

Current & Future Stent Design for Drug-eluting Stent

– Focused on the Updated Resolute
Program –

**Seung-Woon Rha, MD, PhD,
FACC, FAHA, FESC, FSCAI, FAPSIC**

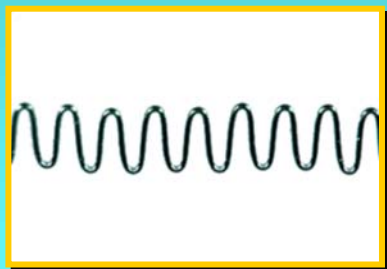
**Cardiovascular Center,
Korea University Guro Hospital, Seoul, Korea**

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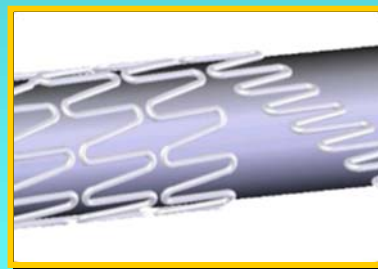
1. Endeavor Resolute vs. Resolute Integrity
2. Brief Summary of Recent Clinical Data
 - 1) Data from TCT 2010
 - 2) Data from ACC 2011

Unique Manufacturing Process

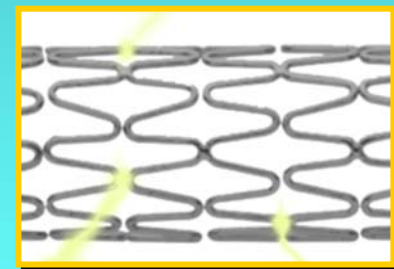
- Resolute Integrity DES uses Continuous Sinusoid Technology, a unique manufacturing process pioneered by Medtronic.
 - Continuous Sinusoid Technology uses a single continuous piece of wire that is formed into the sinusoidal shape.
 - It is then wrapped around a mandrel to give the cylindrical shape of the stent.
 - The stent is then fused in strategic locations to ensure optimum flexibility, conformability and strength.



Sinusoidal Formed Wire



Helical Wrap



Laser Fused

Conventional Laser Cut Stent Manufacturing



Integrity Continuous Sinusoidal Technology



Created with a
non-activated version
www.avs4you.com

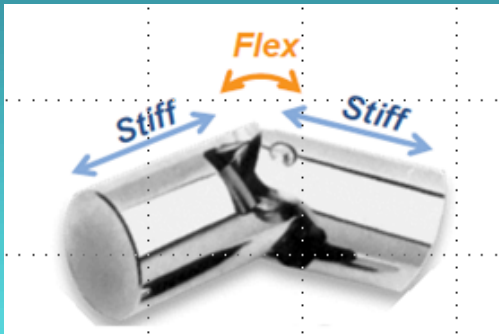
McSonic

Why is Resolute Integrity DES More Deliverable?

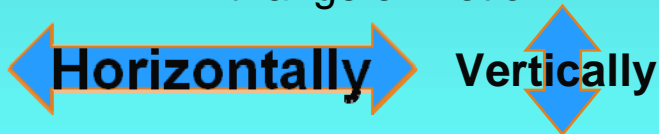
Fluid Range of Motion

CONVENTIONAL LASER CUT STENTS

Xience Prime DES & Promus Element DES



Separate stiff segments connected by flexible connectors limit range of motion

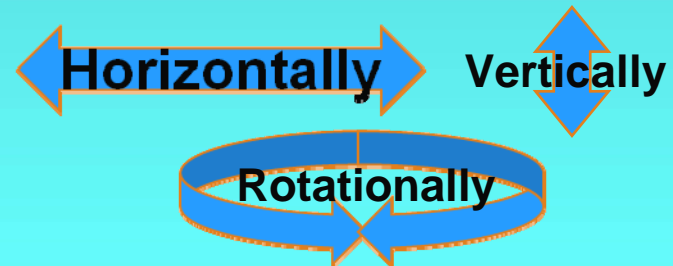


CONTINUOUS SINUSOID

Resolute Integrity DES



Continuous sinusoid technology will flex continually



⇒ Fluid range of motion for streamlined delivery in 3D anatomy.

Fluid Range of Motion

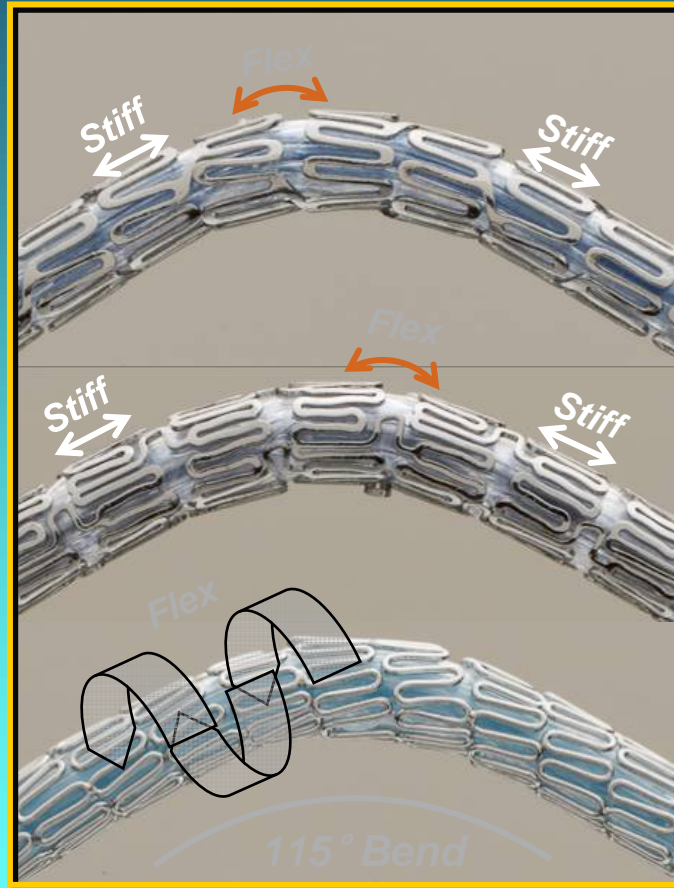
Integrity stent platform provides continuous range of motion.

DES:

Promus
Element

Xience
Prime

Resolute
Integrity



Separate stiff
segments in laser
cut stents limit the
range of motion.

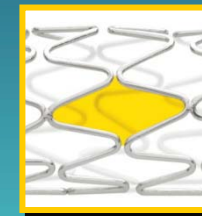
The helical design
of Integrity
continually flexes.

Similarities in Cell Design, Stent Pattern & Scaffolding

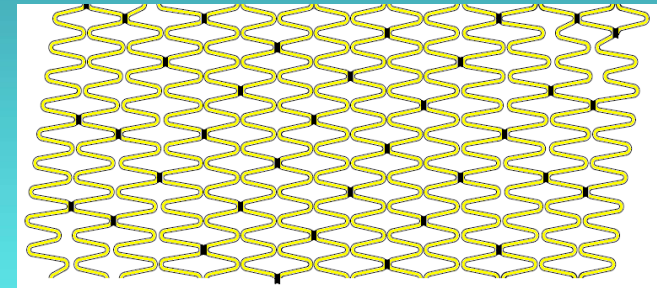
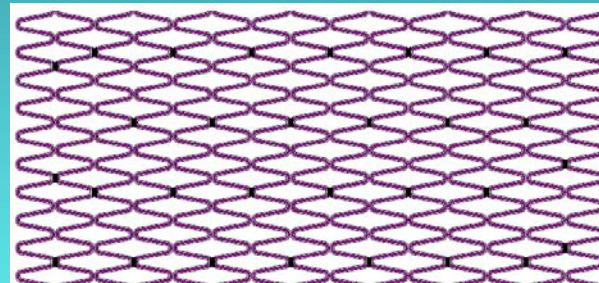
Resolute DES

Resolute Integrity DES

Cell Design



Stent Pattern



Scaffolding



Coating Layer Comparison – Resolute DES vs. Resolute Integrity DES

Resolute DES

Resolute Integrity DES

Coating Composition

Primer: Parylene
35% Zotarolimus
65% BioLinx

SAME

Primer: Parylene
35% Zotarolimus
65% BioLinx

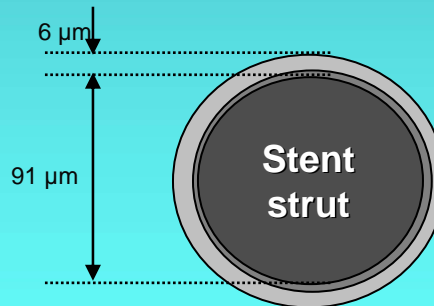
Dose Density

~1.6 $\mu\text{g}/\text{mm}^2$

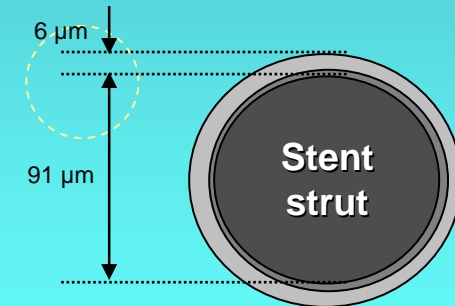
SAME

~1.6 $\mu\text{g}/\text{mm}^2$

Coating Thickness



SAME



Strut Dimensions

Drug Load Comparison

Resolute Integrity DES has
~.9 mm helical wraps with
nominal dose density of
~1.6 $\mu\text{g}/\text{mm}^2$



Continuous Wire



**Resolute
Integrity DES**

180 μg

Individual Rings



Resolute DES has
1.0mm segments with
nominal dose density of
~1.6 $\mu\text{g}/\text{mm}^2$

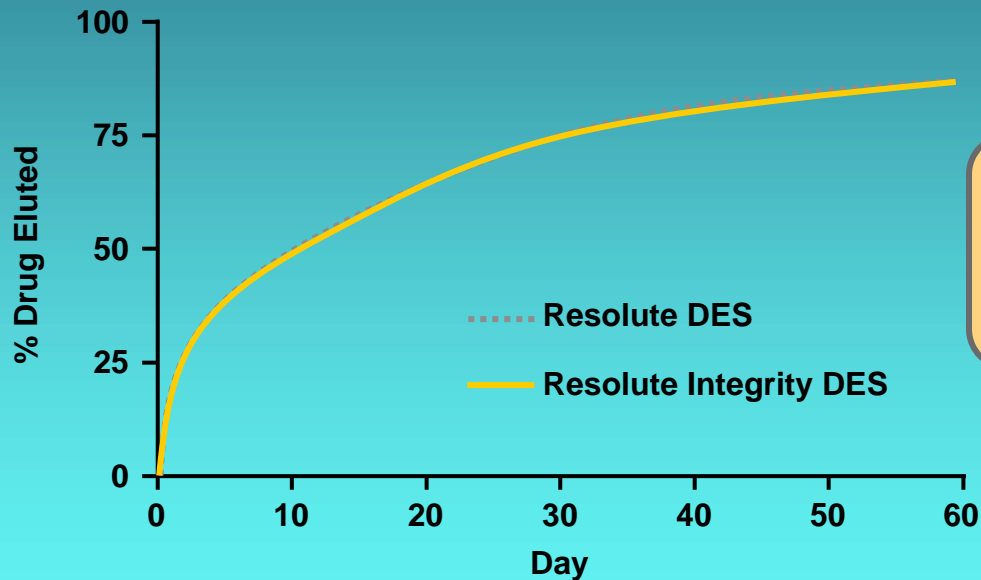


**Resolute
DES**

**Total drug load is
identical
for both stents**

In-Vivo Drug Delivery: Resolute DES vs Resolute Integrity DES

**In-Vivo Elution:
Comparison of Resolute DES and
Resolute Integrity DES through Day 60**

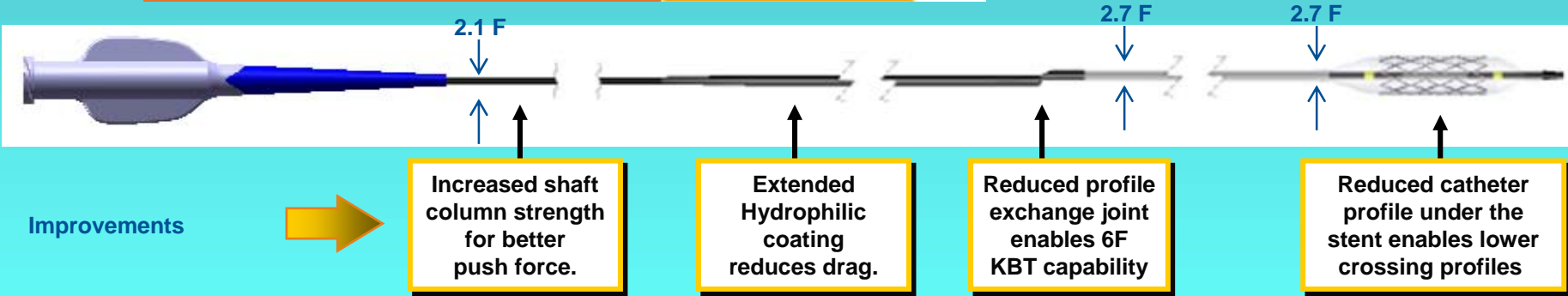
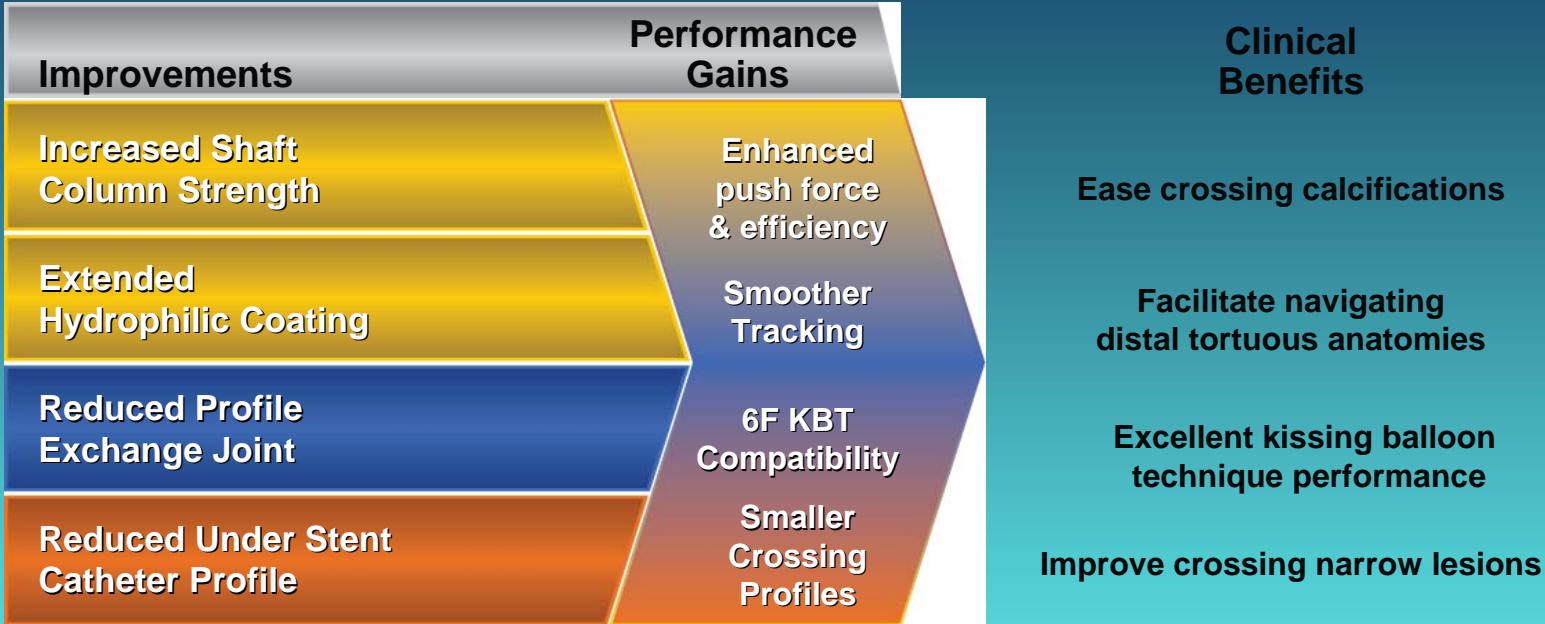


**In-Vivo Bioequivalence Testing:
Comparison of Resolute DES and
Resolute Integrity DES**

EQUIVALENT in-vivo drug release profile
EQUIVALENT zotarolimus arterial tissue level
EQUIVALENT blood drug levels

⇒ **In-Vivo Bioequivalence Testing demonstrated equivalent drug delivery characteristics between Resolute DES and Resolute Integrity DES.**

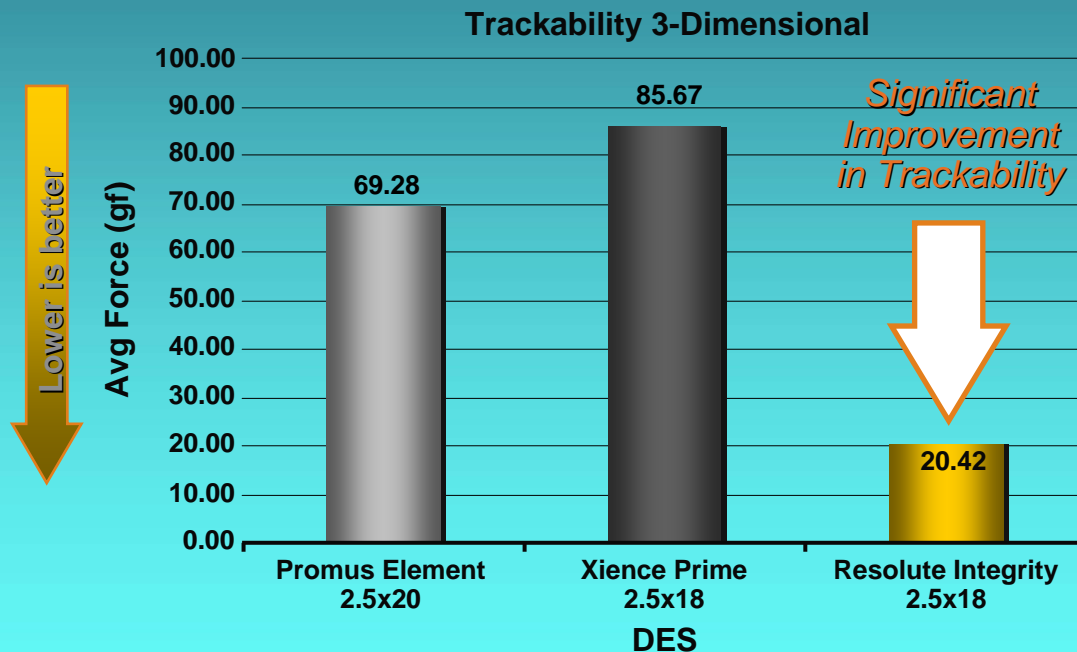
MicroTrac Delivery System Enhances Capabilities



⇒ MicroTrac delivery system enhances device performance.

Trackability




- Trackability assesses the amount of effort required to track a DES through a 3-dimensional tortuous path.
- Challenging curvature differentiates stent designs.



⇒ **Resolute Integrity DES is significantly more trackable.**

Crossing Profile

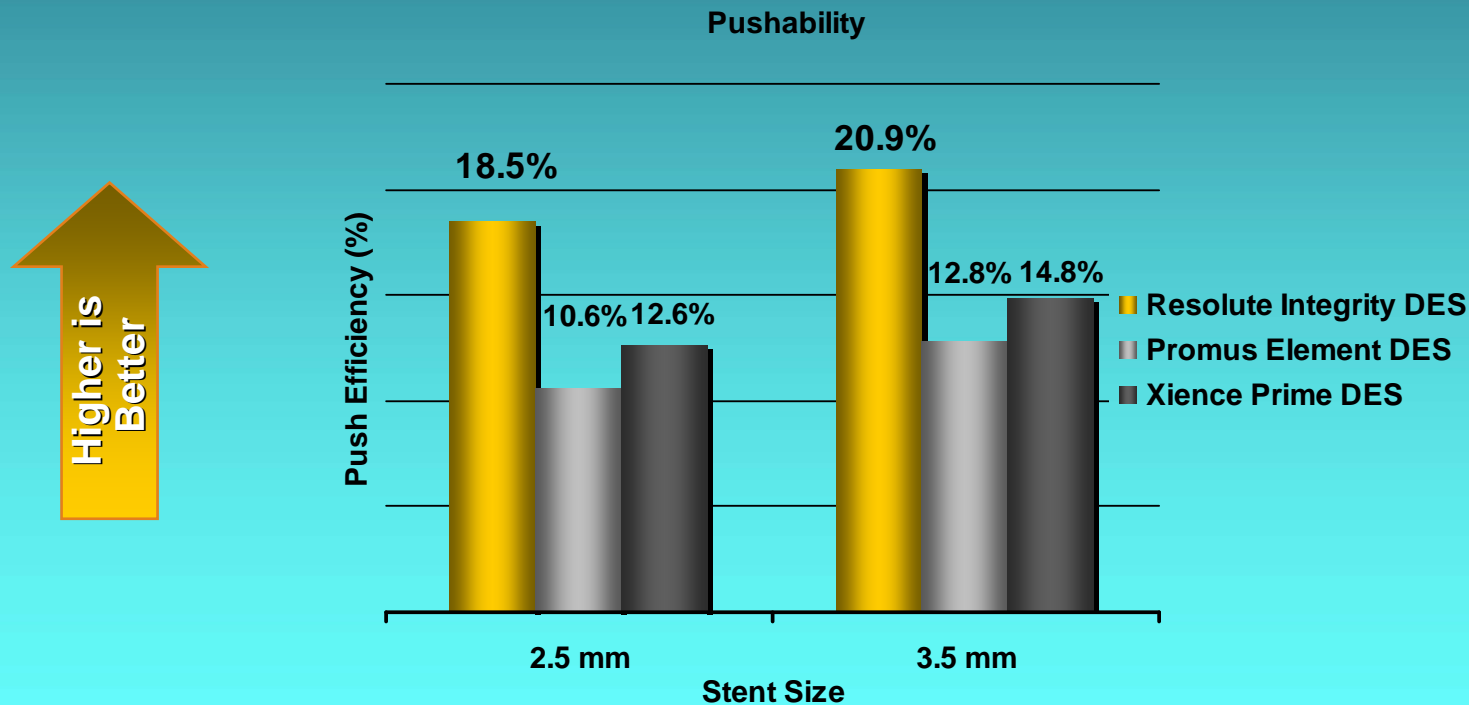
- The smaller a DES's crossing profile, the better able it is to cross through narrow stenoses.

<i>DES</i>		<i>Stent Crossing Profile, 2.5 mm (mm)</i>	<i>Stent Crossing Profile, 3.5 mm (mm)</i>
Resolute Integrity		1.01(0.039")	1.17(0.046")
Promus Element		1.01	1.17
Xience Prime		1.05	1.24

⇒ **Resolute Integrity DES has an excellent crossing profile.**

Pushability

- Pushability measures the ability to transfer force applied by the operator at the proximal end of the catheter to the distal end.
- With greater push efficiency, the Resolute Integrity system may ease the crossing of narrow and/or calcified lesions.



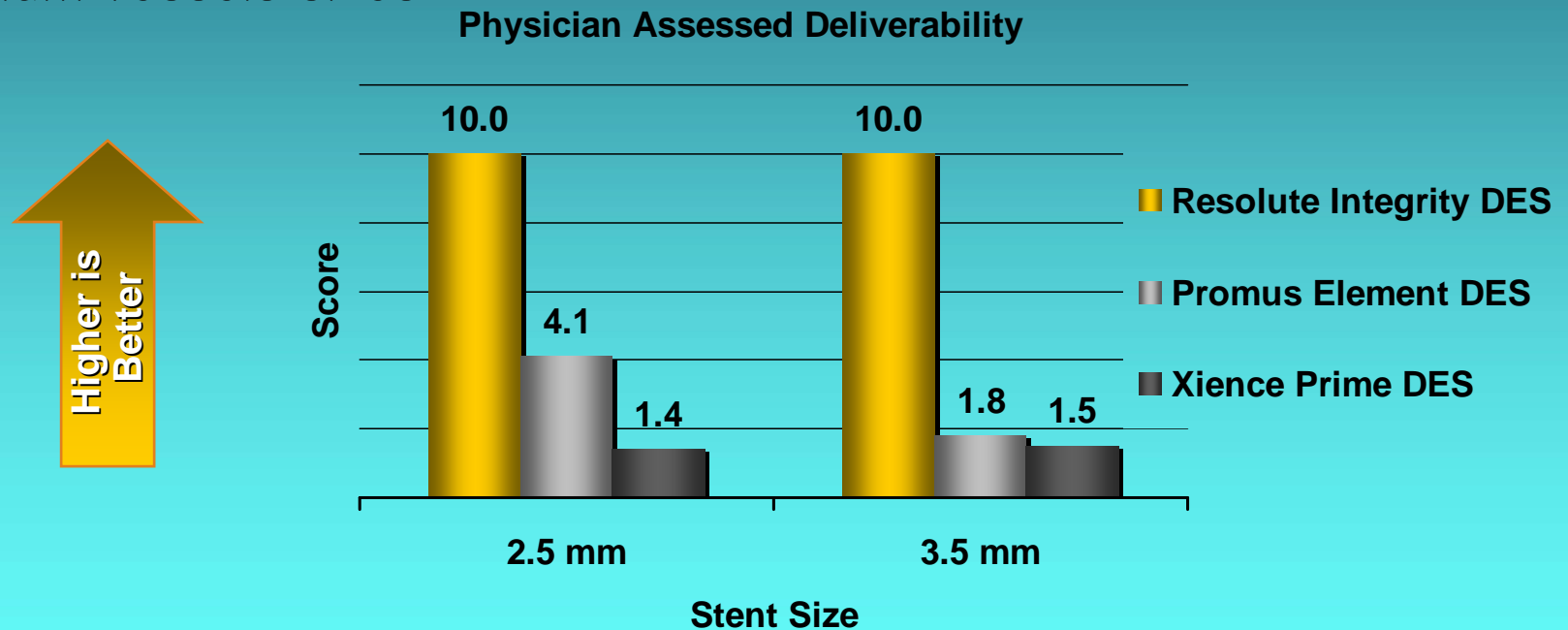
⇒ **Resolute Integrity DES is significantly more pushable.**

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc.
These tests may not be indicative of clinical performance.

Lesion Access

Blinded Physician Assessment of Deliverability

- Physicians rated Resolute Integrity DES significantly higher than Xience Prime DES and Promus Element DES in both small and medium vessels sizes



⇒ **Resolute Integrity DES significantly outperformed competition in blinded in-vivo studies.**

Placement Accuracy: Radiopacity

Physician Assessed Radiopacity in In-vivo Animal Studies

RADIOPACITY

Promus Element DES was most radiopaque, followed by Resolute Integrity DES, then Xience Prime DES. Promus Element DES uses platinum enriched alloy material that increases radiopacity.

TRADEOFFS

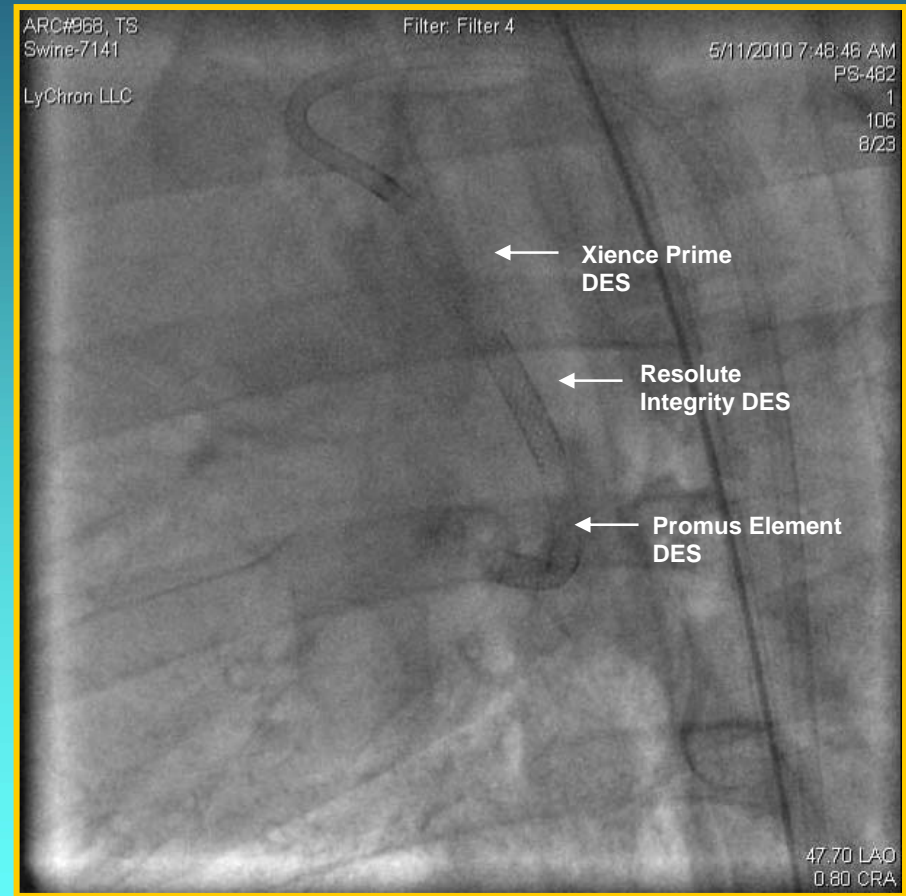
Promus Element DES alloy material does have tradeoffs:

- Unknown strength and fatigue resistance
- New alloy with no prior history of human use

RESOLUTE INTEGRITY DES vs Xience Prime DES and Resolute DES

Radiopacity of Resolute Integrity DES is better than Xience Prime DES.

Radiopacity was also assessed against Resolute DES and determined to be similar; Resolute DES & Resolute Integrity DES have similar strut thicknesses and surface area.

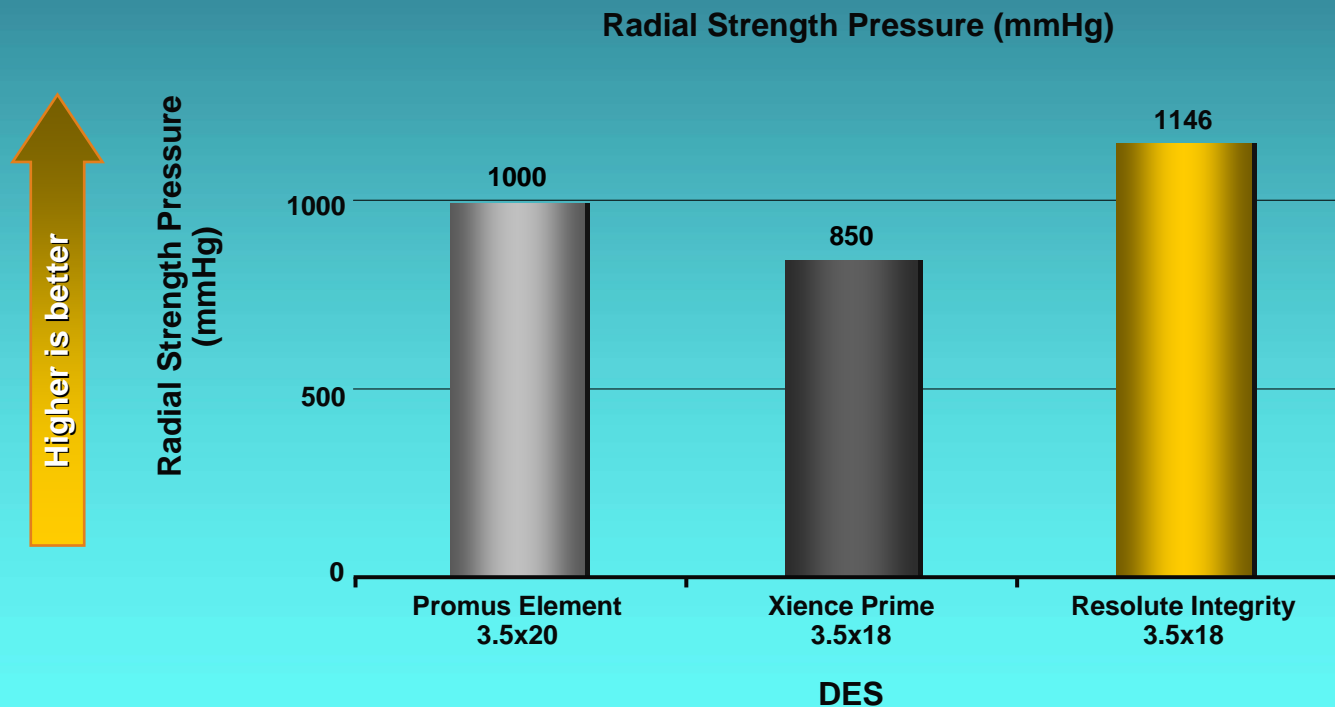


⇒ Resolute Integrity DES has better radiopacity than Xience Prime DES.

Lesion Coverage

Radial Strength

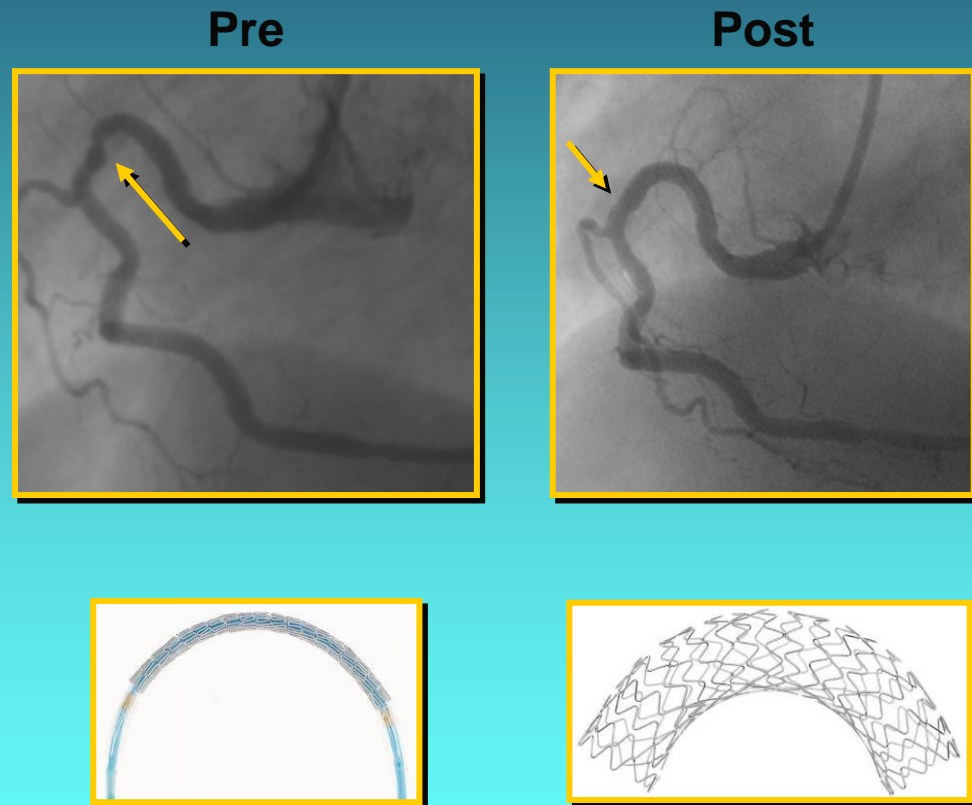
- Radial strength is the ability of the stent to resist external forces and maintain its diameter.



⇒ **Resolute Integrity DES has excellent radial strength.**

Conformability Case Study

- A conformable stent will provide excellent strut apposition to the vessel wall while minimizing vessel straightening.
- Conformability Challenge:
 - Physician Assessment
 - Prof. Stephen WL Lee, Queen Mary Hospital, Hong Kong.
- Case, 3 November 2009:
 - Proximal RCA
 - Very severe tortuosity
 - Severe calcification
 - Type C lesion
 - 80% stenosis



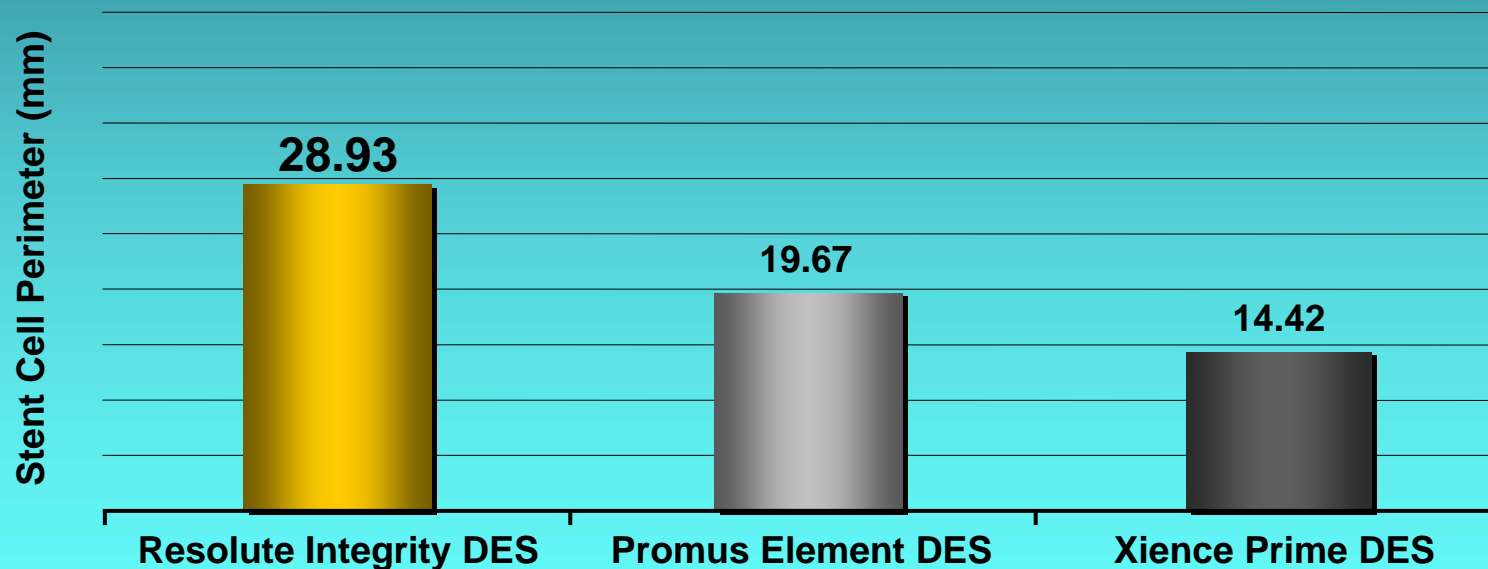
⇒ **Resolute Integrity DES is highly conformable.**

Excellent Side Branch Access

- A maximum cell perimeter will allow you to address a wide range of side branch diameters and angulations.
- Resolute Integrity DES's round struts facilitate wire access and balloon and stent crossing into a side branch.



Stent Cell Perimeter @ Nominal Pressure



⇒ **Resolute Integrity DES provides excellent side branch access.**

Resolute Integrity DES Expanded Size Matrix

Diameter (mm)	Stent Length (mm)								
	8	12	14	18	22	26	30	34	38
2.25									
2.50									
2.75									
3.00									
3.50									
4.00									

22-mm and 26-mm lengths expand the size matrix and replace the 24-mm Resolute DES stent length.

- Resolute Integrity DES adds 3 new lengths to the size matrix, expanding product offering from 39 sizes to 48 sizes.

⇒ More even spacing and additional longer lengths allow more optimal lesion matching.

Overview of Packaging Improvements

- Only DES among market leaders to have a single pouch package.
- A single pouch configuration simplifies access to product in a sterile field, especially when time is a critical factor.
- A smaller box facilitates product handling and frees up more shelf space in the stock room.

Reduced box size



Single Pouch

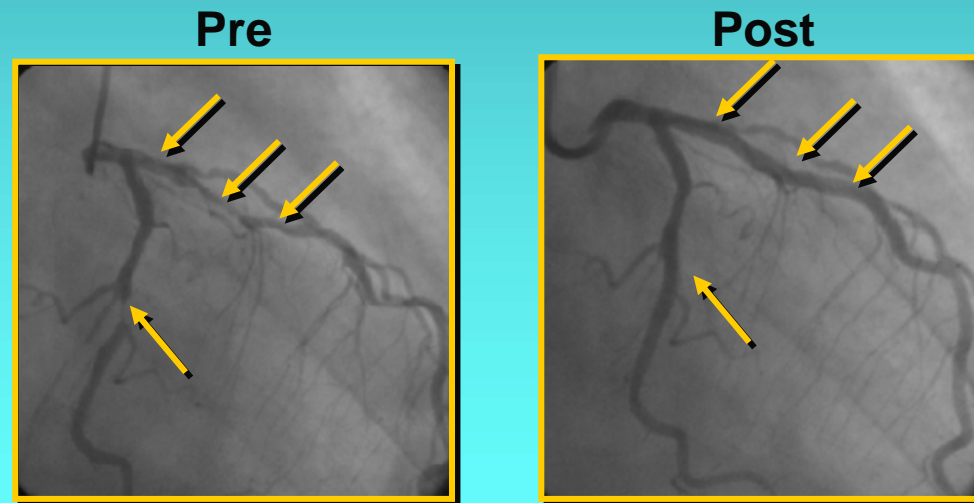


Summary; Make the Complex Simple

Resolute Integrity offers you:

- Superior deliverability¹ without compromise.
- Identical drug delivery characteristics to a platform proven for complex daily practice.
- Powerful DES therapy made even easier to deliver to complex lesions.
- Latest in DES innovation that redefines performance.
- Designed for the needs of an increasingly complex clinical practice.

The Resolute Integrity stent system will help you navigate tortuous anatomies and deliver powerful efficacy, making it easier for you to address the needs of your complex cases.



¹Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc.
These tests may not be indicative of clinical performance.
RESOLUTE All Comers 12-month data.
Case conducted using Integrity BMS.

Korea University Guro Hospital



I am one of known CTO guy...



SAVE THE DATE!

Date: January 9, 2010 (Sat.)
Venue: Main Auditorium, Asan Medical Center, Seoul, Korea

Course Directors :
Hee-Yeol Kim, MD, Nae Hee Lee, MD,
Seung-Whan Lee, MD, Seung-Woon Rha, MD

CTO Club

The 12th Seminar of
Angioplasty of Chronic Total Occlusions

June 11 fri. - 12 sat., 2010

Hotel Nikko Toyohashi,
Aichi, Japan

International Faculty Members

Chi-Kin Chan
United Christian Hospital
(Hong Kong)

Alfredo R. Galassi
Ferravento Hospital, University of Catania
(Italy)

Junbo Ge
Zhongshan Hospital, Fudan University
(People's Republic of China)

J. Aaron Grantham
Mid America Heart Institute St. Luke's Hospital
(USA)

Yong Huo
First Hospital Peking University
(People's Republic of China)

Hweung Kon Hwang
Sejong General Hospital
(Korea)

Hsien-Li Kao
National Taiwan University Hospital,
Yueh-Lin Branch
(Taiwan, R.O.C.)

NaeHee Lee
Seoncheong University Bucheon Hospital
(Korea)

Sum Kim Leung
Kwong Wah Hospital
(Hong Kong)

Xiankun Li
The China-Japan Friendship Hospital
(People's Republic of China)

William Lombardi
North Cascade Cardiology PLLC/
Stanford University
(USA)

Sudhir Rathore
Liverpool Heart and Chest Hospital
(UK)

Nicolaus J. Reifart
Main Tazara Heart Institute
(Germany)

Seung-Woon Rha
~~Korea University Guro Hospital~~
(Korea)

Georgios Sianos
ARIEPA University Hospital
(Greece)

Khalid Tamam
National Heart Institute
(Egypt)

Craig A. Thompson
Yale University School of Medicine
(USA)

Gerald S. Werner
Klinikum Darmstadt
(Germany)

R. Michael Wyman
Tennessee Memorial Medical Center
(USA)

e-CTO Club

e-Chronic Total Occlusion Club

1. CTO PCI Expert & Preceptorship
2. Director in Scientific Committee
3. CTO live in many hospitals...

CCI Program

Complex Cardiovascular Intervention Program

COURSE OVERVIEW

- Instructor : Dr. Rha Seung Woon
- Technical Improvement in Complex Coronary & Peripheral Intervention
- Clinical Research in Cardiovascular Field

REGISTRATION

Personal Information

Name _____

Hospital & Specialty _____

E-mail address _____

Telephone/Mobile _____

Areas of Interests

- How to get out of trouble (procedural complication)
- How to get accesses in difficult CTO Case
- Current treatment strategies and device selection
- Clinical Research in Cardiovascular Field

Korean Visiting Professors



Prof. Park SH & Cho YH's Live

Visiting Professor 2011; Young & Ambitious Drs



Never Give Up & Until Happy Ending



Korean Visiting Professors; Happy Endings!!



Strong New Data from TCT 2010

- Strong Performance in More All Comer Patients
 - RESOLUTE International 12-month results
- Valuable Evidence in Complex Patient Subgroups
 - RESOLUTE All Comers 12-month subgroup results
- Strong Results in the Long-Term
 - RESOLUTE 4-yr results

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for complex patient subgroup analysis

RESOLUTE International

Prospective, Multicenter, Real World Study

PI: J. Belardi, F-J. Neumann, P. Widimský

All patients with symptomatic coronary artery disease eligible for DES implantation (no lesion/vessel limitations)

Resolute Stent
N = 2200

88 sites International
No angiographic follow-up
25% randomly assigned to 100% monitoring

Clinical endpoints



30d

6mo

12mo

2yr

3yr

Primary Endpoint: Composite of Cardiac Death & Target Vessel MI at 12mo
Key Secondary Endpoint: ARC Definite and Probable Stent Thrombosis at 12mo
Drug Therapy: ASA and clopidogrel/ticlopidine \geq 6mo (per guidelines)

RESOLUTE International

Patient Eligibility

Inclusion Criteria

Coronary artery disease

- **Stable angina**
- **Silent ischemia**
- **Acute coronary syndrome including UA, NSTEMI and STEMI**

Intention to electively implant at least one Resolute stent

Lesion characteristics

- **Number of lesions: no limitation**
- **Number of vessels: no limitation**
- **Lesion length: no limitation**

Written informed consent

Exclusion Criteria

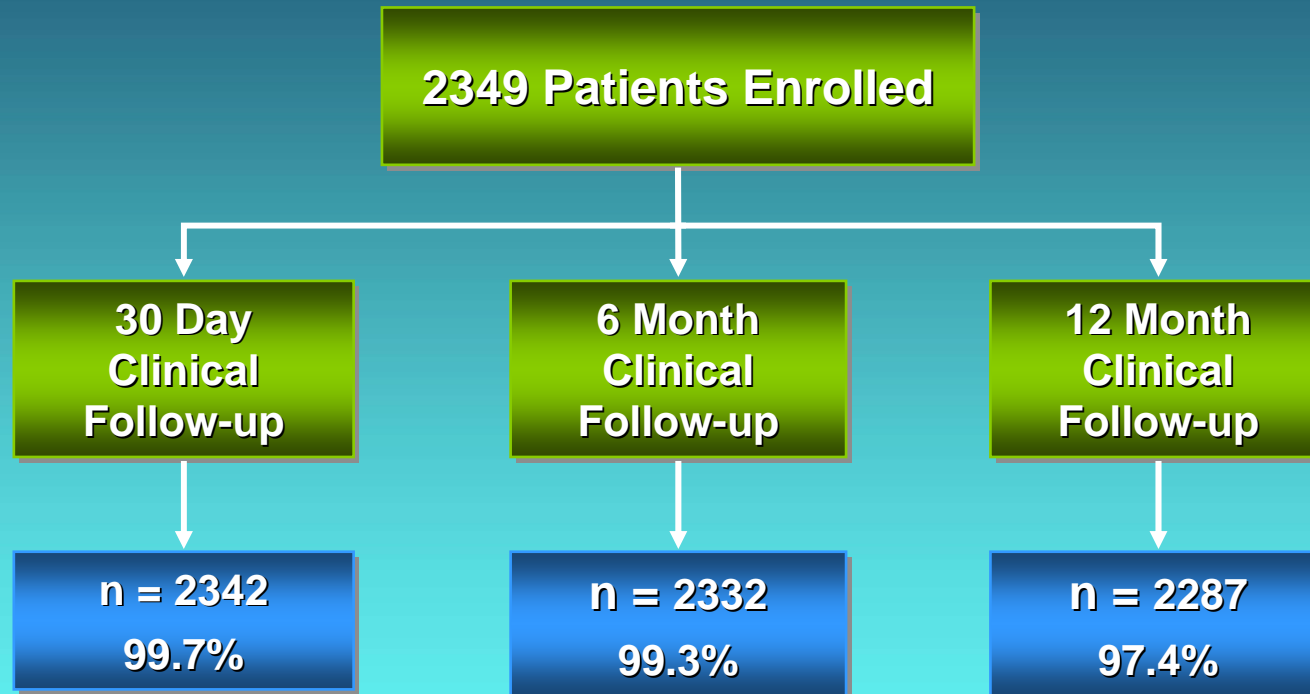
Pregnancy

Inability to comply with follow-up requirements

Participation in another trial

RESOLUTE International

Patient Follow-up

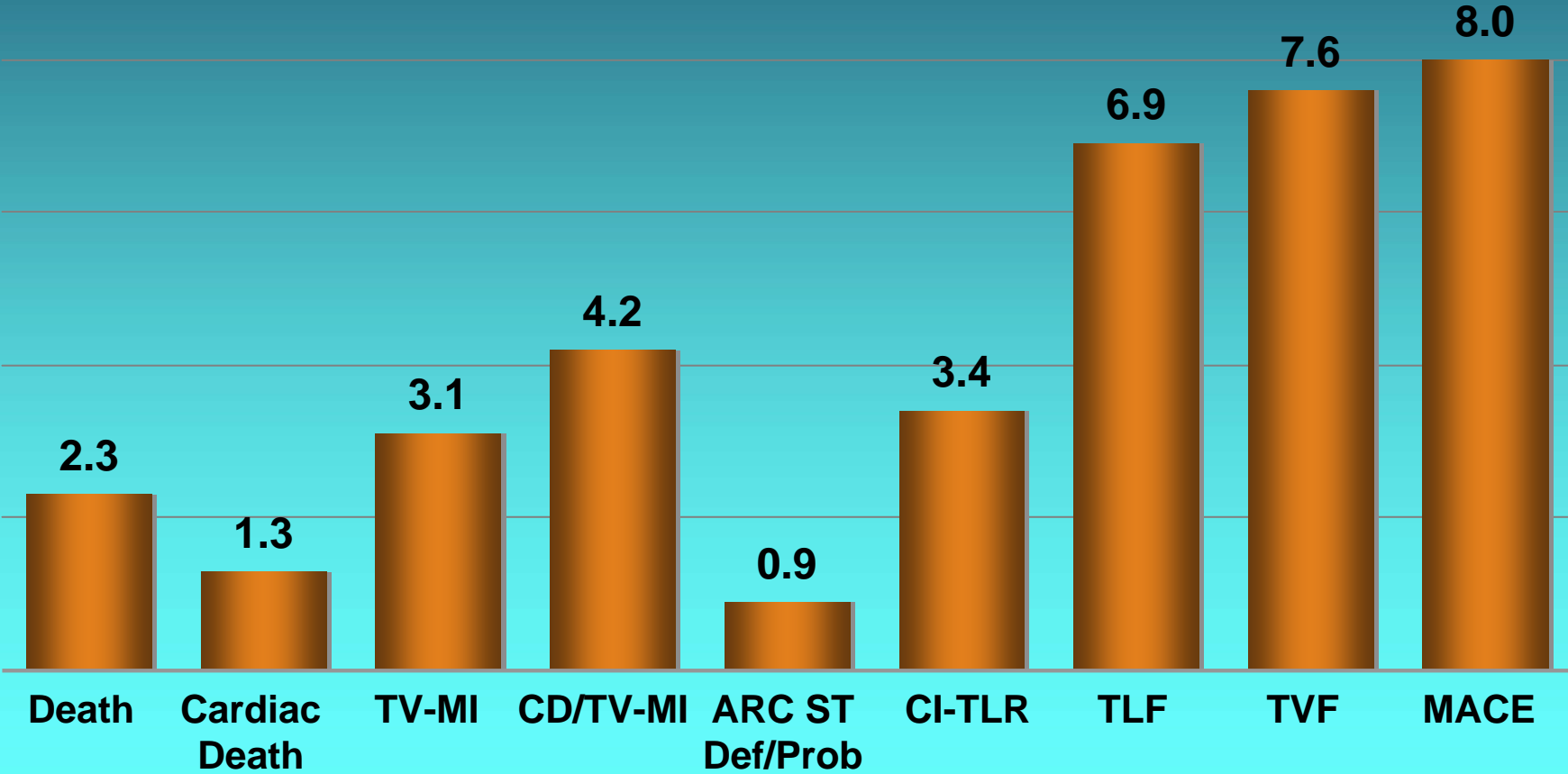


RESOLUTE International

Clinical Outcomes to 1 Year

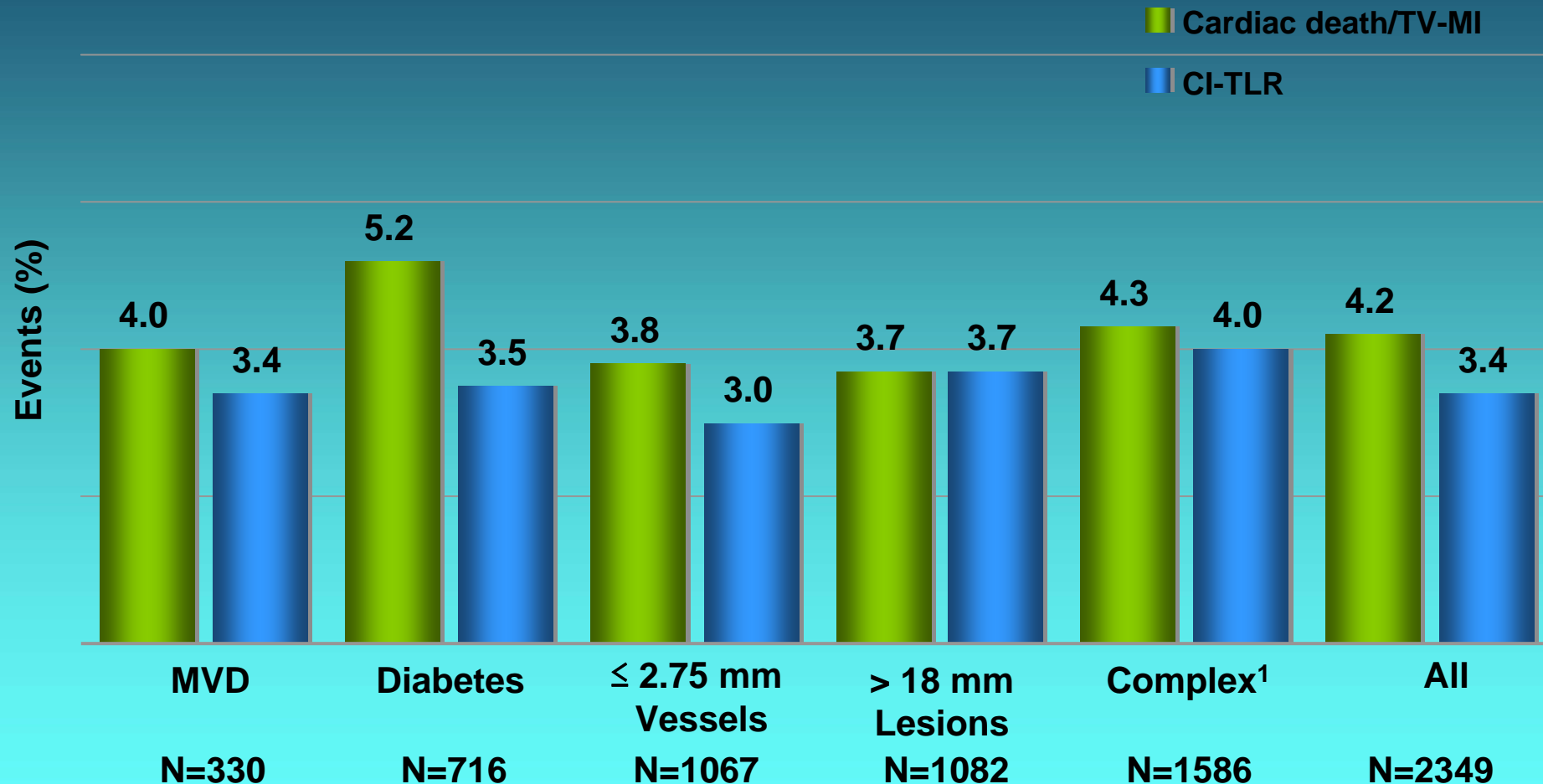
N = 2349

Percentage [%]



RESOLUTE International

Performance Across Subgroups at 12 Months



Complex patient definition: bifurcation, bypass grafts, ISR, AMI <72 hr, LVEF <30%, unprotected LM, >2 vessels stented, renal insufficiency or failure (creatinine >140 μmol/L), lesion length >27 mm, >1 lesion per vessel, lesion with thrombus or TO (preprocedure TIMI = 0). With the exception of long lesions (treatable with a single 38-mm length stent), Resolute DES currently is not specifically approved or the patient subsets noted above. RESOLUTE International was not specifically designed or powered for patient subset analysis shown above.

Belardi J. TCT 2010

RESOLUTE All Comers

Clinical Trial Design

Co-PIs: Profs. Serruys, Silber, Windecker



Clinical endpoints



Angio/OCT endpoints

Primary Endpoint:

- 12-month target lesion failure (TLF), composite of cardiac death, target vessel MI & clinically driven TLR

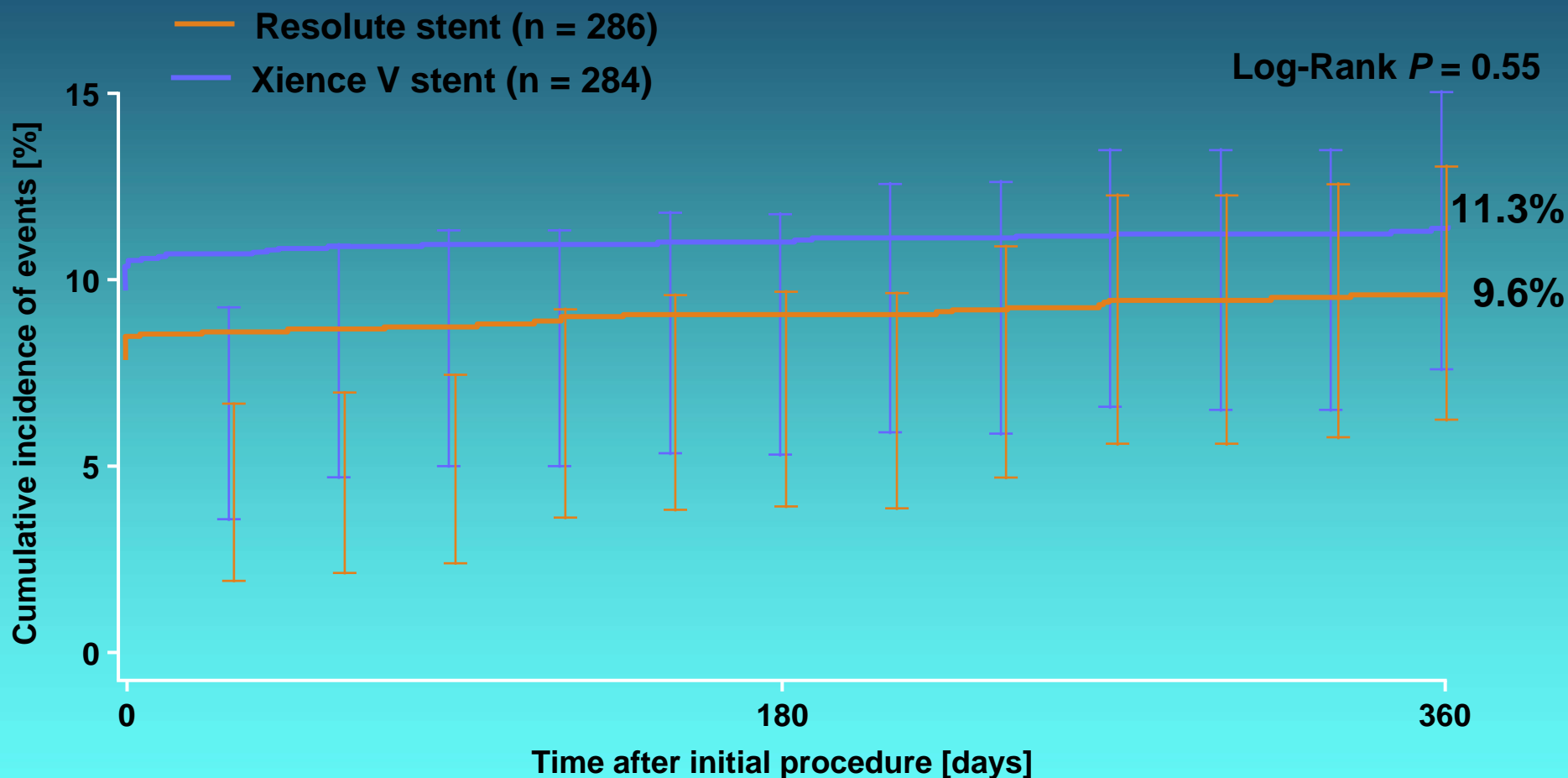
Secondary Endpoints:

- Clinical: Patient composite of any death, any MI, & any repeat revascularisation
- QCA (powered): 13-month in-stent % diameter stenosis
- QCA: % diameter stenosis, late loss, and binary restenosis

Drug Therapy: ASA and clopidogrel/ticlopidine > 6mo (per guidelines)

RESOLUTE All Comers: Multi-Vessel Stenting

TLF (Cardiac Death, Target Vessel MI, Clinically Driven TLR) at 1 Year



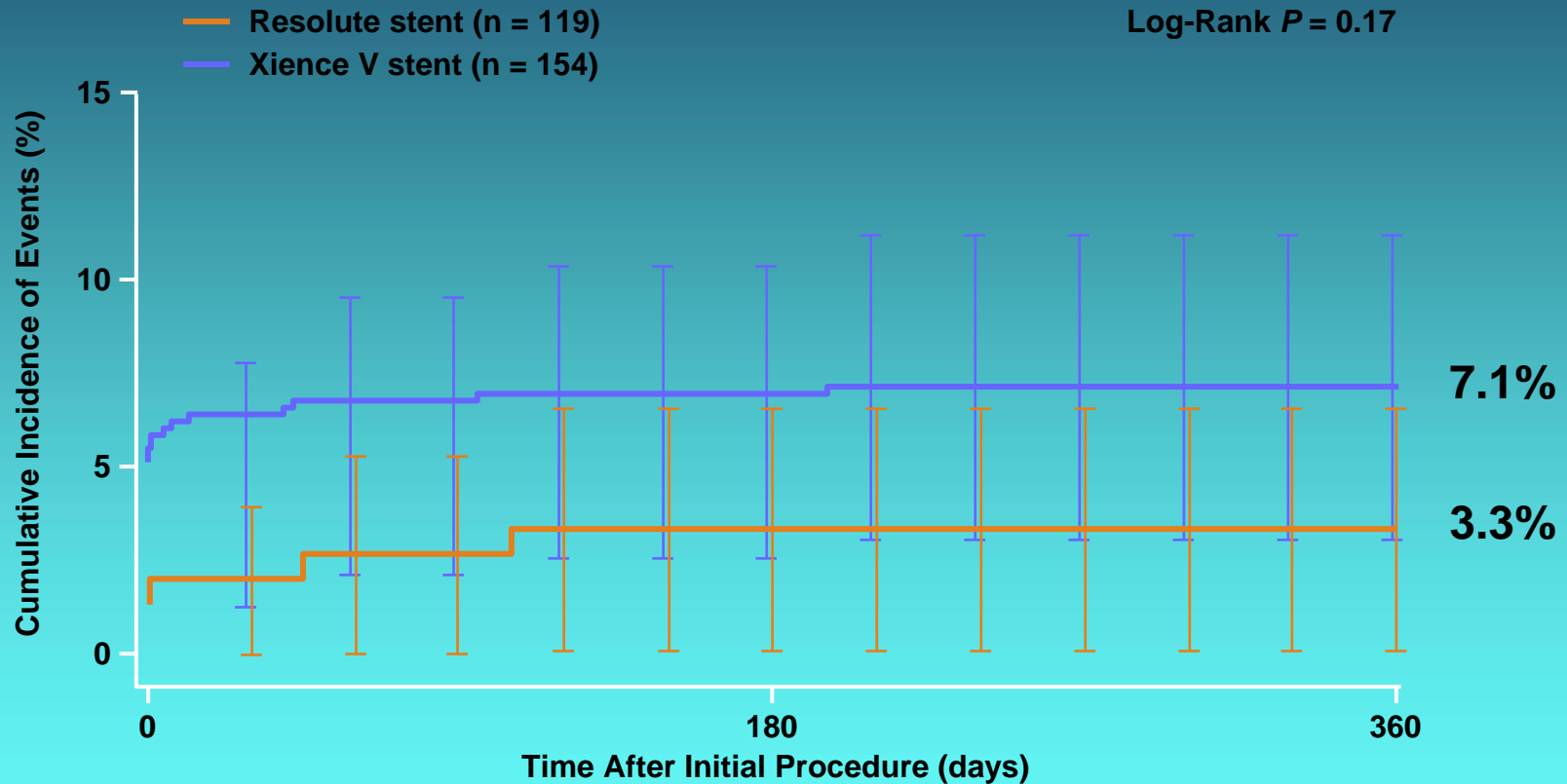
No. at risk	0	30	60	90	120	150	180	210	240	270	300	330	360
Resolute	286	280	270	268	267	263	262	262	260	257	254	254	252
Xience V	284	272	265	261	259	259	258	257	254	253	249	249	248

Error bars indicate a point-wise two-sided 95% confidence interval ($\pm 1.96 \cdot SE$). Standard Error based on the Greenwood Formula. RESOLUTE All Comers was not specifically designed or powered for multi-vessel subset analysis. Resolute DES is not specifically approved for the treatment of multi-vessel disease.

Silber S. TCT 2010

RESOLUTE All Comers: STEMI Subgroup

TLF (Cardiac Death, Target Vessel MI, Clinically Driven TLR) at 1 Year



<i>No. at risk</i>	0	30	60	90	120	150	180	210	240	270	300	330	360
Resolute	122	120	118	117	117	116	116	116	116	116	116	116	115
Xience V	159	156	146	144	143	142	142	142	141	141	141	141	141

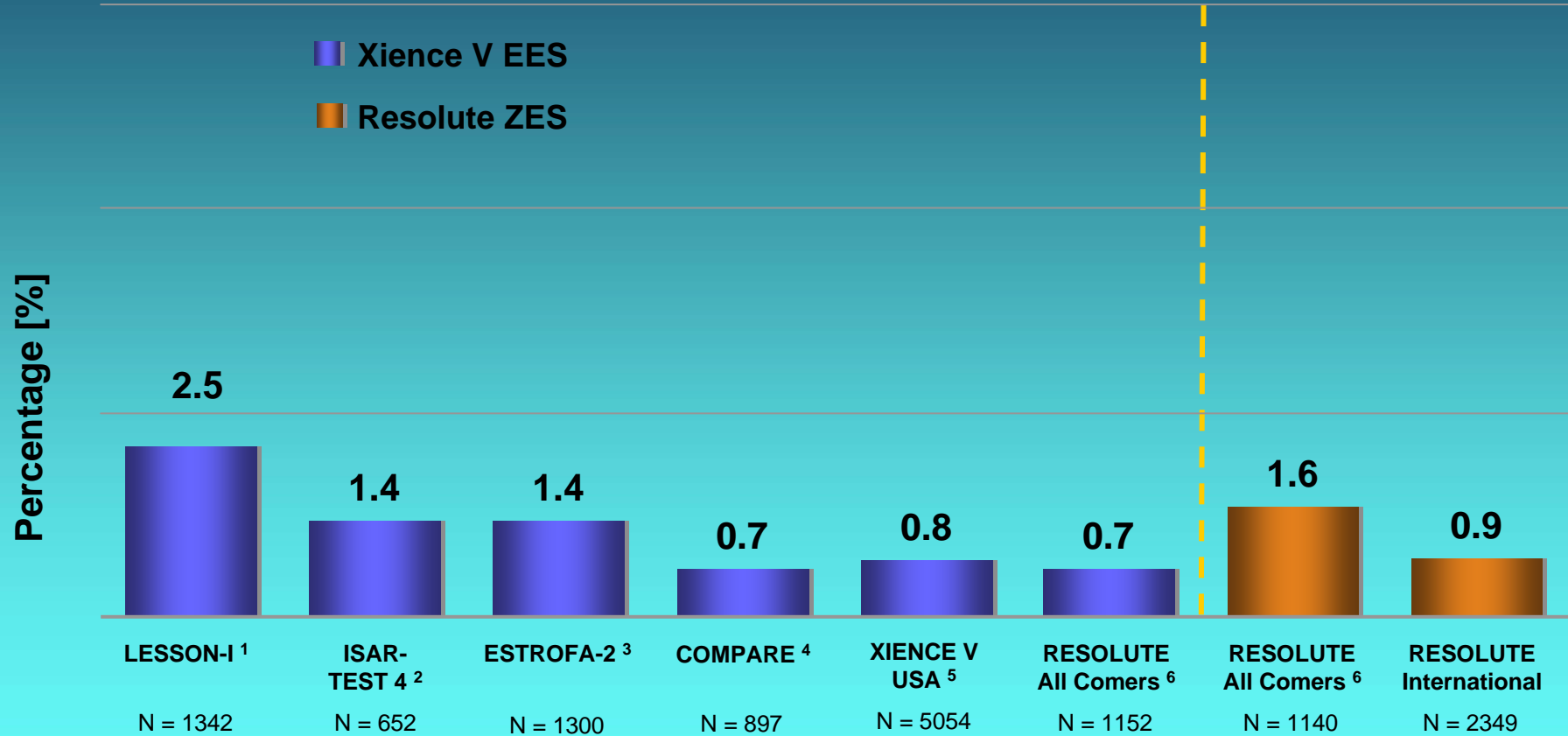
Error bars indicate a point-wise two-sided 95% confidence interval ($\pm 1.96 * SE$). Standard Error based on the Greenwood Formula.

RESOLUTE All Comers was not specifically designed or powered for STEMI subset analysis. Resolute DES is not specifically approved for STEMI patients.

Windecker S. TCT 2010

All-Comer Trials

ARC Definite/Probable ST at 12 Months



¹ Windecker S./Räber L. ESC2010. ² Kastrati A. TCT 2009. ³ de la Torre-Hernández JM. *J Am Coll Cardiol Intv.* 2010;3:911–9. ⁴ Kedhi E, et al. *Lancet.* 2010;375:201-9. ⁵ Hermiller J. EuroPCR 2010. ⁶ Serruys PW, et al., *N Engl J Med.* 2010;363(2):136-46. Results from clinical trials are not directly comparable. Information is provided for educational purposes only.

RESOLUTE

Clinical Trial Design

PI: I. Meredith

Single *De Novo* Native Coronary Artery Lesions
Lesion Length: 14–27 mm
Stent Diameters: 2.5, 3.0, 3.5 mm
Stent Lengths: 18, 24, 30 mm (8/9 mm bailout)
Drug Dose: 1.6 $\mu\text{g}/\text{mm}^2$ stent surface area
Pre-dilatation required

Resolute Stent
n = 139

130 patients (9 additional PK Sub-Study patients
enrolled after original 130 patients)
12 sites in New Zealand / Australia

Clinical endpoints

30d 4mo 6mo 9mo 12mo 2yr 3yr 4yr 5yr

Angio/IVUS endpoints

n = 30

n = 30

Primary Endpoint: Late lumen loss (in-stent) at 9mo by QCA

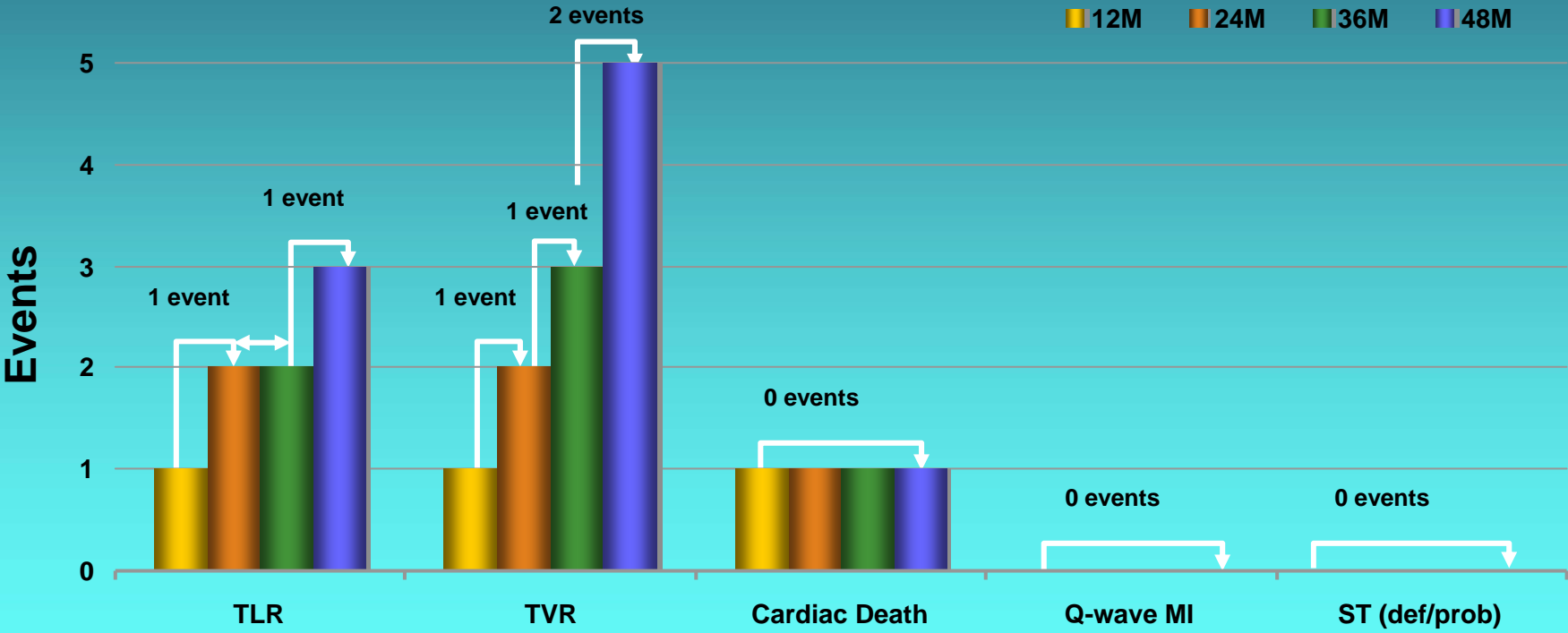
Secondary Endpoints: MACE at 30d, 6, 9 and 12mo and IVUS and angiographic parameters at 9mo

30 pt subset: 4mo MACE and angiographic, IVUS parameters

Drug Therapy: ASA and clopidogrel/ticlopidine \geq 6mo (per guidelines)

RESOLUTE Trial

Events Between Year 1 – 4





Resolute Integrity

Zotarolimus-Eluting Coronary Stent System



RESOLUTE US 12-Month Summary
RESOLUTE All Comers 2-Year Summary

ACC 2011

Resolute DES Shows Powerful Clinical Performance Across the Patient Spectrum

RESOLUTE US 12-Month Summary

- Robust trial design that enrolled a broad range of patients and lesions
 - High percentage of challenging cases: 34% diabetics and 70% small vessels
 - Resolute DES shows a very low rate of events for all safety and efficacy outcomes

RESOLUTE All Comers 2-Year Summary

- Resolute DES matches Xience V DES in all clinical endpoints at 2 years
 - No significant difference in clinical outcomes or stent thrombosis rates
- Resolute DES shows powerful performance in complex patients

Make the Complex Simple

- Revolutionary stent engineering with Resolute Integrity DES provides superior deliverability¹ and better conformability² vs. major competitors with enhanced procedural confidence.

Powerful clinical performance with superior deliverability

RESOLUTE US and All Comers trials studied Resolute DES.

RESOLUTE All Comers was not specifically designed or powered for complex patient subset analysis.

¹Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc.

²Simulated FEA studies Resolute Integrity DES vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES were performed by Dr. Peter Mortier, FEops / Ghent University-Belgium (Manuscript in preparation).

These tests may not be indicative of clinical performance.

RESOLUTE US Trial Design

PI: M. Leon, L. Mauri, A. Yeung

De Novo Native Coronary Lesions
Vessel Diameter: 2.25–4.00-mm
Lesion Length: ≤ 27-mm (38-mm arm: ≤ 35 mm)

Resolute DES
2.25–3.5 Clinical (n = 1242)
2.25–3.5 Angio/IVUS (n = 100)
4.0 Angio (n = 60)
38-mm Clinical (n = 110–175)¹

N = 1402 patients
116 US sites

100% data monitoring
Independent data adjudication

**Historical (Hx) Controls
Performance Goals**

Clinical endpoints



Angio/IVUS endpoints

Primary endpoints:

- 2.25–3.50-mm clinical → Target lesion failure at 12 months
- 2.25–3.50-mm angio/IVUS → In-stent LL at 8 months
- 4.0-mm angio → In-segment LL at 8 months
- 38-mm clinical → Target lesion failure at 12 months

Drug therapy: ASA and clopidogrel/ticlopidine ≥ 6 months (per guidelines)

RESOLUTE US 38-mm substudy is still enrolling.

Baseline Characteristics

Broad range of patients with high percentage of challenging lesions

Patient Characteristics

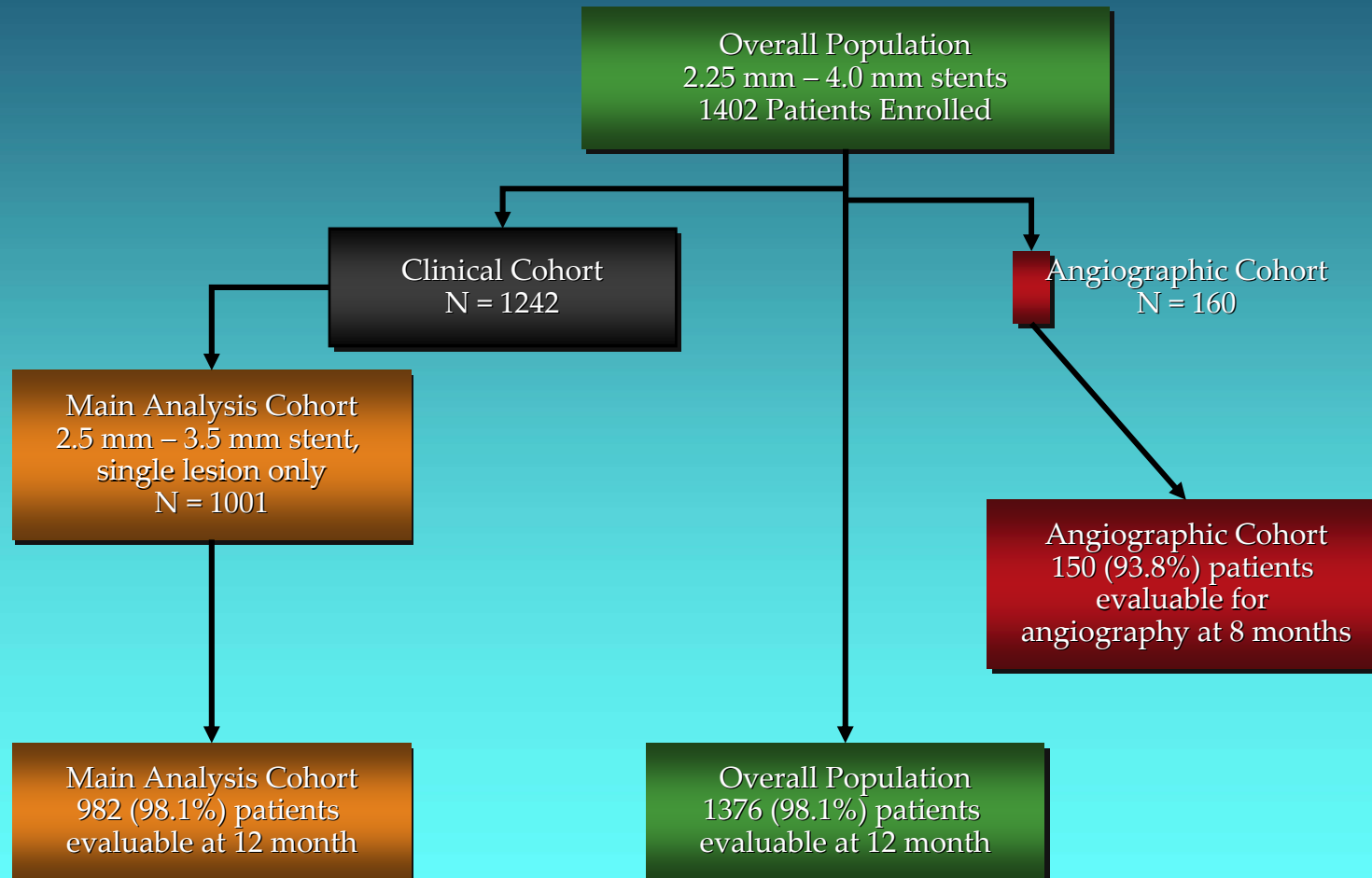
	<i>Resolute DES</i> (<i>n</i> = 1402)
Age (yr)	64
Men (%)	68
Diabetes mellitus (%)	34.4
Insulin dependent (%)	9.6
Prior MI (%)	21.6
Prior PCI (%)	32.7
Prior CABG (%)	8.8
Mean ejection fraction (%)	58.0 ±9.2
Hyperlipidemia (%)	87.7
Hypertension (%)	84.2
Current smokers (%)	20.9
Stable angina (%)	56.1
Unstable angina (%)	41.9
MI (%)	2.1

Lesion Characteristics

	<i>Resolute DES</i> (<i>n_L</i> = 1573)
RVD (mm)	2.59 ±0.47
Minimal lumen diameter (mm)	0.77 ±0.35
Lesion length (mm)	13.06 ±5.88
Lesions treated per patient	1.13 ±0.35
Average DS (%)	70.67 ±11.52
Type B2/C lesion	75.2
Two vessel treated (%)	10.4
≥ small vessel (RVD ≤2.75 mm) (%)	68.5
≥ lesion length > 18 mm (%)	19.9
Vessel location	
LAD (%)	45.9
LCX (%)	32.2
RCA (%)	31.2
LMCA (%)	0.6

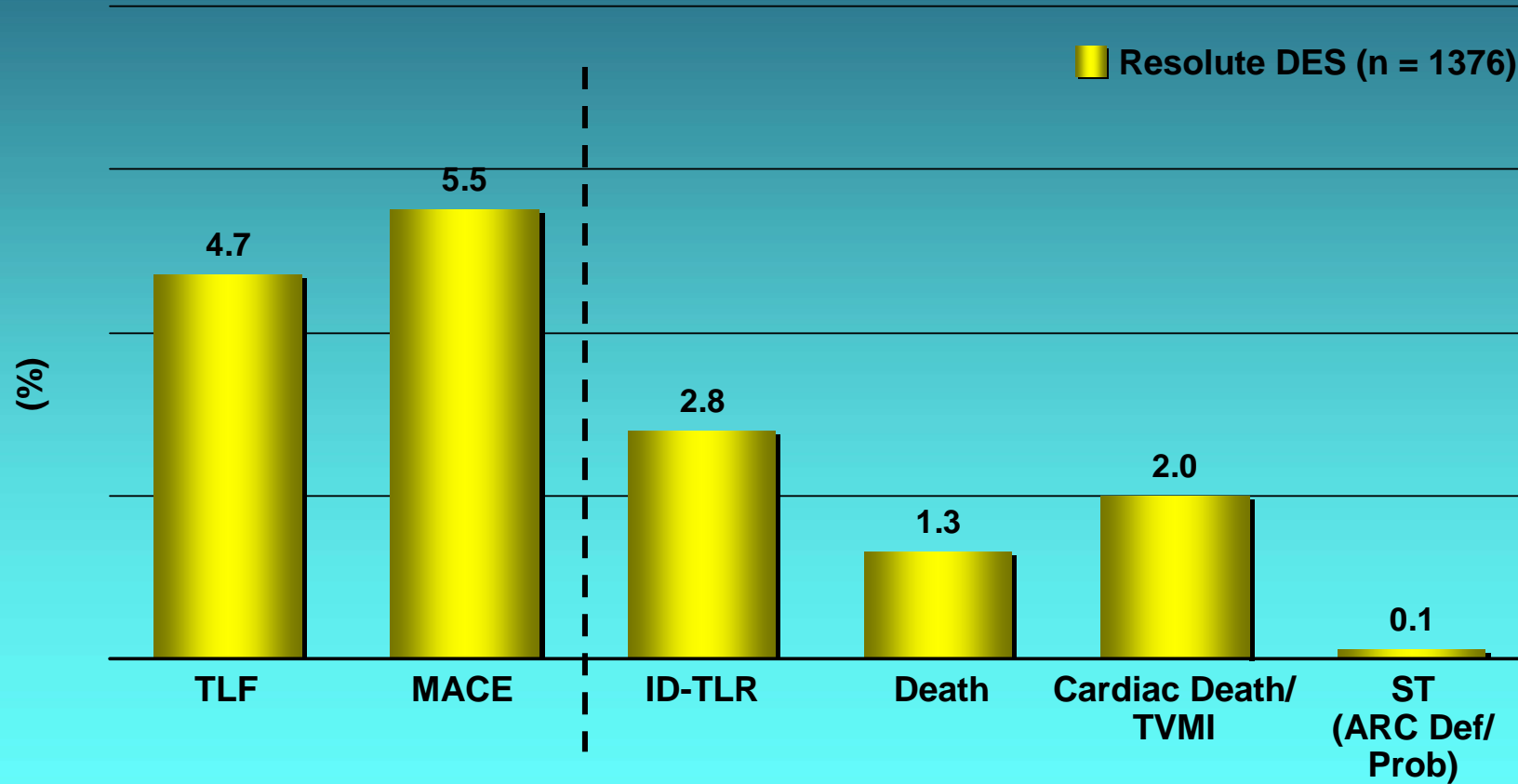
Patient Follow-Up

Robust clinical and angiographic statistical analysis of multiple study arms



Low Rates in All Safety and Efficacy Endpoints

RESOLUTE US 12-Month Data
Overall Cohort (2.25–4.00-mm diameter)

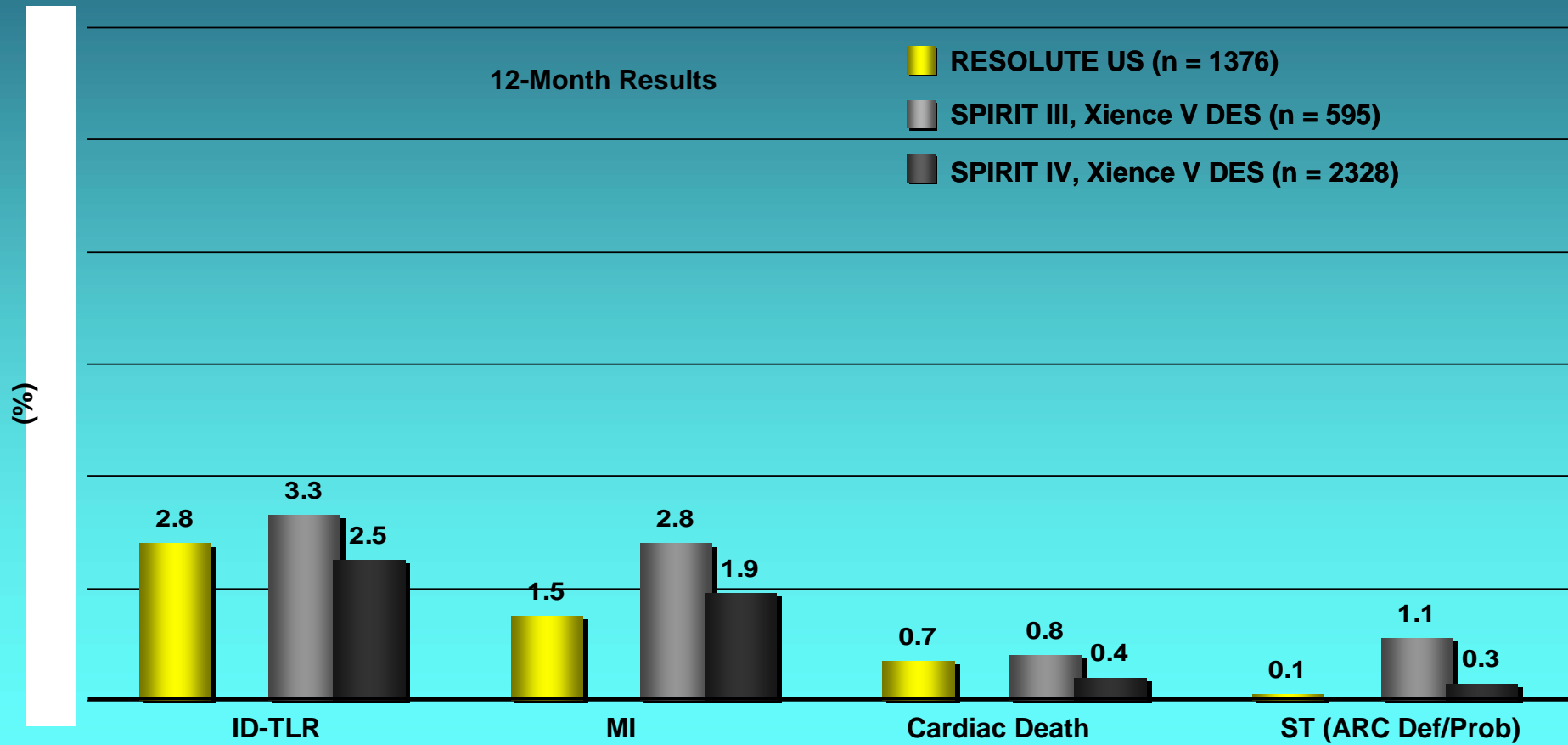


US Trials for Second-Generation DES

	<i>RESOLUTE US</i>	<i>SPIRIT III/SPIRIT IV</i>
Study type	Resolute DES pivotal study Nonrandomised multistudy trial	SPIRIT III–Xience V pivotal study SPIRIT IV–more complex population Both randomised to Taxus Express
N, sites	1402 Resolute DES patients 116 US sites	SPIRIT III–669 Xience V pt; 65 US sites SPIRIT IV–2458 Xience V pt; 66 US sites
Multivessel treatment	Up to 2 vessel treatments	SPIRIT III–up to 2 vessels SPIRIT IV–up to 3 vessels
Angiographic follow-up	8 mo for angio cohort (n = 160)	SPIRIT III–8 mo all patients SPIRIT IV–none
Lesion/stent sizes (mm)	2.25–4.00 (diameter) Up to 38 (length)	2.50–3.75 (diameter) Up to 28 (length)
Primary endpoint	TLF at 12 mo	SPIRIT III–LL at 8 mo; SPIRIT IV–TLF at 12 mo
Diabetes mellitus (%)	34.4 (9.6 IDDM)	SPIRIT III–29.6; (7.8 IDDM) SPIRIT IV–32.0; (8.5 IDDM)
Prior MI (%)	21.6	SPIRIT III–19.9; SPIRIT IV–21
Unstable angina (%)	41.9	SPIRIT III–18.7; SPIRIT IV–27.7
RVD (mm)	2.59	SPIRIT III–2.77; SPIRIT IV–2.75
Lesion length (mm)	13.06 ± 5.88	SPIRIT III–14.7; SPIRIT IV–14.8 ± 6.7
Age (yr)/men (%)	64/68	SPIRIT III–63.2/70.1; SPIRIT IV–63.3/67.7

Clinical Outcomes: RESOLUTE US Overall Cohort

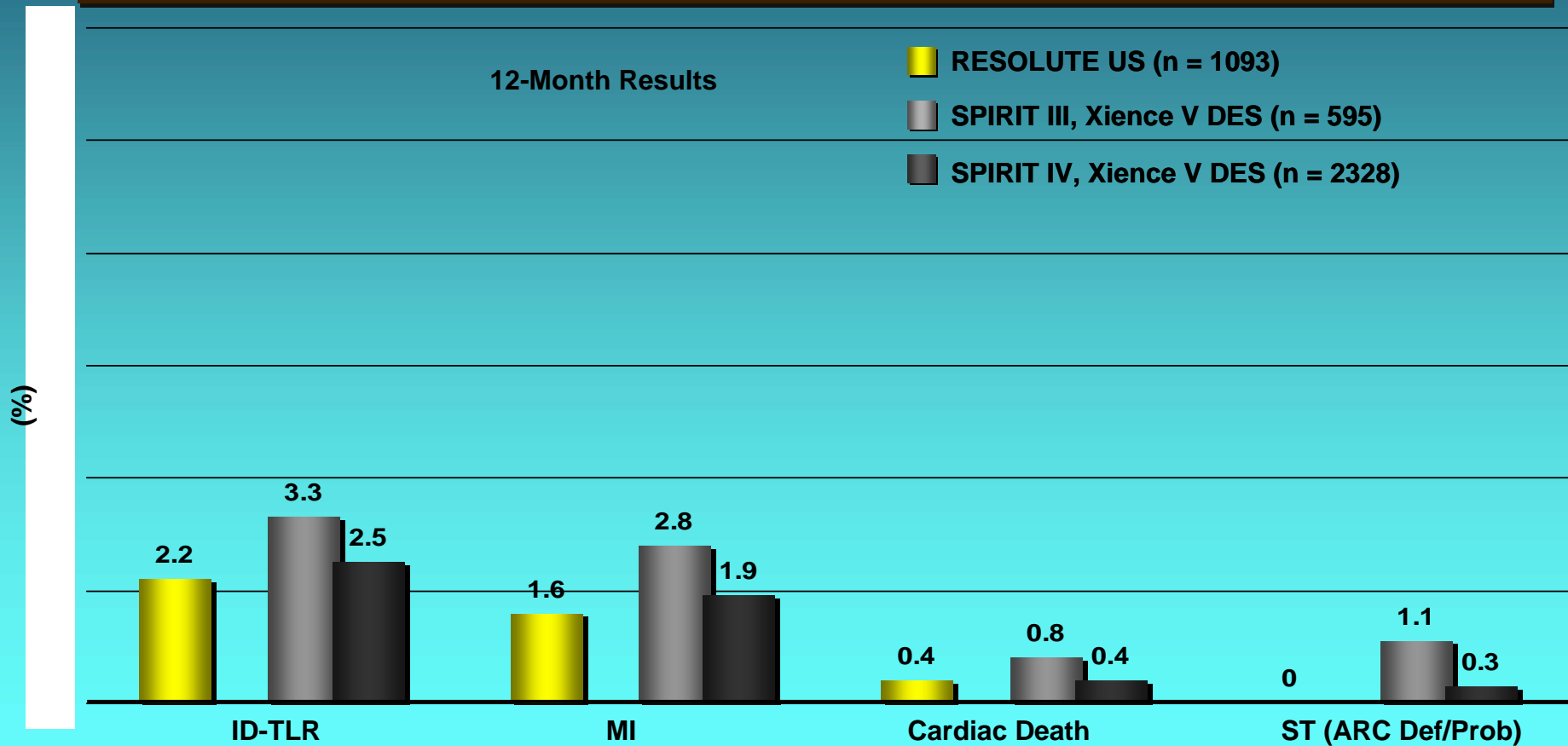
All patients from RESOLUTE US (2.25–4.00-mm diameter)
All patients from SPIRIT III and SPIRIT IV (2.50–3.75-mm diameter)



Results come from separate clinical trials. Data may differ in a head-to-head comparison.

Clinical Outcomes: RESOLUTE US Main Cohort

Main cohort from RESOLUTE US (2.50–3.50-mm diameter)
All patients from SPIRIT III and SPIRIT IV (2.50–3.75-mm diameter)

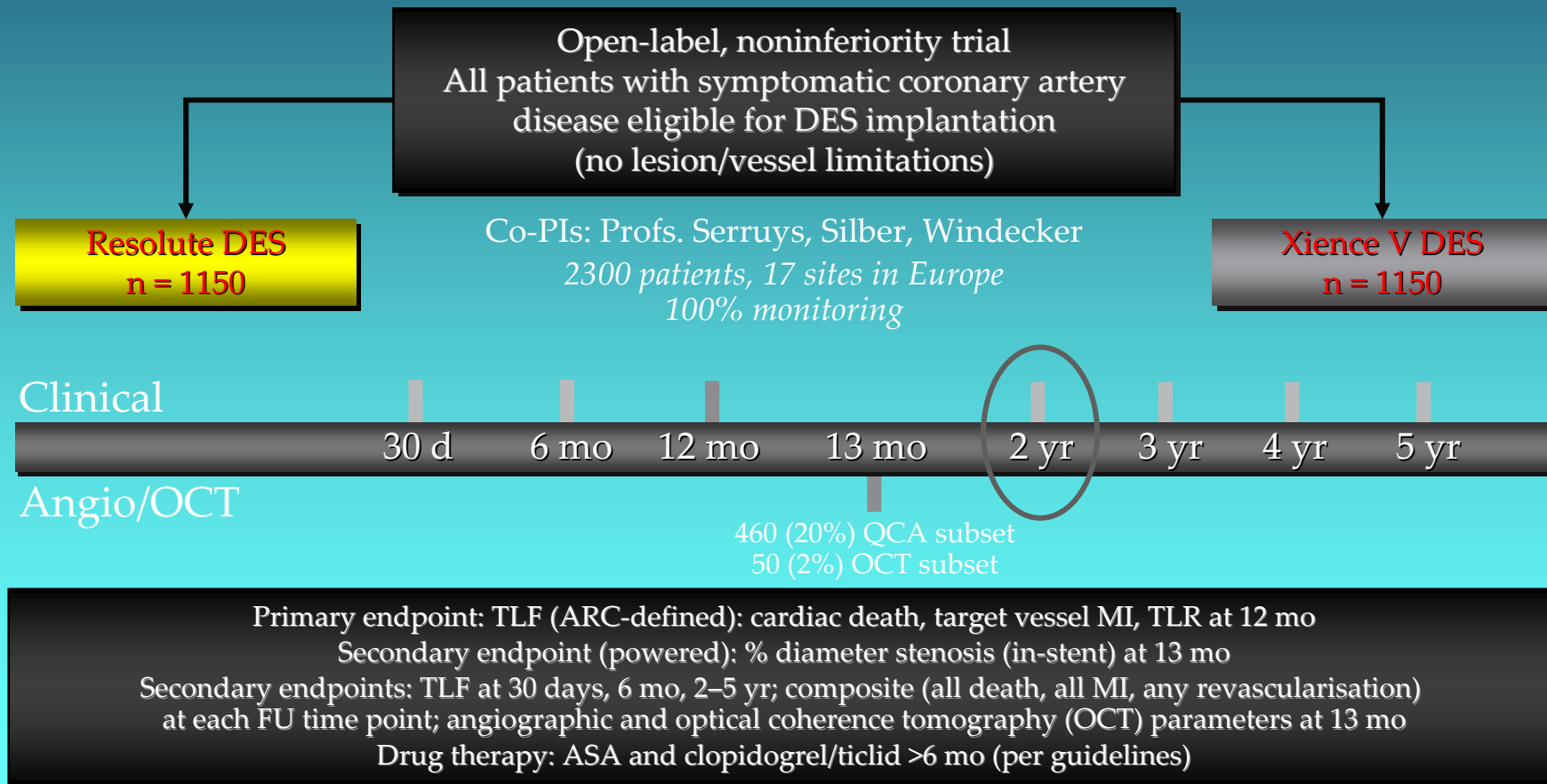


Results come from separate clinical trials. Data may differ in a head-to-head comparison.

Innovative Trial Design

Large, real-world study that reflects complexities of daily clinical practice

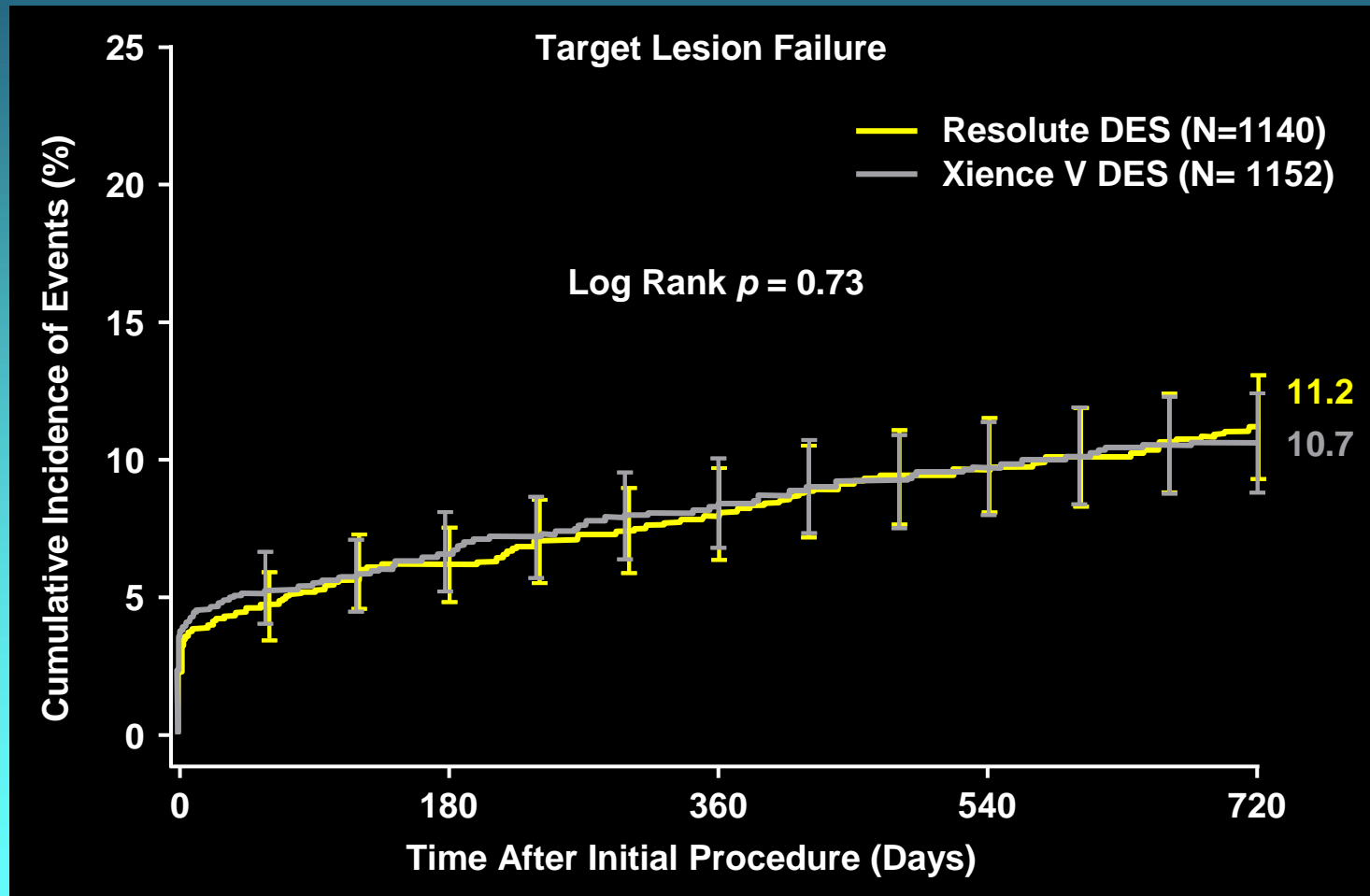
RESOLUTE All Comers Trial Design



Excellent Clinical Follow-Up at 2 Years

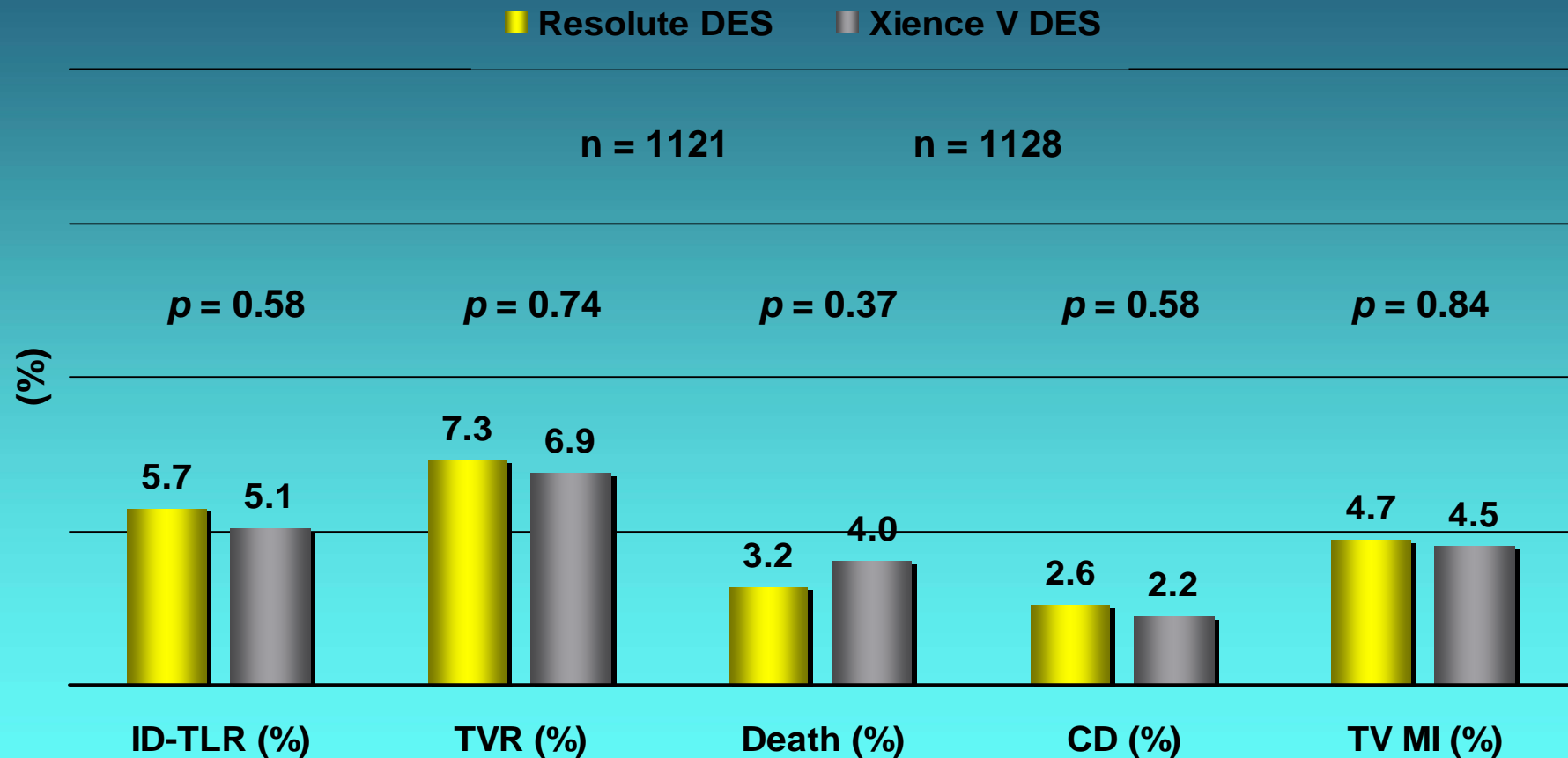


Resolute DES Continues to Match Xience V DES in Primary Endpoint at 2 Years



TLF = cardiac death, target vessel MI, TLR
Error bars indicate a pointwise, two-sided 95% confidence interval ($1.96 \pm SD$).
Standard error is based on the Greenwood formula.

Similar Results in All Efficacy and Safety Endpoints at 2 Years

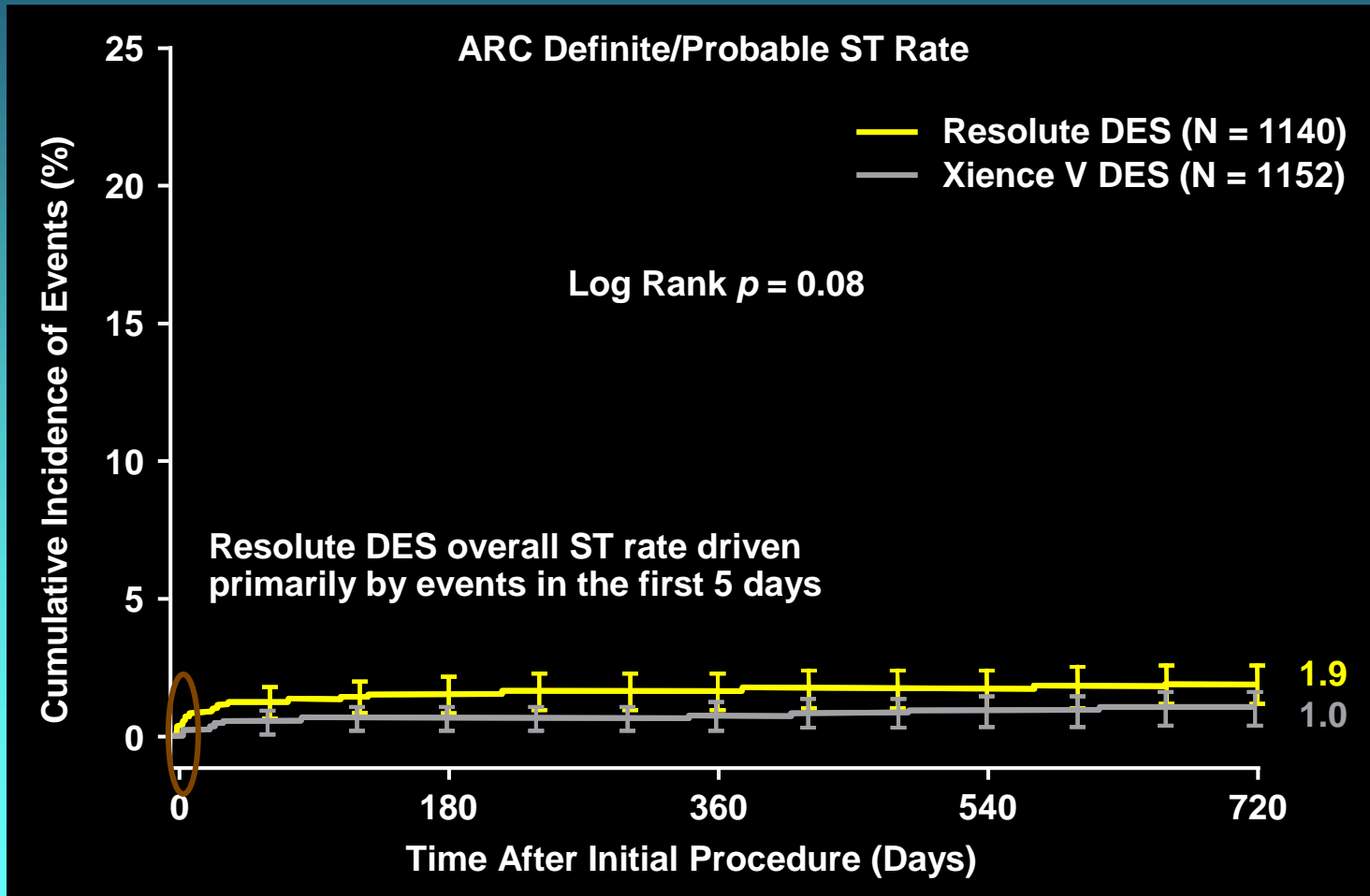


p-Values are based on Fisher Exact Test.

p-Values for outcome differences are unadjusted for multiple comparisons.

RESOLUTE All Comers was not specifically designed or powered to individually compare endpoints shown above.

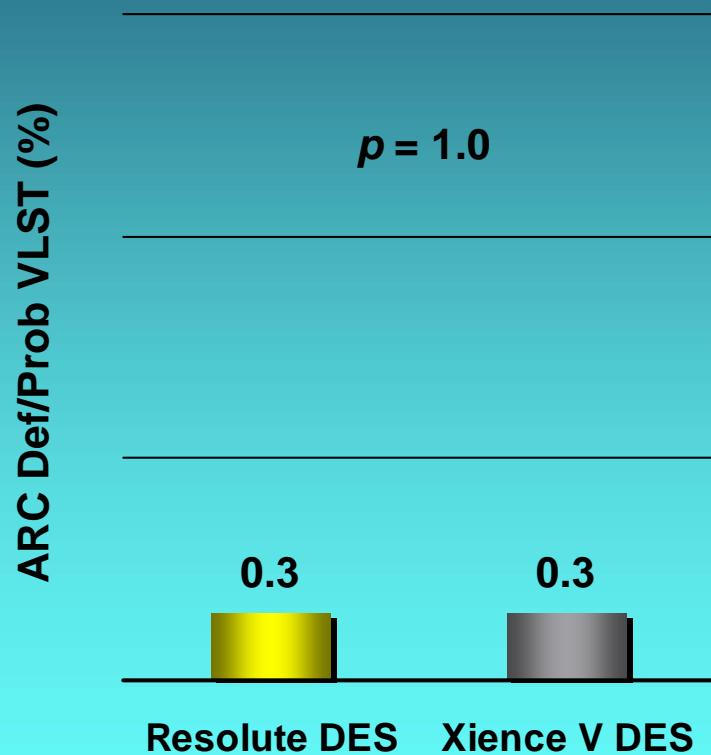
No Significant Difference in Stent Thrombosis Rates



RESOLUTE All Comers was not specifically designed or powered to individually compare endpoints shown above.

No Difference in Very Late Stent Thrombosis (VLST)

No difference in VLST rates



No difference in DAPT compliance

Length of DAPT	Resolute ZES	Xience V EES	p-Value
30 days on (%)	93.8	94.6	0.419
180 days on (%)	93.1	93.3	0.933
360 days on (%)	84.1	83.8	0.908
720 days on (%)	18.6 ²	18.1 ²	0.781

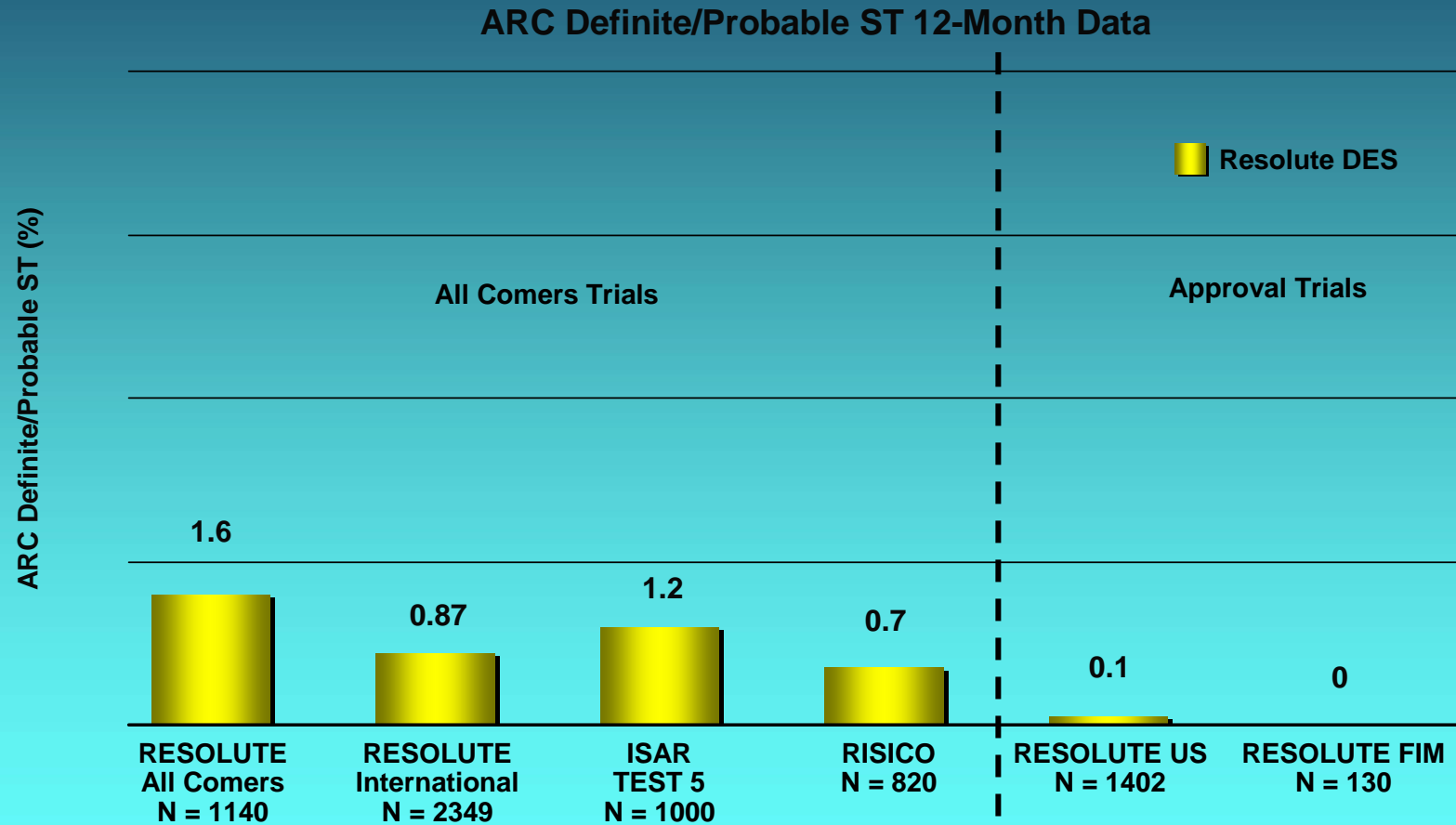
p-Values are based on Fisher Exact Test.

p-Values for outcome differences are unadjusted for multiple comparisons.

RESOLUTE All Comers was not specifically designed or powered to individually compare endpoints shown above.

²Majority on DAPT considered complex or ACS at time of procedure

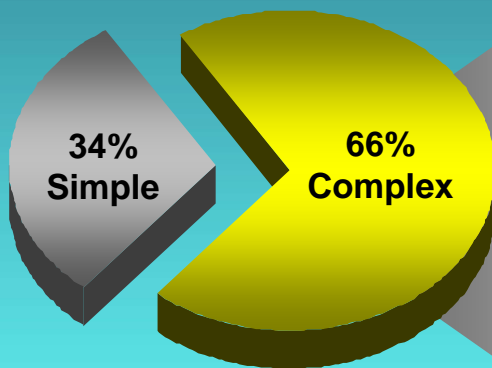
Stent Thrombosis Rates for Resolute DES Across the Patient Spectrum



Studies not powered for this low-frequency ST event.

Almost 70% of RESOLUTE All Comers Patients are Complex

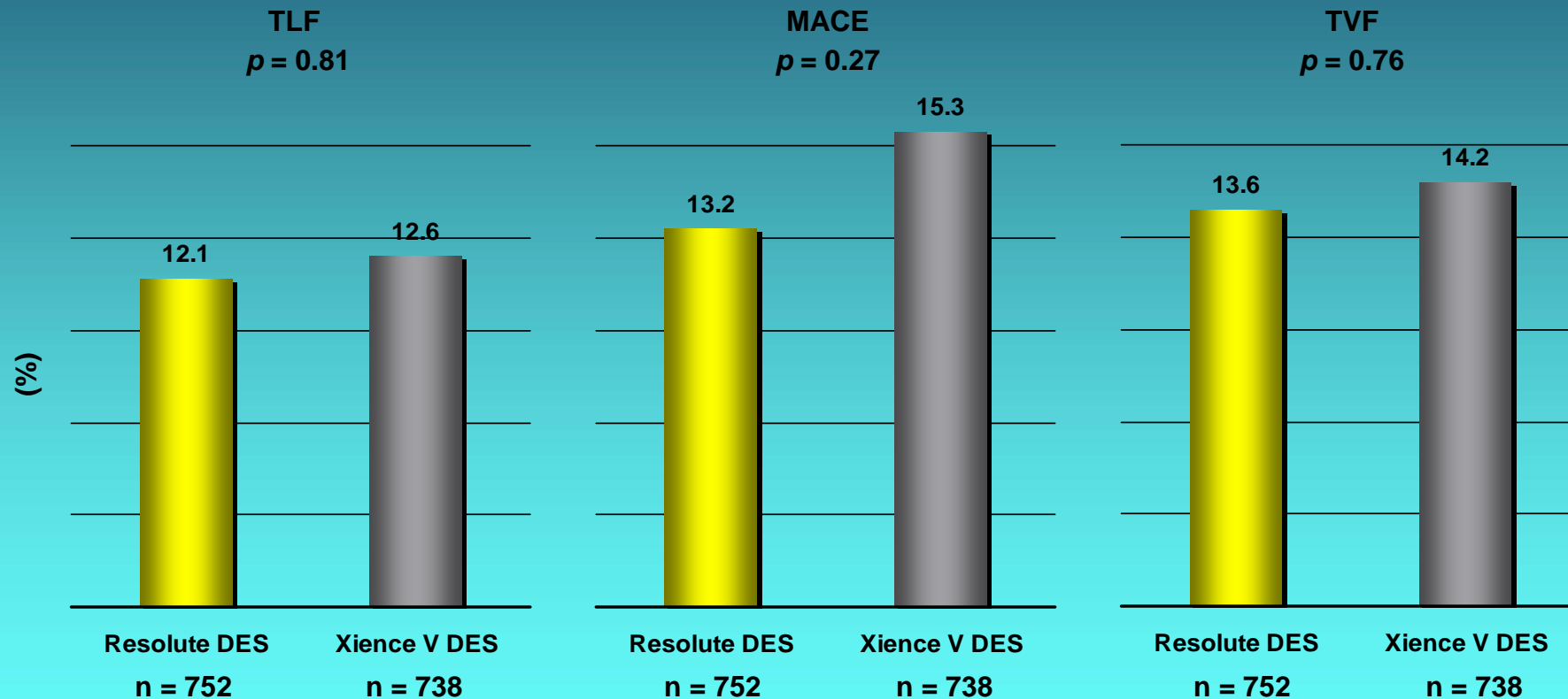
**All Patients
N = 1520/2292**



<i>Patient Characteristics</i>	<i>Resolute DES N = 1140 (%)</i>	<i>Xienc V DES N = 1152 (%)</i>	<i>p-Value</i>
Complex	67.0	65.6	NS
AMI (within 72 hours)	28.9	28.8	NS
Multivessel treatment (>2)	25.1	24.7	NS
Renal insufficiency	4.0	3.1	NS
ISR	8.1	8.0	NS
Bifurcation	16.9	17.7	NS
Unprotected left main	1.6	1.3	NS
Bypass graft	2.5	2.4	NS
LVEF <30%	2.8	2.1	NS
Long lesion (>27 mm)	5.7	6.0	NS
Total occlusion	16.3	17.2	NS
>1 lesion per vessel	16.4	17.7	NS
Thrombus lesion	7.4	6.9	NS

With the exception of long lesions (treatable with a single 38-mm length stent), Resolute DES currently is not specifically approved for the patient subsets noted in this complex patient definition.

Resolute Strength: Powerful Performance in Complex Patients at 2 Years

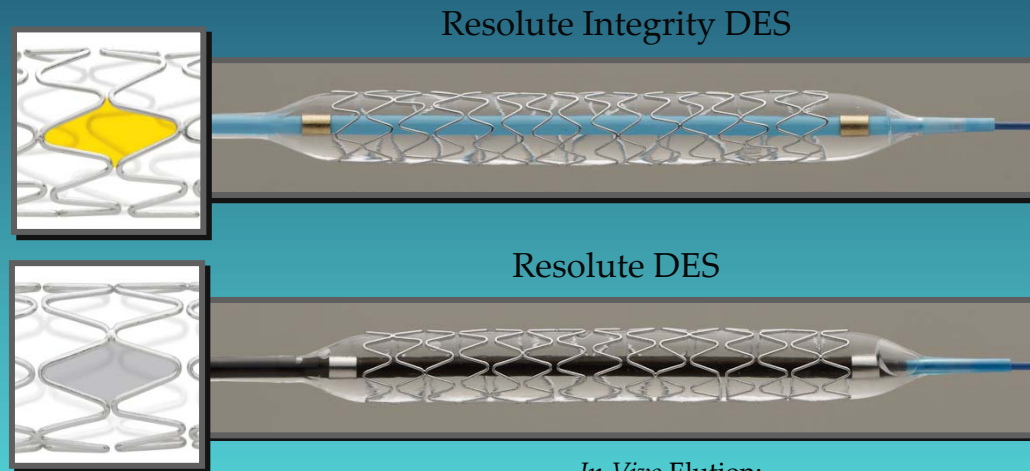


Complex patient definition: Bifurcation, SVG, ISR, AMI <72 hr, LVEF <30%, unprotected LM, >2 vessels stented, renal insufficiency or failure (creatinine >140 $\mu\text{mol/L}$), lesion length >27 mm, >1 lesion/vessel, lesion with thrombus or TO (preprocedure TIMI = 0). Currently, Resolute DES is not specifically approved for the subsets noted in this complex patient definition. *p*-Values are based on Fisher Exact Test. *p*-Values for outcome differences are unadjusted for multiple comparisons. RESOLUTE All Comers was not specifically designed or powered for complex patient subset analysis.

Resolute Integrity DES Provides Identical Drug Delivery to Resolute DES

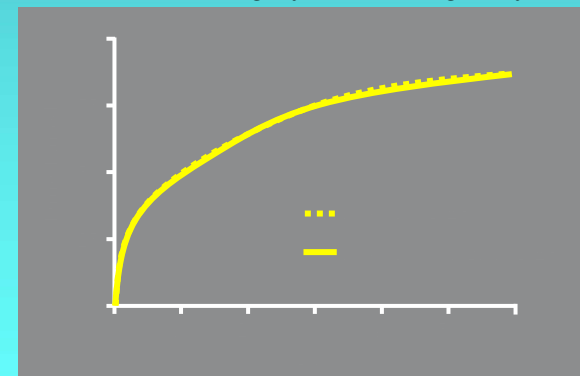
This is achieved by having highly similar:

- Surface area
- Scaffolding
- Strut thickness
- Cell area
- Drug load and drug distribution
- Drug elution



In-vivo elution³ results for Resolute Integrity DES provide confidence that you can expect the same powerful clinical performance as Resolute DES

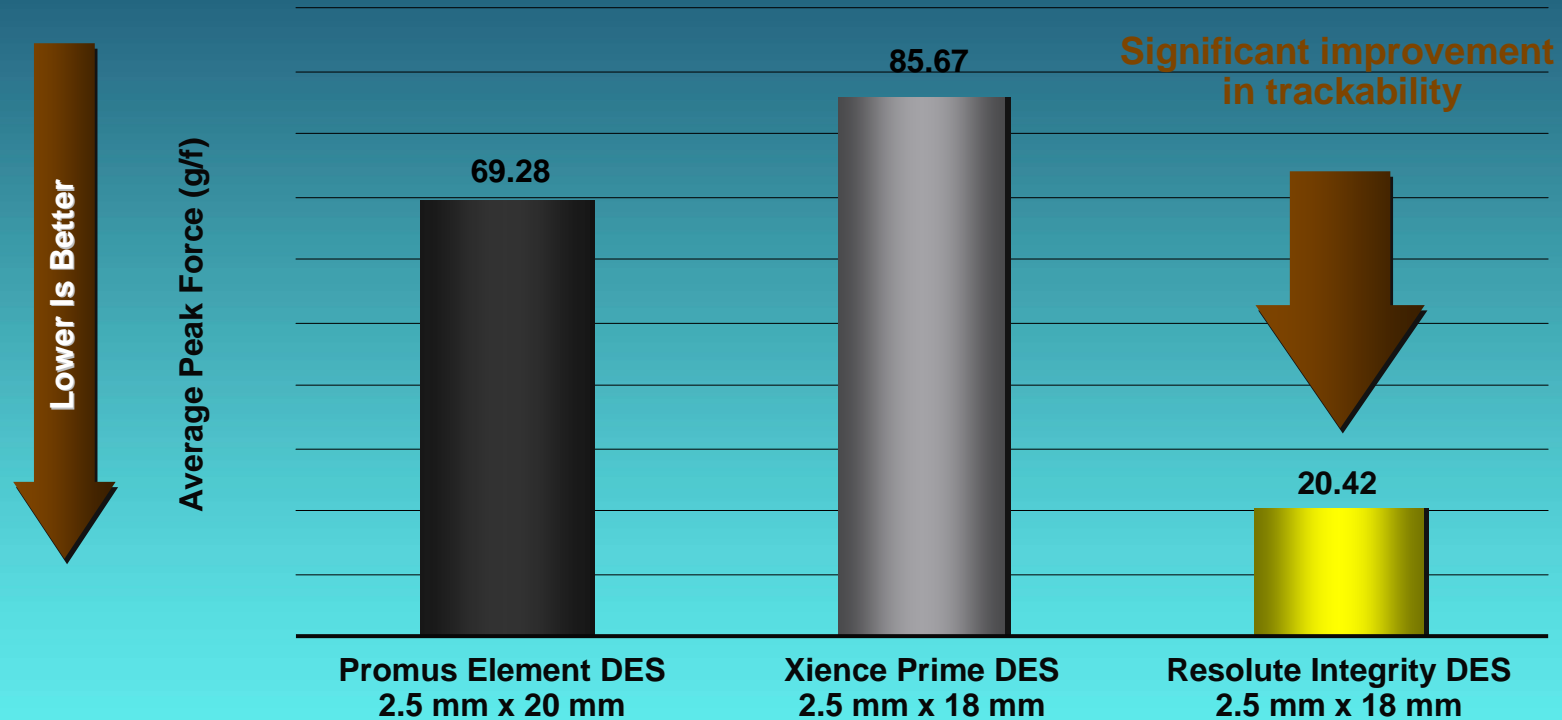
In-Vivo Elution:
Comparison of Resolute DES and
Resolute Integrity DES Through Day 60



³Porcine coronary artery model.
Data on file at Medtronic, Inc. and may not be indicative of clinical performance.

Resolute Integrity DES Redefines Performance

Trackability 3D: DES



The Resolute Integrity stent's unique helical design and new delivery system provide **breakthrough deliverability that is superior to leading DES.**

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance.

Comparison of Device Performance for Market-Leading DES

	<i>Resolute Integrity DES</i>	<i>Xience Prime DES</i>	<i>Promus Element DES</i>	
LESION ACCESS				Best
Trackability				Average
Crossing profile				Worst
Pushability				
PLACEMENT ACCURACY				
Radiopacity				
Stent foreshortening				
LESION COVERAGE				
Scaffolding				
Radial strength				
Strut apposition				
ANATOMICALLY COMPLEX LESIONS				
Sidebranch access				
Vessel conformability ⁴				

Resolute Integrity DES redefines performance.

Bench test data on file at Medtronic

⁴Simulated FEA studies Resolute Integrity DES vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES were performed by Dr. Peter Mortier, FEops/Ghent University, Belgium (manuscript in preparation). These tests may not be indicative of clinical performance.

Summary & Conclusion

; Resolute DES Shows Powerful Clinical Performance Across the Patient Spectrum

RESOLUTE US 12-Month Summary

- Robust trial design that enrolled a broad range of patients and lesions
 - High percentage of challenging cases: 34% diabetics and 70% small vessels
 - Resolute DES shows a very low rate of events for all safety and efficacy outcomes

RESOLUTE All Comers 2-Year Summary

- Resolute DES matches Xience V DES in all clinical endpoints at 2 years
 - No significant difference in clinical outcomes or stent thrombosis rates
- Resolute DES shows powerful performance in complex patients

Make the Complex Simple

- Revolutionary stent engineering with Resolute Integrity DES provides superior deliverability¹ and better conformability² vs. major competitors with enhanced procedural confidence

Powerful clinical performance with superior deliverability

RESOLUTE US and All Comers trials studied Resolute DES.

RESOLUTE All Comers was not specifically designed or powered for complex patient subset analysis.

¹Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc.

²Simulated FEA studies Resolute Integrity DES vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES were performed by Dr. Peter Mortier, FEops / Ghent University-Belgium (Manuscript in preparation).

These tests may not be indicative of clinical performance.