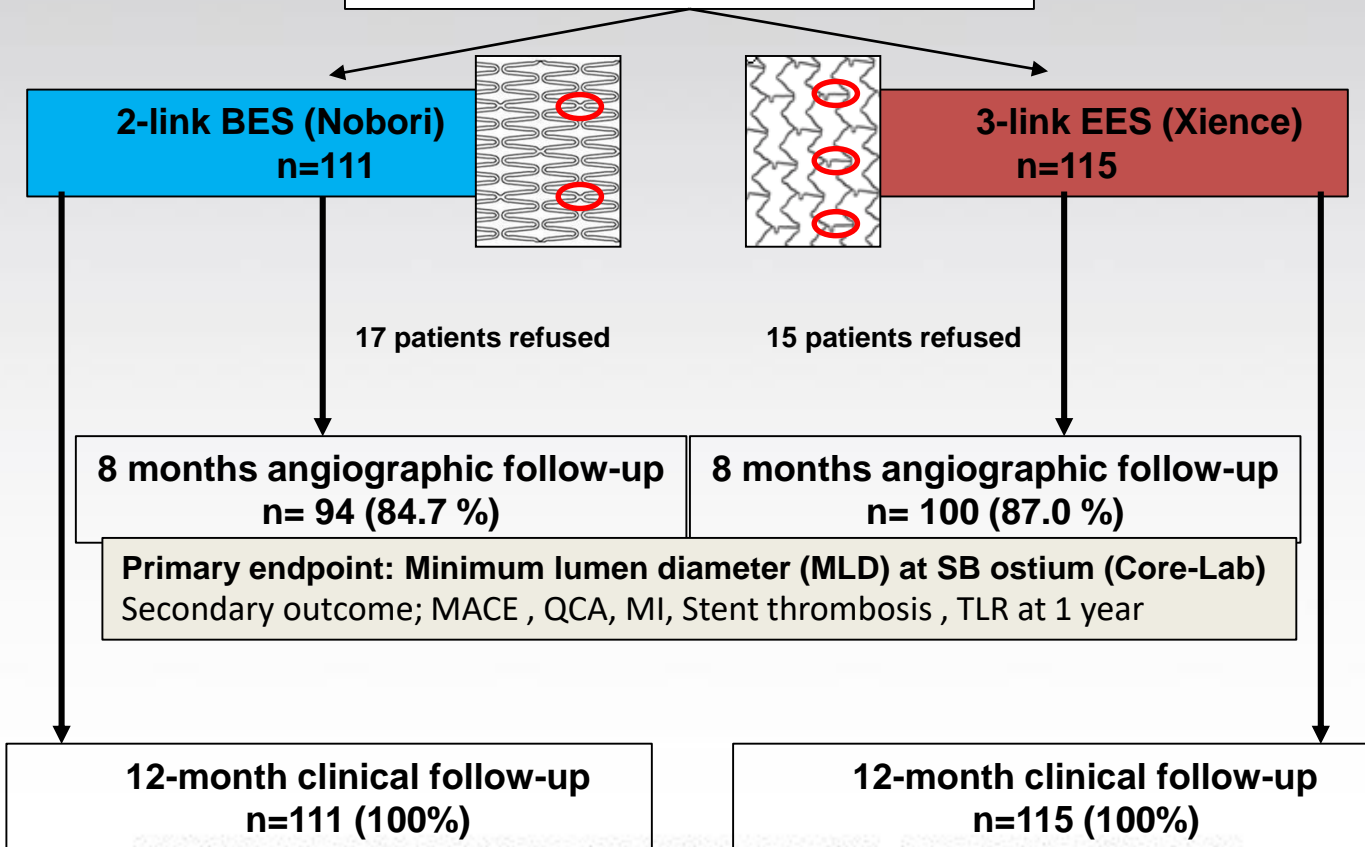
- Final kissing inflation** is recommended.

- SB endpoint : diameter stenosis <50% in visual**





BEGIN trial (NCT01574586)
226 patients enrolled and randomized
Between April 2012 and May 2014





Patient background

	2-link BES (n = 111)	3-link EES (n = 115)	P value
Age, years	70 ± 10	69 ± 10	0.676
Male	87 (78.4)	83(72.2)	0.286
Hypertension	88 (79.3)	71 (61.7)	0.005
Dyslipidemia	84 (75.7)	89 (77.4)	0.875
Diabetes mellitus	43 (38.7)	50 (43.5)	0.501
Current smoking	18 (16.2)	14 (12.2)	0.310
Previous			
- PCI	45 (40.5)	41 (35.7)	0.494
-CABG	2 (1.8)	3 (2.6)	1.000
-myocardial infarction	23 (20.7)	20 (17.4)	0.611
Family history of CAD	13 (11.7)	13 (11.3)	1.000
LV ejection fraction, %	61.7 ± 11.2	62.9 ± 10.0	0.413
Present status			
-Stable angina pectoris	83 (74.8)	90 (78.3)	0.430
-Unstable angina pectoris	8 (7.2)	11 (9.6)	
-Silent MI	20 (18.0)	14 (12.2)	



Lesion and procedural background

	2-link BES (n = 111)	3-link EES (n = 115)	P value
Target vessel			
Left main coronary artery	15 (13.5)	15 (13.0)	0.843
Left descending anterior artery	70 (63.1)	69 (60.0)	
Left circumflex artery	14 (12.6)	14 (12.2)	
Right coronary artery	11 (9.9)	16 (13.9)	
Medina classification			
(0.1.1)	22 (19.8)	27 (23.5)	0.813
(1.0.1)	11 (9.9)	11 (9.6)	
(1.1.1)	78 (70.3)	77 (67.0)	
IVUS use (both pre- and post-procedure)	105 (94.6)	103 (89.6)	0.539
Pre-dilation for main vessel	106 (95.5)	109 (94.8)	1.000
Pre-dilation for side branch*	61 (55.5)	60 (54.1)	0.608
Proximal optimization technique*	5 (4.5)	11 (9.9)	0.112



Lesion and procedural background

	2-link BES (n = 111)	3-link EES (n = 115)	P value
Stent deployment technique			0.496
Single crossover stenting with FKI	74 (66.7)	84 (73.0)	
Single crossover stenting without FKI	2 (1.8)	5 (4.3)	
Provisional culottes stenting	21 (18.9)	16 (13.9)	
Provisional T-stenting	2 (1.8)	1 (0.9)	
Elective culottes stenting	9 (8.1)	9 (7.8)	
Elective T-stenting	2 (1.8)	0 (0)	
Stent diameter in main vessel, mm	3.1 ± 0.4	3.0 ± 0.4	0.544
Stent inflation pressure in main vessel, atm	11.0 ± 3.4	12.0 ± 3.8	0.045
Final kissing balloon inflation	108 (97.3)	110 (95.7)	0.722
-balloon diameter in main vessel, mm	3.0 ± 0.4	3.0 ± 0.4	0.358
-balloon pressure in main vessel, atm	10.0 ± 3.6	10.7 ± 4.3	0.254
-balloon diameter in side branch, mm	2.4 ± 0.3	2.4 ± 0.4	0.809
-balloon pressure in side branch, atm	9.5 ± 3.4	10.0 ± 3.7	0.248
Dissection in side branch ostium*	5 (4.5)	8 (7.2)	0.284
Max CPK-MB, ng/mL	16.5 ± 21.8	16.0 ± 25.2	0.582

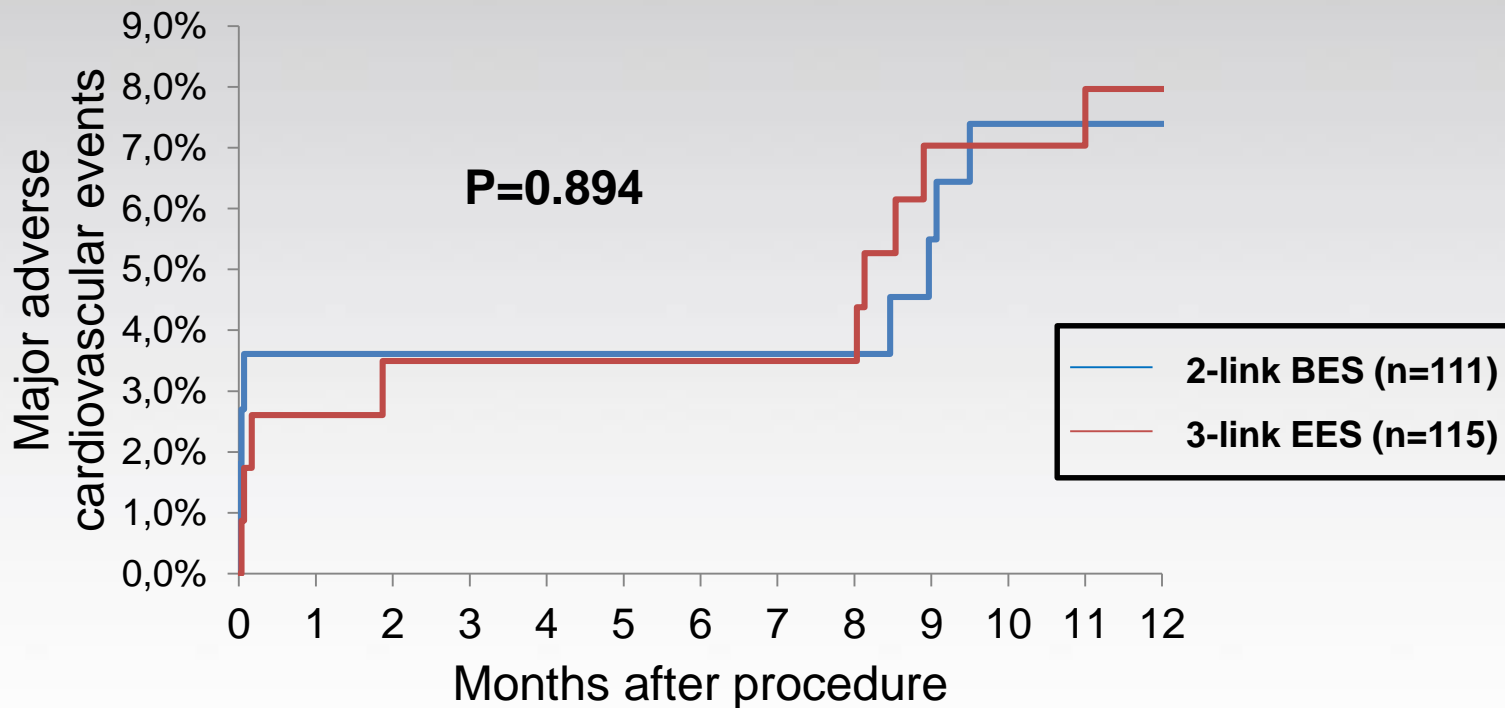


Clinical outcome at 1 year

	2-link BES (n = 111)	3-link EES (n = 115)	P value
Major adverse cardiovascular events	8 (7.4)	9 (8)	0.894
Cardiac death	0 (0)	1 (0.9)	0.339
Non-cardiac death	0 (0)	0 (0)	-
Myocardial infarction	4 (3.6)	3 (2.6)	0.654
Target vessel revascularization	8 (7.6)	7 (6.2)	0.573
Target lesion revascularization	5 (4.8)	3 (2.7)	0.280
TLR for target bifurcation	4 (3.8)	2 (1.8)	0.378
Stent thrombosis	1 (0.9)	2 (1.7)	1.000



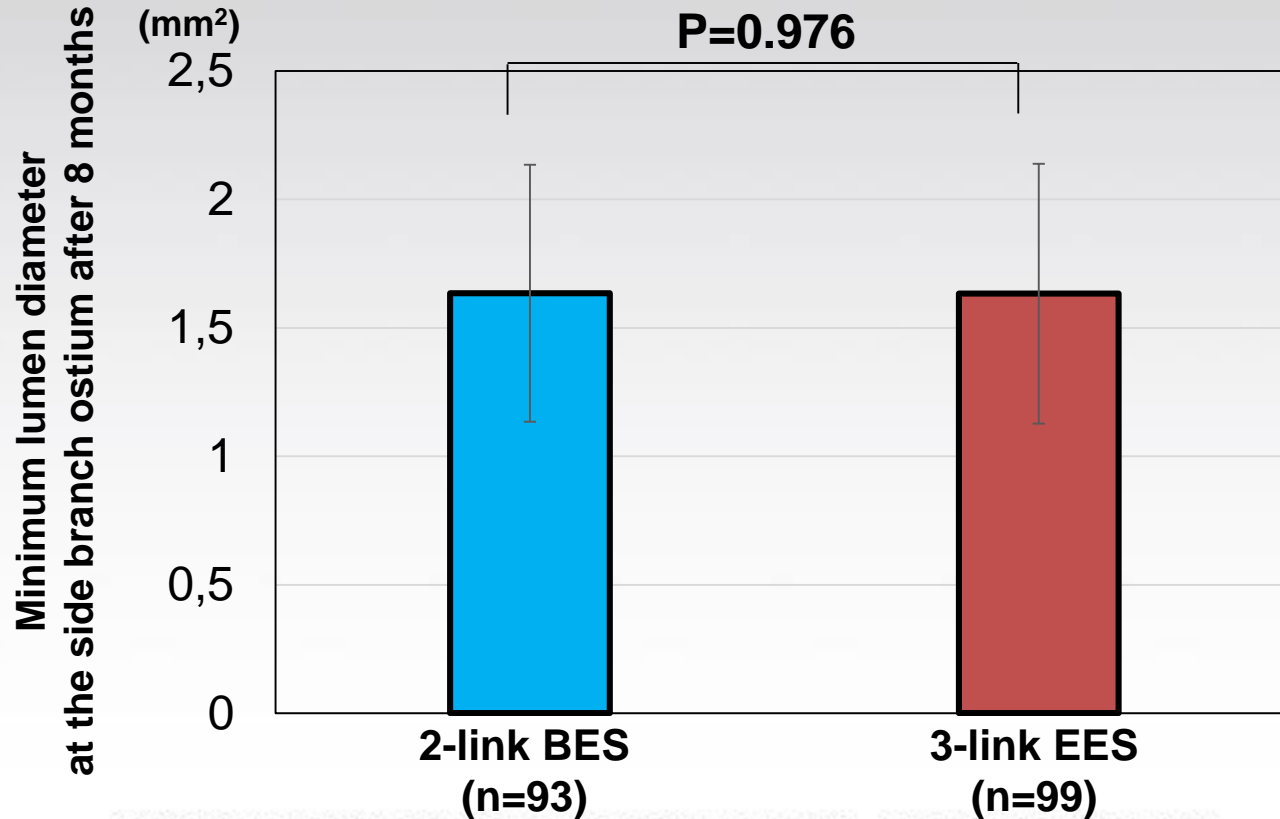
MACE during 1 year



Number at risk	0	1	2	3	4	5	6	7	8	9	10	11	12
2-link BES	109	106	106	106	105	105	104	104	103	100	97	90	69
3-link EES	115	110	109	109	109	109	109	109	109	105	102	98	73



Primary endpoint: MLD at SB ostium at 8-month follow up CAG

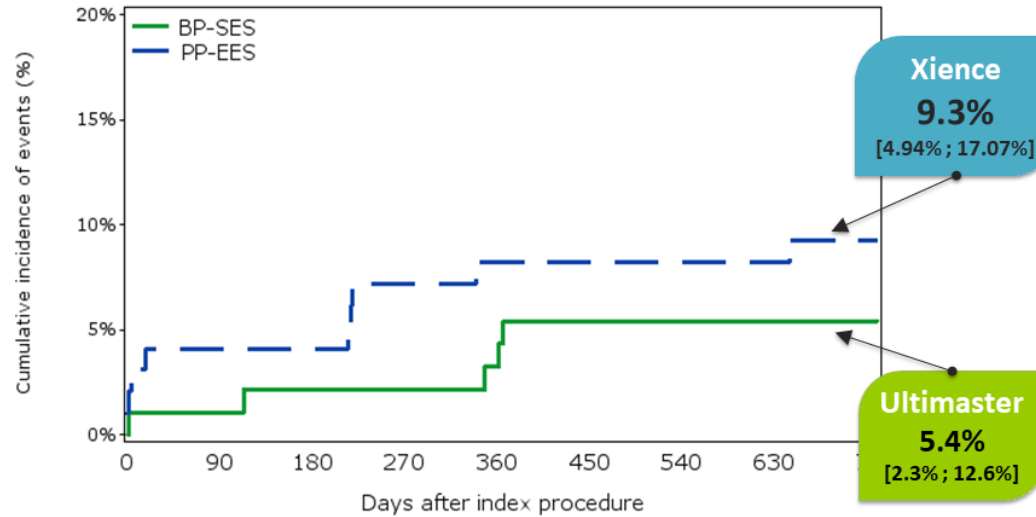




Discussion

CENTURY II Bifurcation lesions Target Lesion Failure at 24 months

CENTURY-II - Kaplan-Meier survival curves - Cumulative Events
Target Lesion Failure Composite (TLF)



Number at Risk

BP-SES	92	91	90	90	90	88	88	88	88
PP-EES	97	93	93	93	93	93	93	93	92

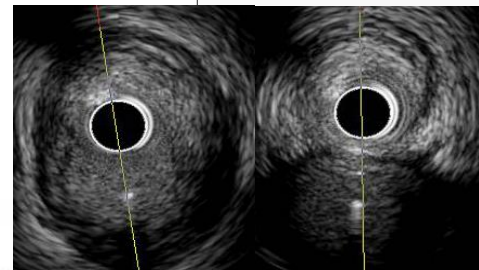
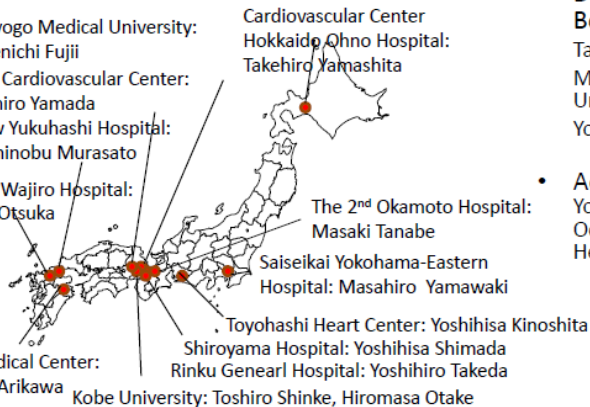
Log-rank: p=0.3048

Merkely B , EuroPCR2015

Japanese registry of IVUS guided bifurcation stenting

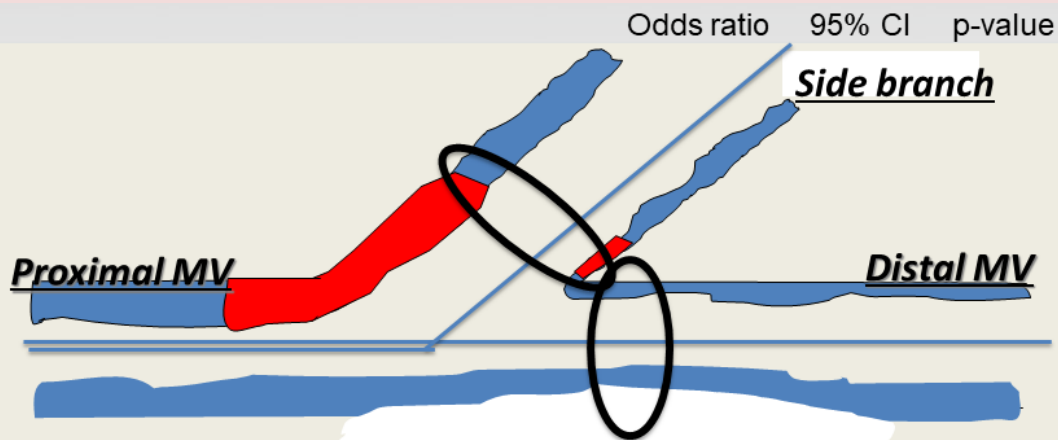
J-REVERSE: Study Organization

- **Principal Investigator**
 - Yoshinobu Murasato (New Yukuhashi Hospital)
 - Yoshihisa Kinoshita (Toyohashi Heart Center)
- **Participating institutes & members of steering committee**
 - Hyogo Medical University: Kenichi Fujii
 - Himeji Cardiovascular Center: Shinichiro Yamada
 - New Yukuhashi Hospital: Yoshinobu Murasato
 - Fukuoka Wajiro Hospital: Yoritaka Otsuka
 - Oita Medical Center: Masaya Arikawa
 - Kobe University: Toshiro Shinke, Hiromasa Otake
 - Cardiovascular Center Hokkaido: Ohno Hospital: Takehiro Yamashita
 - The 2nd Okamoto Hospital: Masaki Tanabe
 - Saiseikai Yokohama-Eastern Hospital: Masahiro Yamawaki
 - Toyohashi Heart Center: Yoshihisa Kinoshita
 - Shiroyama Hospital: Yoshihisa Shimada
 - Rinku General Hospital: Yoshihiro Takeda
- **Core laboratory**
 - Angiography Cardiovascular Imaging Center
 - OCT Kobe University
- **Data and Safety Monitoring Board**
 - Takahiko Suzuki (Toyohashi HC)
 - Masato Tsutsui (Ryukyuu University)
 - Yoshinori Takajyo (Takajyo Clinic)
- **Adviser of statistical analysis**
 - Yoshihisa Fujino (Univ. Occupational & Environmental Health)





Pre-procedure plaque distribution affected SB enlargement after 1 stenting with final kissing



Residual SB ostium stenosis after FKI

Negative remodeling in distal MV before intervention	8.78	1.67-46.1	<0.05
Plaque burden at distal MV before intervention	1.12	1.00-1.25	<0.05
Plaque burden at SB ostium before intervention	1.06	1.00-1.12	<0.05

10th European Bifurcation Club meeting - Bordeaux, France - 17th & 18th October 2014

Yamawaki M et al, EBC 2014
Published by J.Interve Cardiol 2016

XIV European Bifurcation Club meeting - Brussels, Belgium - 12th & 13th October 2018



試験概要

3D-OCT Bifurcation Registry



冠動脈分岐部病変に対するステント留置術の3D-OCTによる検討

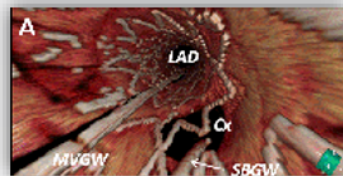
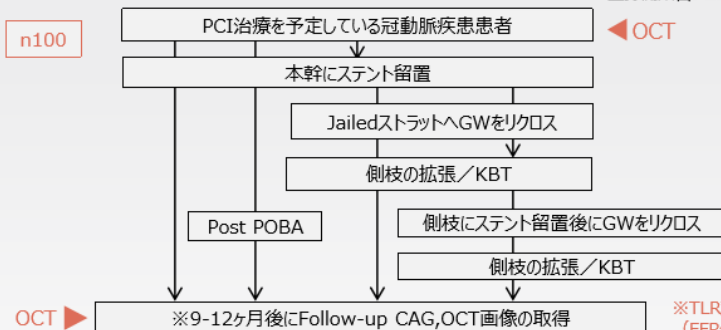
- デザイン
- 目的
- 対象
- 方法

多施設共同（国内10施設）、前向き、介入・観察、非ランダム化試験

冠動脈分岐部病変のPCIにおいてステント留置後に起きるJailedストラットに対し、最適なワイヤーリクロスポイントを検討して分岐部ステントの問題点を2D/3D-OCTを用いて明らかにすること

冠動脈分岐部病変患者 100例

登録開始日: 2014/06/01~



Okamura et.al EuroIntervention 2014; 9- online publish-ahead-of-print February 2014

※TLR施行は可能な限り虚血の客観的根拠 (FFR値や心筋シンチグラフィなど) を得るようにすること

評価項目

ステント留置後の2D/3D-OCT所見から側枝拡張とワイヤーリクロスポイントとの関連を評価

側枝部位のJailedストラットのリンクパターン、Jailedストラットへのワイヤーリクロスポイント、側枝を拡張後のJailedストラットのセル/側枝入口部面積の比率、Incomplete Stent Apposition (ISA) の頻度および定量的評価

[副次的評価項目]9-12ヶ月FOLLOW-UP時に、冠動脈造影およびステント内の2D/3D-OCTによる解析を実施
angiographic late loss, binary restenosis (>50% DS)、ストラットの新生内膜による被覆率・被覆厚、血栓、ISA頻度および定量的評価、MACE (major adverse cardiac events) :主要心血管イベントの有無

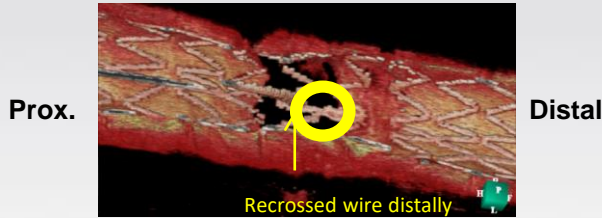
研究責任者:志手淳也先生 (大阪府済生会中津病院)、岡村誉之 (山口大学)
研究主体組織:3D-OCT研究会
サポーター企業:セント・ジュード・メディカル株式会社、他

Confidential. For internal use only. Not for distribution

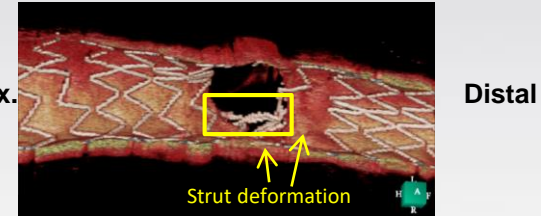
“Link on carina” and “proximal re-wiring” were associated with higher rate of strut malapposition at the SB ostium.

Link on carina

GW crossed distally

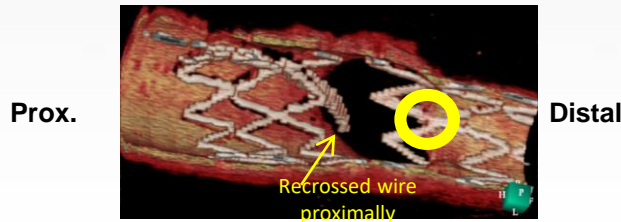


After Kissing Ballooning



Proximal re-wiring

GW crossed proximally



After Kissing Ballooning

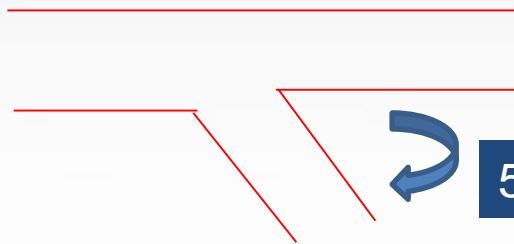


Okamura et al, CVIT-3D OCT 2016

Parallel angle



Perpendicular angle



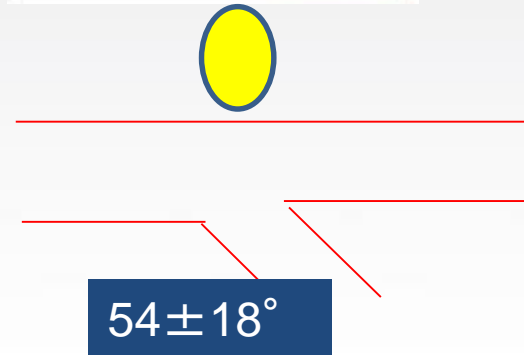
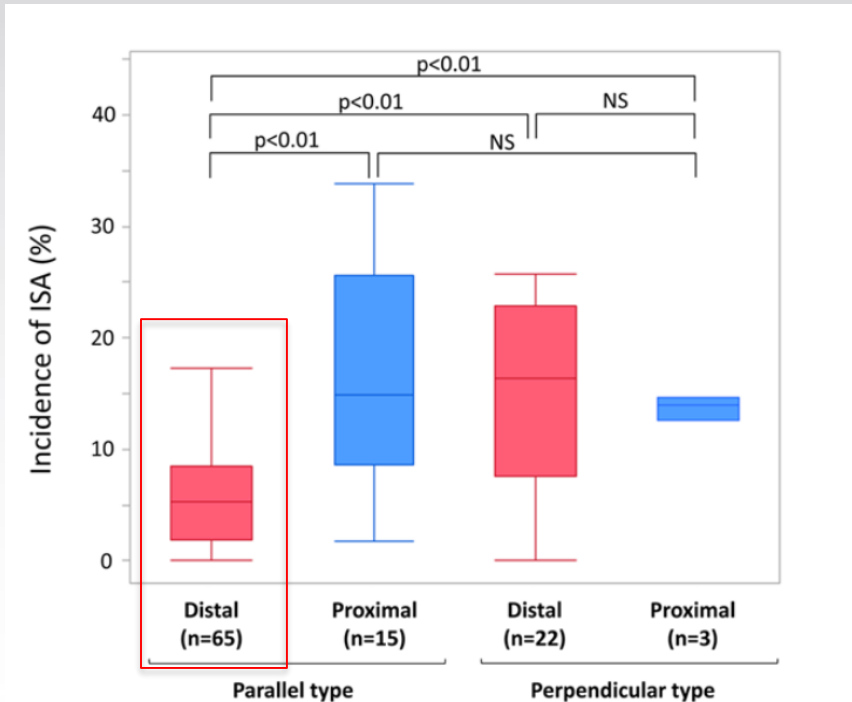
$54 \pm 18^\circ$



$77 \pm 23^\circ$

Okamura et al EuroIntervention 2017

Parallel bifurcation and Distal wiring were related to lower rate of stent malaposition.



Okamura et al EuroIntervention 2017



Conclusion

- ☑ 2-link BES did not appear superior to 3-link EES with respect to mid-term maintenance of SB ostial enlargement despite aggressive treatment for SB.**

- ☑ Factors other than stent platform design (pre-procedure plaque distribution, location of link on the carina before kissing, bifurcation angle, and strut thickness) might affect ostial SB angiographic and clinical outcome.**



Thank you !



Sakaiminato



Yokohama

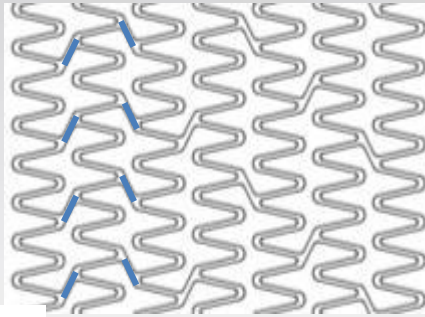


Amstelveen



Yokohama

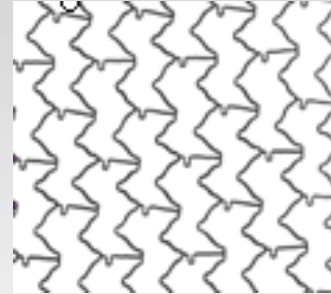
The second-generation DES platform is based on a thinner strut structure with a 2–3-link cell design.



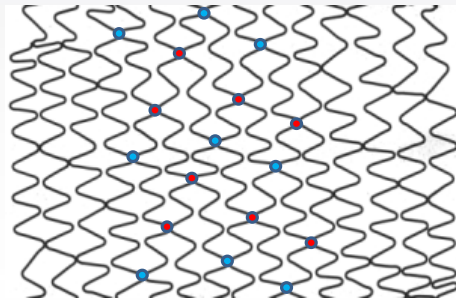
2-2.5 link

SYNERGY
(Pt)

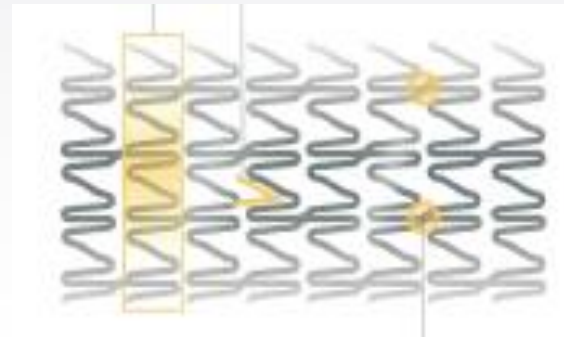
3 link



Xience Alpine
(CoCr)



Resolute Onyx
(CoNi + Pt)



Ultimaster
(CoCr)





