Vergängliche Stents von der Hand zum Herz

Burkhard Hornig

Herzpraxis Warteckhof

Vergängliche Stents

von der Hand zum Herz

Burkhard Hornig

Herzpraxis Warteckhof

Hintergrund

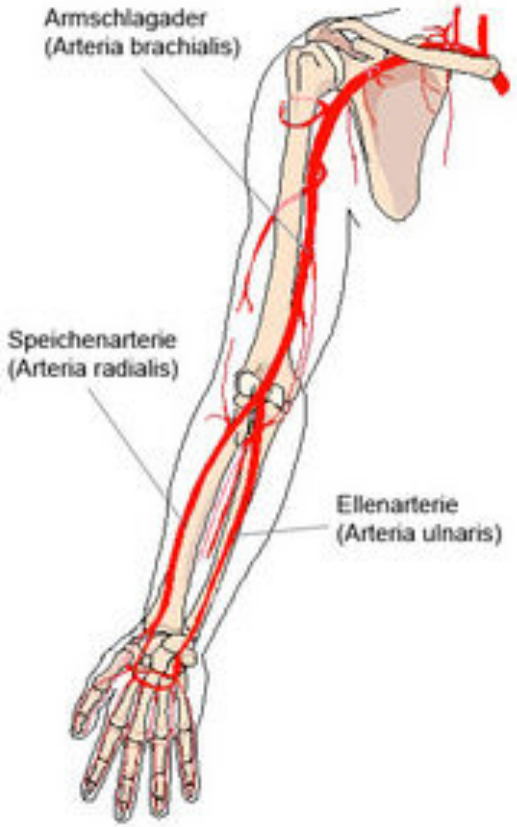
- Seit 1977 werden Koronarangiographien und Interventionen (PTCA/Stentimplantation) überwiegend über einen Zugang in der A. femoralis durchgeführt
- Anschliessend bekommt der Patient einen Druckverband und hat Bettruhe ≥6h

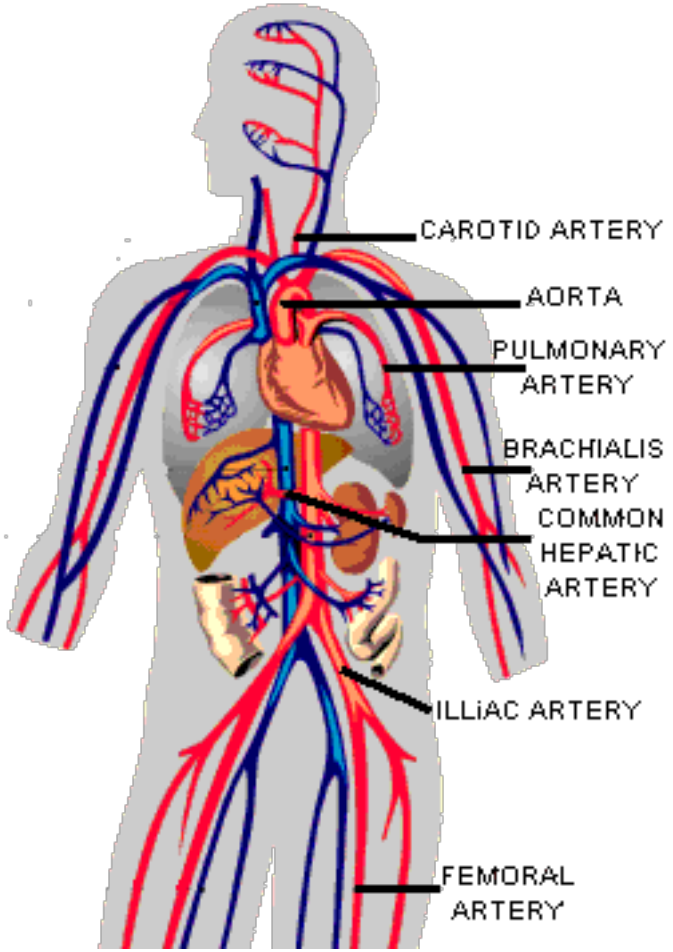
Kardiologe 2012 · 6:423–426
DOI 10.1007/s12181-012-0451-6
Online publiziert: 26. September 2012

H. Thiele
Klinik für Innere Medizin/Kardiologie, Universität Leipzig – Herzzentrum, Leipzig

Herzkatheter via A. radialis: Ist der femorale Zugangsweg noch zeitgemäß?

Zugangswege zum Herz

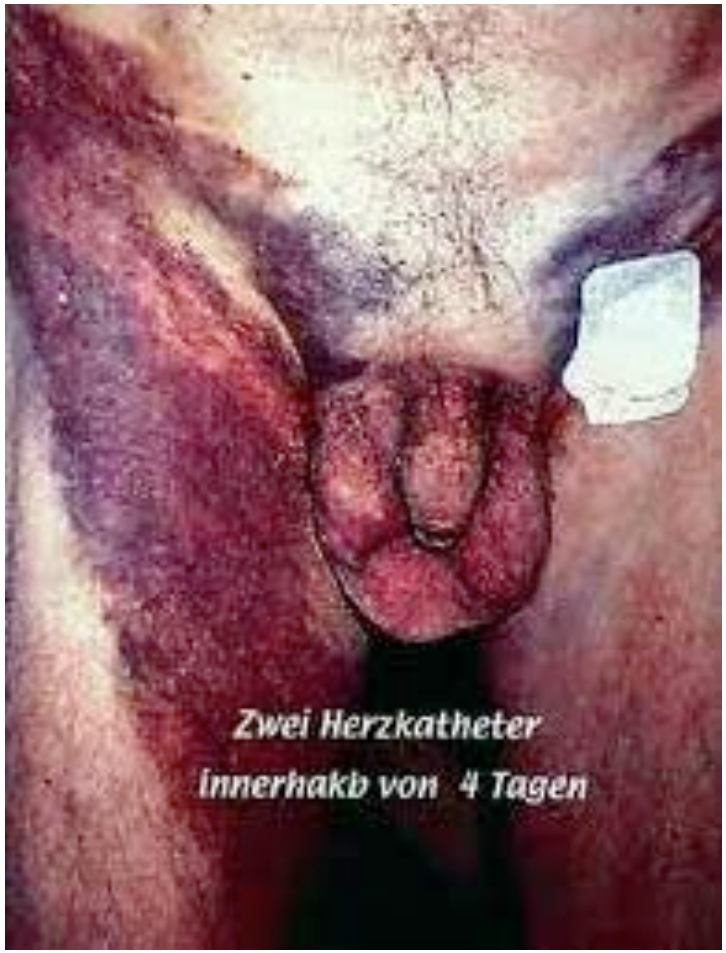


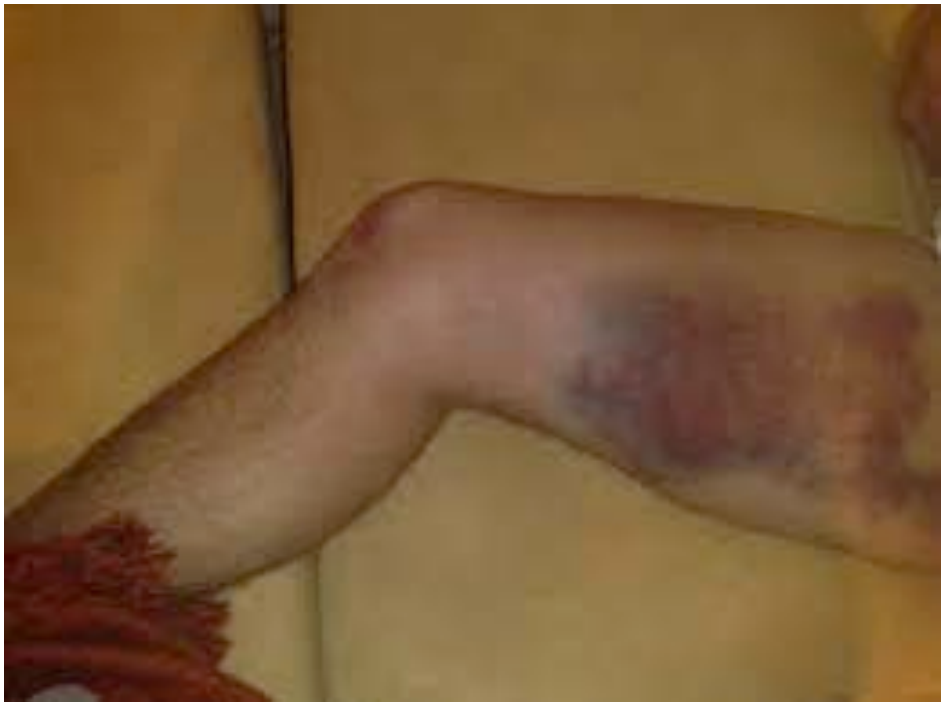


Vorteile Zugang A. femoralis

- Grosser Gefässdiameter erlaubt grosskalibrige Katheter
- Untersuchung einfacher zu erlernen als via A. radialis
- Gefäss kann unkompliziert und mehrfach punktiert werden

Nachteile des Zugangsweg via A. femoralis





Vorteile Zugangsweg A. radialis

- Weniger Blutungskomplikationen
- Patient kann sofort nach Koro/PTCA/Stent mobilisiert werden
- Reduziert Mortalität bei Patienten mit Herzinfarkt im Vgl. zum Zugangsweg A. femoralis
- Untersuchung rechte und linke Koronararterie mit dem gleichen Katheter möglich

Nachteile Zugangsweg A. radialis

- Gefässdiameter kleiner, kleinkalibrige Katheter erforderlich (Koro/PTCA/Stent in 5F)
- Untersucher braucht mehr Erfahrung
- (Anfangs) Höhere Strahlenbelastung
- Nicht günstig bei Patienten mit Zn. Bypass-OP
- A. ulnaris muss gut funktionieren (Allen-Test)
- Selten: asymptomatischer Verschluss der A. radialis als Folge

Herzkatheter via A. radialis

Durchführung und Anlage des Luftkissen-Verbands

Herzkatheter via A. radialis

Durchführung und Anlage des Luftkissen-Verbands

Umdenken erforderlich!

- Empfehlung der Europäischen Gesellschaft für Kardiologie (ESC)
- In allen Kardiol. Zentren sollten > 50% der Untersuchungen (Koro und PCI) via A. radialis durchgeführt werden
- Insbesonders Patienten mit akutem Myokardinfarkt profitieren
- EuroIntervention. 2013 Mar;8(11):1242-51. doi: 10.4244/EIJV8I11A192

Umdenken erforderlich!

- **Achtung Pflege:** bei Patienten, die eine Koro via A. radialis rechts erhalten sollen, ist ein Venflow am rechten Handrücken, Handgelenk oder Unterarm nicht geeeignet! **Venflo immer am linken Arm**

- Nach Ende der Koro/PTCA wird ein ca. 5cm breiter, Luft-gefüllter Druckverband um das rechte Handgelenk angelegt!

- Aus einem venösen Zugang an der rechten Hand/ Handgelenk/Unterarm würde es herausbluten, eine Infusion würde nicht laufen, der Druckverband könnte nicht korrekt angelegt werden

Umdenken erforderlich!

- **Achtung Pflege:** Patienten, die eine Koro/PTCA via A. radialis rechts erhalten haben, dürfen und sollen auch direkt nach der Untersuchung mobilisiert werden (zB Mittagessen am Tisch)

- Bitte Schema beachten: 4 Stunden nach Ende Koro/PCI beginnen, Luft aus cuff-Verband abzulassen

- Cuff in der Regel mit 15-18ml Luft gefüllt

ERWEITERUNG UND REINIGUNG DER PUMPENLEITUNGEN VON KALK UND FETT DURCH HOCHDRUCK UND STENT.

Vergängliche Stents

von der Hand zum Herz

Burkhard Hornig

Herzpraxis Warteckhof

Hintergrund

- Ab 1977: Ballonangioplastie
  Limitation: Restenose ca. 30%

- Ab 1988: coronare Stent Implantation
  (bare metal stent)

  Limitationen:
  In-Stent Restenose ca. 15%
  Stent-Thrombose (akut/spät)
  Fremdkörper-Reaktion in der Gefässwand
  Metall behindert spätere Bypass-Anlage

Hintergrund

- Ab 2001: Drug eluting Stent

  Limitationen:

  In Stent Restenose ca. 5%

  Stent-Thrombose (akut/spät)

  Fremdkörperreaktion in der Gefässwand

  verzögerte Re-Endothelialisierung

  gestörte Vasomotion durch Medikamentenfreisetzung

  Metall behindert spätere Bypass-Anlage

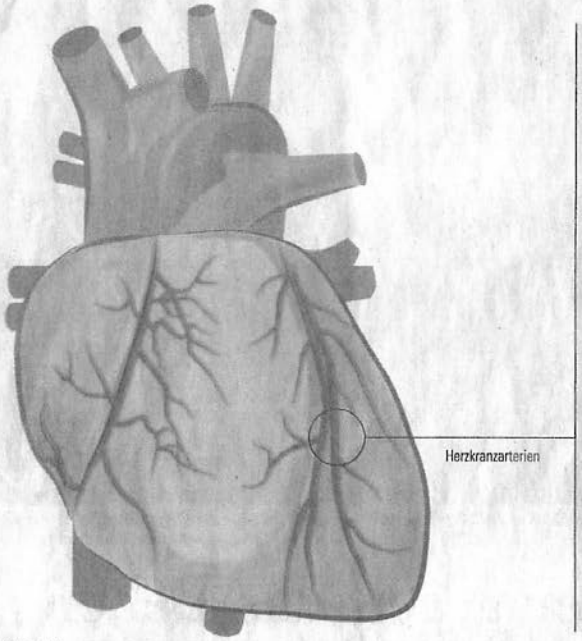
Kriterien für einen „perfekten“ Stent

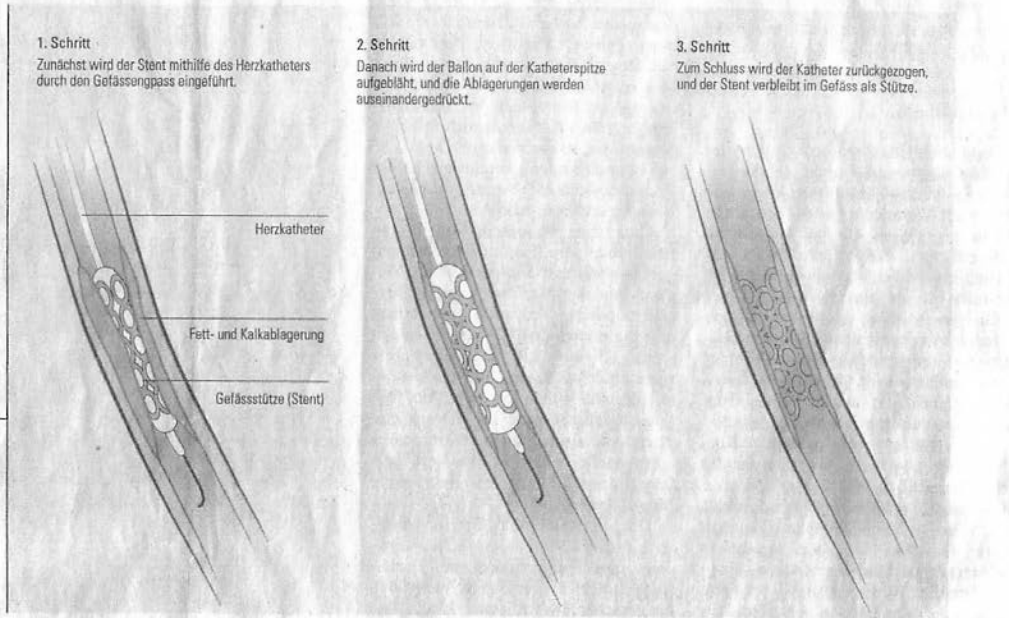
- Hält Gefäss durch mechanische Stabilität für ca. 6 Monate offen (dann ist Wundheilung abgeschlossen) nach Verletzung durch PTCA
- Löst sich anschliessend auf
- Setzt in den ersten 4-6 Wochen antiproliferativ wirkendes Medikament frei, denn Aktivierung von Wachstums-Genen nach PCI nur in den ersten 2(-4) Wochen

Die Suche nach dem perfekten Stent

Neue Zürcher Zeitung

Behandlung verengter Herzkranzarterien mit dem Katheter





ELLE DREAMSTIME, EESOM

NZZ-INFOGRAFIK/lea

Vergängliche Stützen für enge Herzgefässe

Das Interesse am «perfekten» Stent ist ungebrochen

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

New Drugs and Technologies

Bioresorbable Scaffold

The Advent of a New Era in Percutaneous Coronary and Peripheral Revascularization?

Yosinobu Onuma, MD; Patrick W. Serruys, MD, PhD

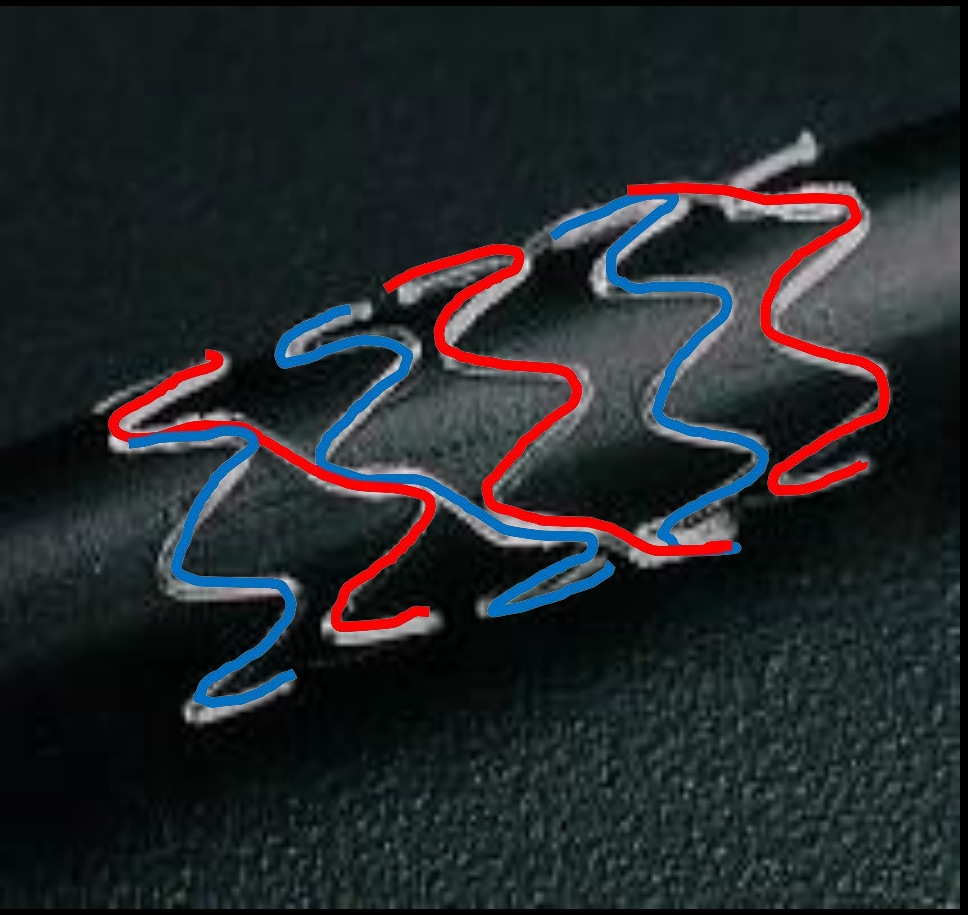
Mechanical properties and degradation time for different polymers and Metals

Polymer composition	Tensile modulus of elasticity (Gpa)	Tensile strength (Mpa)	Elongation at break (%)	Degradation time (months)
Poly(L-lactide)	3.1-3.7	60-70	2-6	>24
Poly (DL-lactide)	3.1-3.7	45-55	2-6	12-6
Poly (glycolide)	6.5-7.0	90-110	1-2	6-12
50/50 DL-lactide/glycolide	3.4-3.8	40-50	1-4	1-2
82/18 L-lactide/glycolide	3.3-3.5	60-70	2-6	12-18
70/30 L-Lactide/ ε -caprolactone	0.02-0.04	18-22	>100	12-24
Cobalt chromium	210-235	1449	~40	Biostable
Stainless steel 316L	193	668	40+	Biostable
Nitinol	45	700-1100	10-20	Biostable
Magnesium alloy	40-45	220-330	2-20	1-3

Real verfügbare biodegradierbare Stents

Company	Product	Material	Development	Preclinical	Clinical	Post clinical
Abbott	ABSORB	PLLA/ PDLLA	✓	✓	✓	✓
Elixir	DESolve	PLLA / PDLLA	✓	✓	✓	✓
Meril	MeRes	PLLA	✓	✓		
Amaranth Medical	FORTITUDE	PLLA	✓	✓	✓	
ART	ART18Z	PDLLA	✓	✓	✓	
Kyoto Medical	IGAKI-TAMAI	PLLA	✓	✓	✓	
Arterius	ReBioStent	PLLA	✓	✓		
Huaan	XINSORB	PLA/PCL/PGA	✓	✓		
OrbusNeich	On-AVS	PLLA/PDLA/TMC/eCAP	✓	✓		

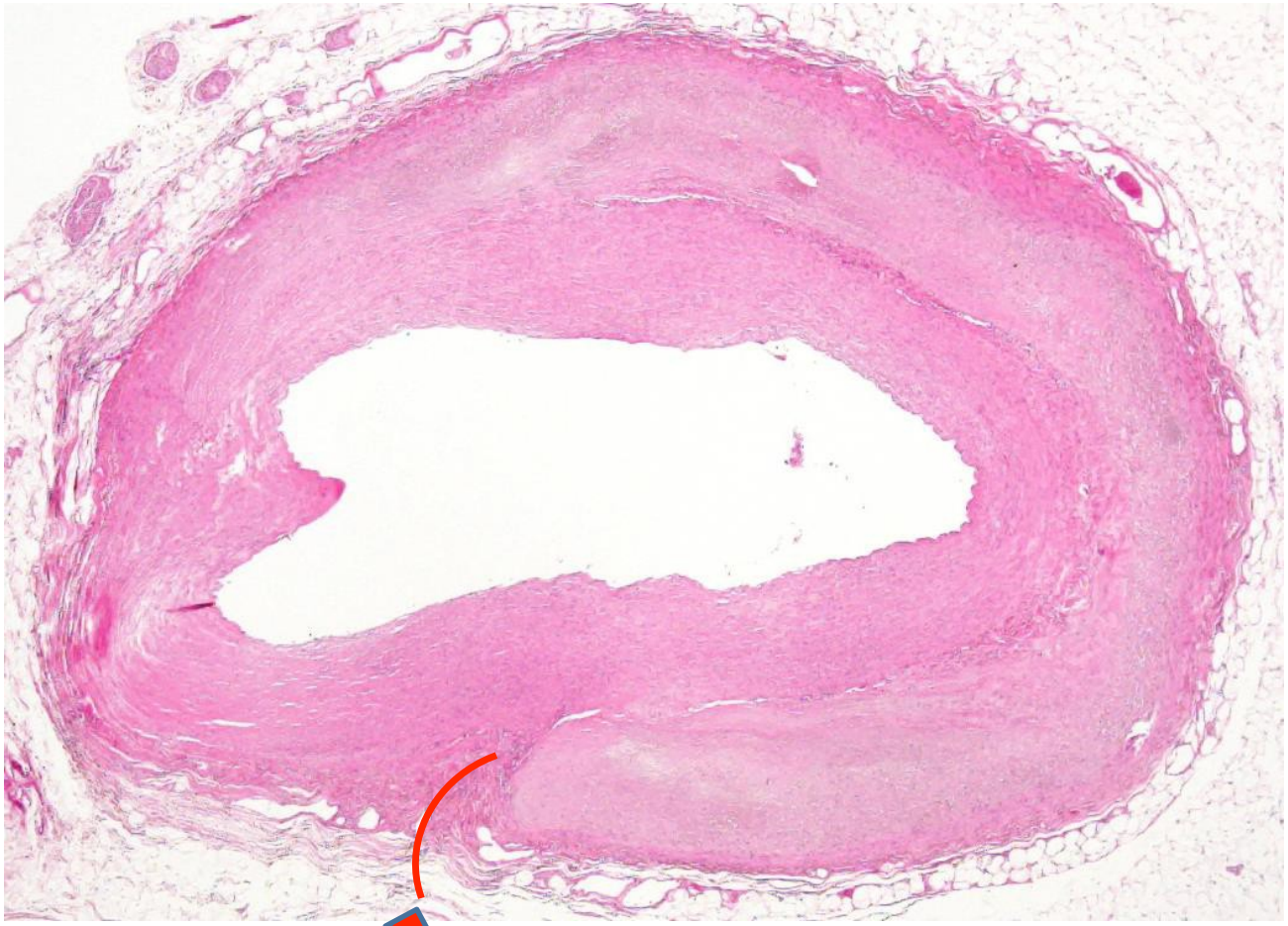
1# Kyoto Medical: Igaki-Tamai Stent



- ✓ Poly-L lactic acid monofilament stent
- ✓ Thickness 170 μ m
- ✓ Balloon expandable stent but also thermoresponsive
- ✓ The 1st BRS stent - implanted in 50 pts in 63 lesions (*BRS = Bare reabsorbable Stent*)
- ✓ Fully absorption on IVUS in 4y

Decade of Histological Follow-Up for a Fully Biodegradable Poly-*l*-lactic Acid Coronary Stent (Igaki-Tamai Stent) in Humans: Are Bioresorbable Scaffolds the Answer?

Histology: 10 years stented LAD with an Igaki-Tamai stent

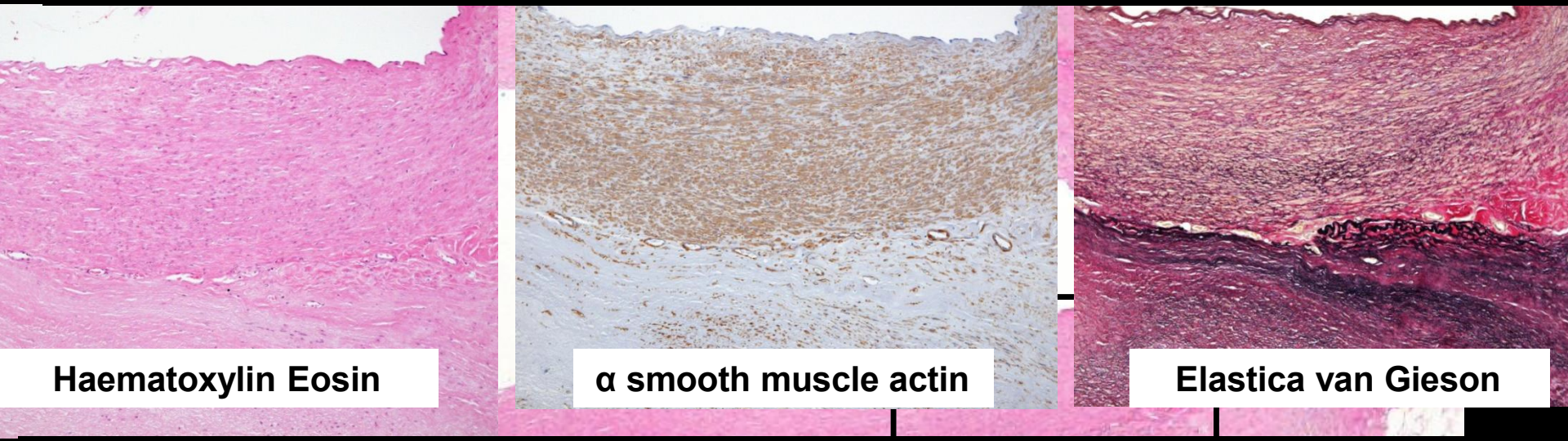


Nishio et al. Circulation 2014;129:534-535

1# Kyoto Medical: Igaki-Tamai Stent

Histology: 10 years stented LAD with an Igaki-Tamai stent

- There were almost no inflammatory cell infiltrations or foreign body reactions in 10-year histology.



- In neo-intima (neo-media), smooth muscle cells and fibrotic tissue were observed.
- Sirolimus-eluting version is under development

Nishio et al. Circulation 2014

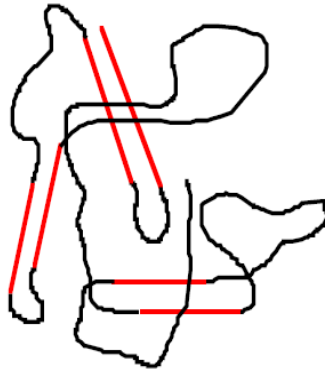
2# Abbott:
Bioabsorbable *Drug Eluting* Stent ("ABSORB")

Poly-lactic Acid (PLA) Polymer

Amorphous

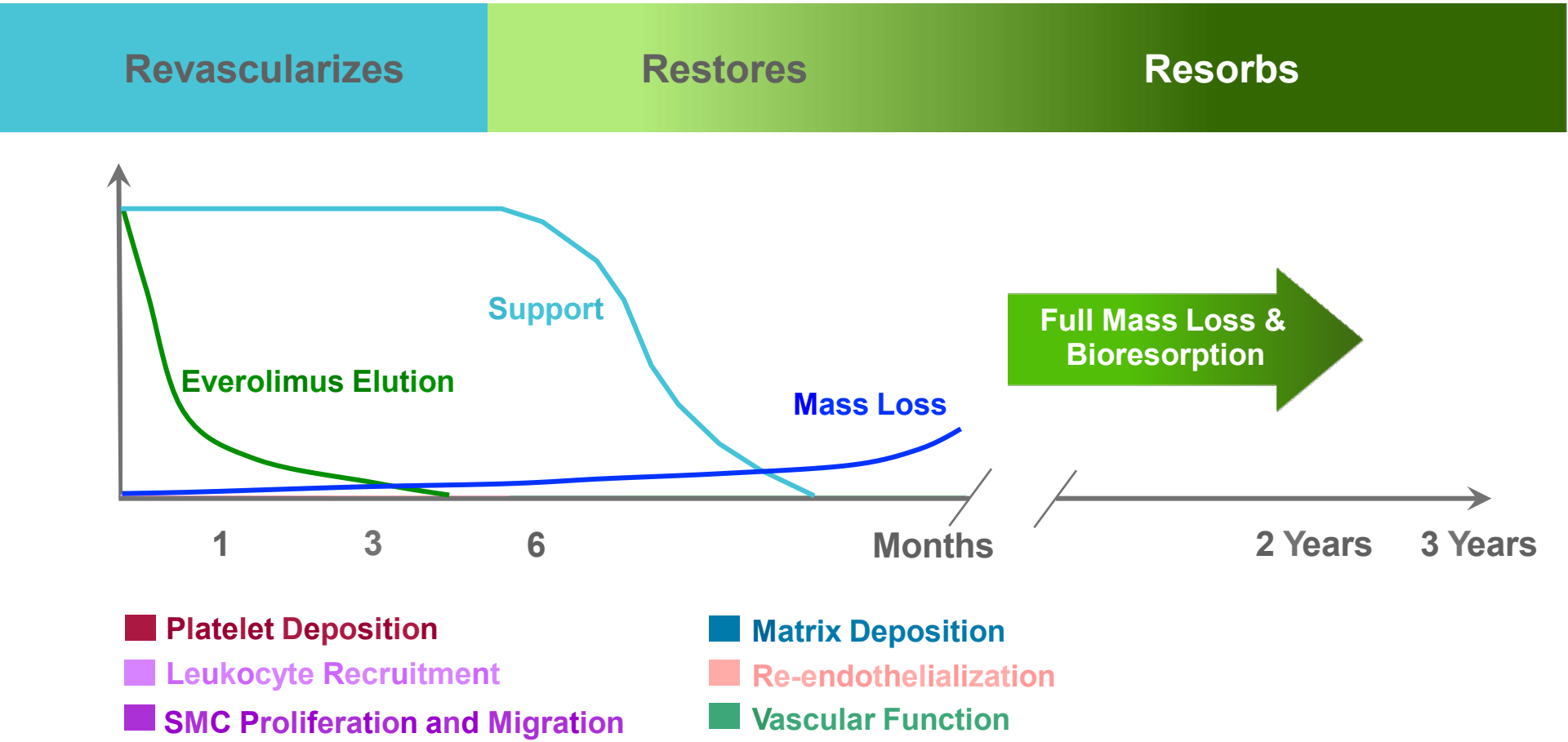
Thin coating of amorphous PDLA **Lower crystallinity** containing Everolimus at a ratio of 1:1
Controlled drug release

Crystalline



PLLA scaffold Backbone
Higher crystallinity
Provides scaffold integrity
Increased radial strength

Design Requirements of a Fully* Bioresorbable Scaffold: Aligning Device Engineering with Vascular Biology



Forrester JS, et al., J. Am. Coll. Cardiol. 1991; 17: 758. / Oberhauser JP, et al., EuroIntervention Suppl. 2009; 5: F15-F22.

*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

Data on file at Abbott Vascular.

The Clinical Need for a Bioresorbable Vascular Scaffold

Rationale

Vessel scaffolding is only needed transiently*

Vision

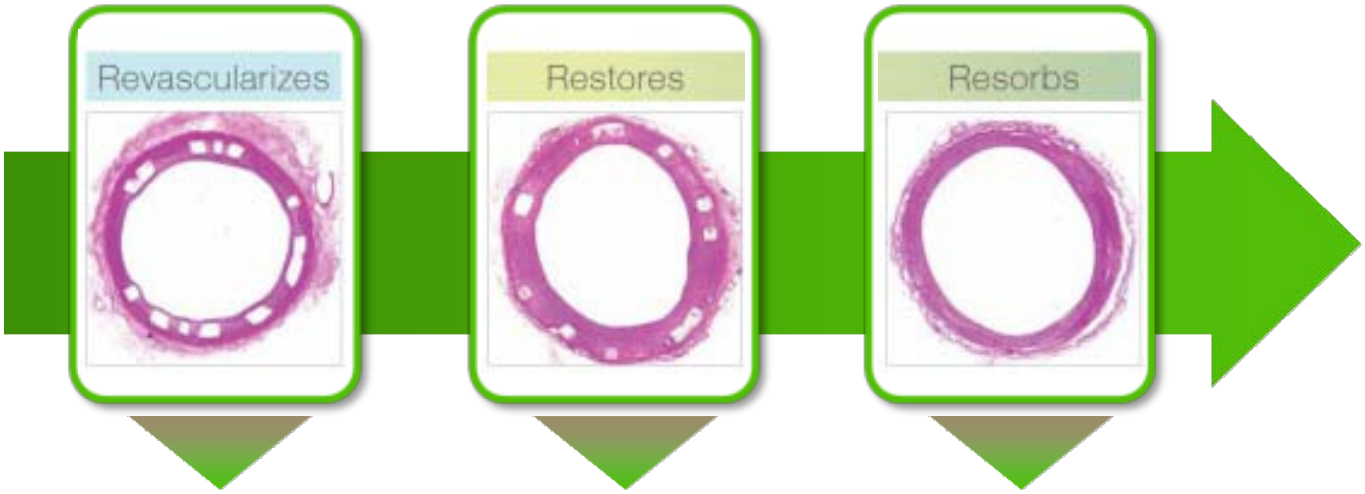
Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind[1]

Potential Benefits

- Restore the vessel to a more natural state, capable of natural vascular function
- Eliminate chronic sources of vessel irritation and inflammation
- Vessels remain free for future treatment options
- Reduce the need for prolonged DAPT[2]
- Allows for use of non-invasive imaging techniques (CCTA)
- Improve patient quality of life

*Serruys PW, et al., Circulation 1988; 77: 361. Serial study suggesting vessels stabilize 3-4 months following PTCA.
1 – Small platinum markers at scaffold edges remain for fluoroscopic landmarking. 2. The Absorb IFU recommends DAPT for a minimum of 6 months.

Absorb Bioresorbable Vascular Scaffold: Three Phases of Functionality



Revascularizes like a best-in-class DES, XIENCE

Preliminary evidence of natural vessel function

Resorbs leaving no scaffold behind*

Preliminary evidence of vasomotion suggests natural vessel function is possible to achieve improved long-term outcomes

Vascular Reparative Therapy

*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

Data on file at Abbott Vascular.

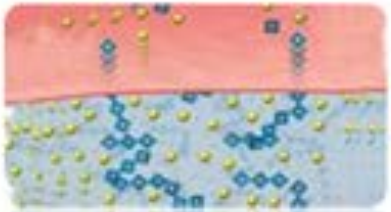
Absorbierbarer DE-Stent: wesentliche Komponenten

Bioresorbable Scaffold

- Poly (L-lactide) (PLLA)
- Based on proven MULTI-LINK pattern
- Naturally resorbed, fully metabolized*

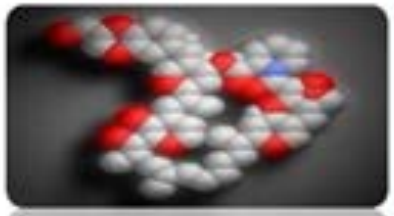
Bioresorbable Coating

- Poly (D,L-lactide) (PDLLA)
- Naturally resorbed, fully metabolized*



Everolimus

- Similar dose density and release rate to XIENCE V



XIENCE V Delivery System

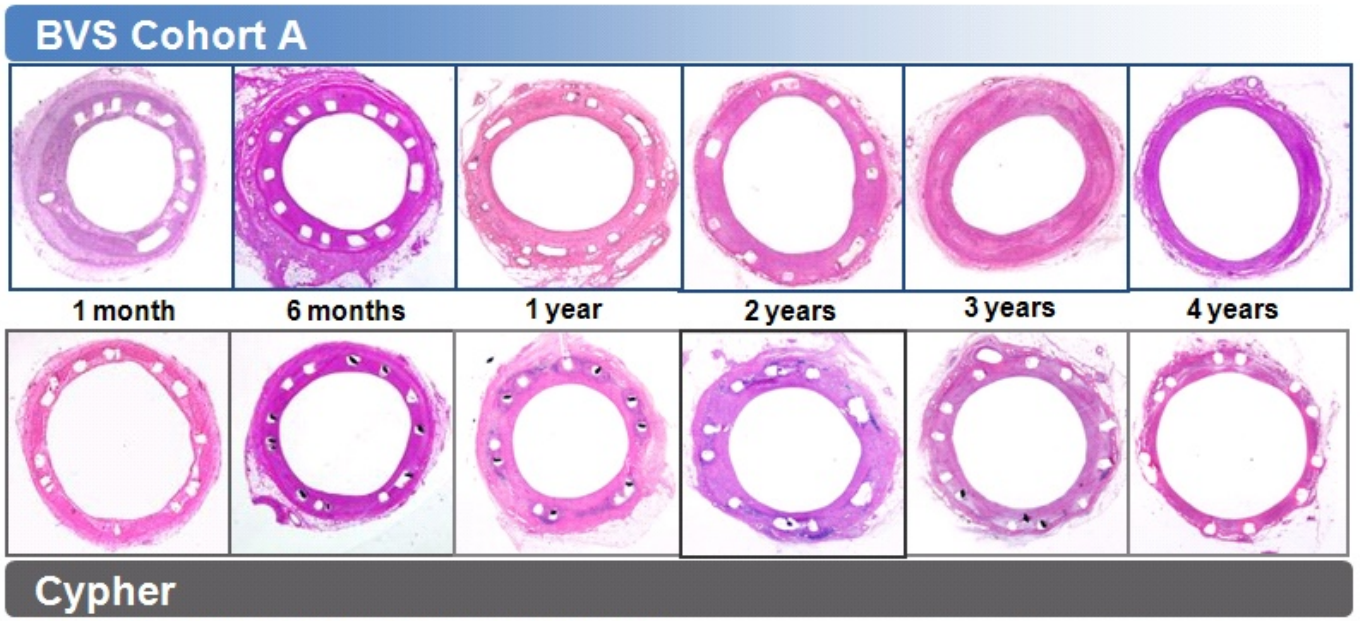
- World-class deliverability

Absorbierbarer DE-Stent

euro PCR

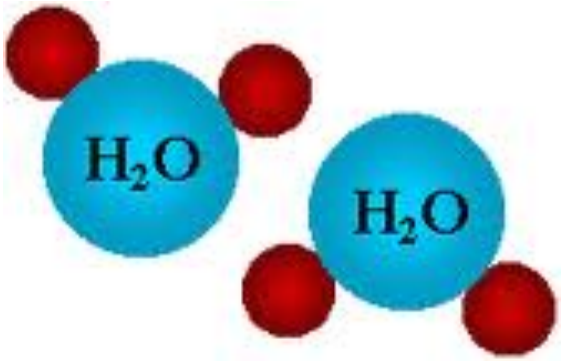
ABSORB BVS Preclinical Safety

Demonstrated in Porcine Coronary Arteries to 48 mos



Representative photomicrographs of porcine coronary arteries, 2x
Images taken by and on file with Abbott Vascular

Absorbierbare Stents



Stent und Beschichtung aus
Poly- L-Lactat-Acid
(=Milchsäure)

Medikament: Everolimus
Freisetzung ca. 6 Wochen

ABSORB Cohort A
Excellent Long-Term Data Out to 5 Years

- **ABSORB Cohort A Clinical Results at Each Phase: Intent to Treat**

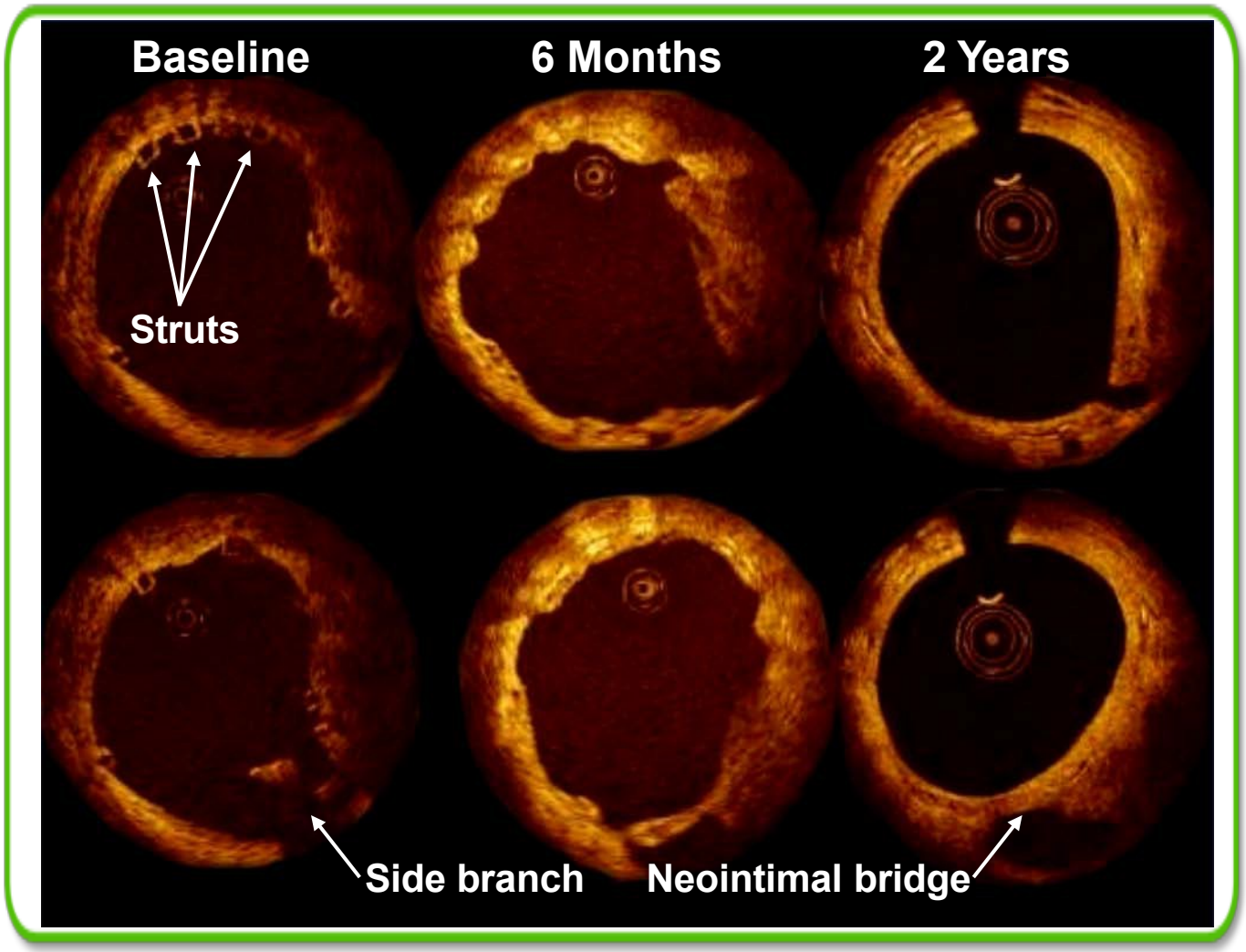
	RESTORATION		RESORPTION	
Hierarchical	**6 Months 30 Patients**	**1 year 29 Patients****	**2 Year 29 Patients****	**5 Year 29 Patients****
Ischemia Driven MACE***	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Cardiac Death	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MI	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Q-Wave MI	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non Q-Wave MI	1 (3.3%)*	1 (3.4%)*	1 (3.4%)*	1 (3.4%)*
Ischemia Driven TLR	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
by PCI	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.%)
by CABG	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.%)

No scaffold thrombosis by ARC or Protocol

*Same patient – this patient also underwent a TLR, not qualified as ID-TLR (DS = 42%). **One patient withdrew consent and missed the 9, 12, 18 month and 2, 3, and 4 year visits; two patients died from a non-cardiac causes, one at 706 days and one at 888 days post procedure. ***MACE – Composite endpoint comprised of cardiac death, myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR) by PCI or CABG.

Serruys, ABSORB Cohort A 5-year results; TCT, 2011

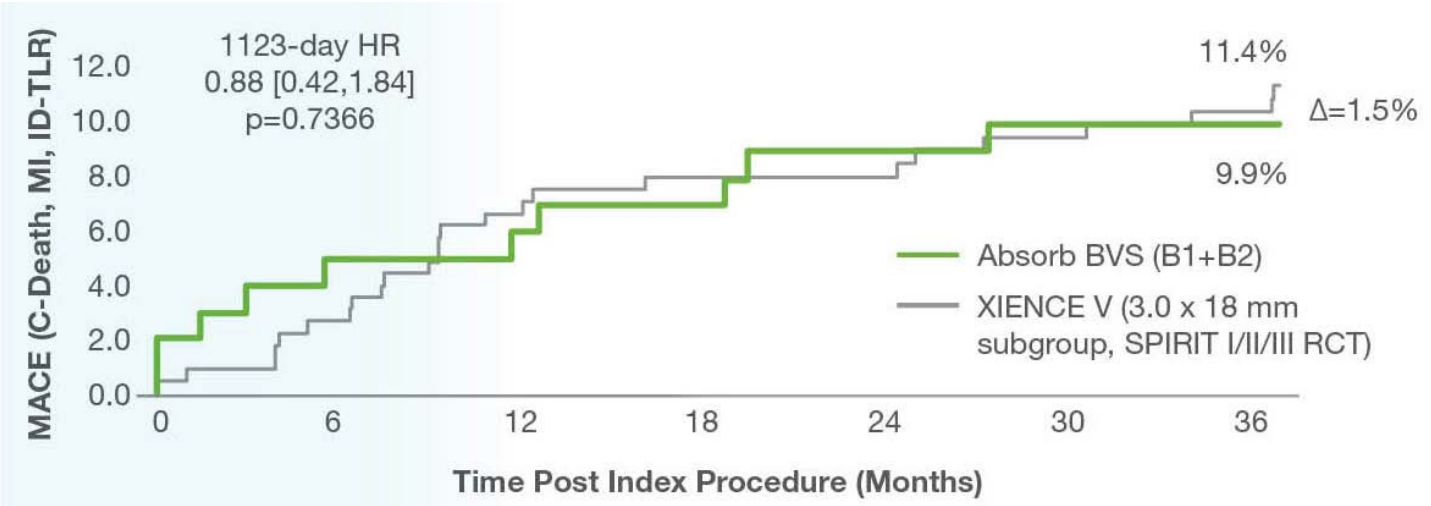
ABSORB Cohort A
OCT Images – Baseline, 6 Months and 2 Years



Serruys. PW .. ABSORB Cohort A 18-month follow-up: ESC 2008.

ABSORB Cohort B Clinical Results – MACE

Numerically Lower Long-Term Event Rates versus a Best-in-Class DES



Number at Risk

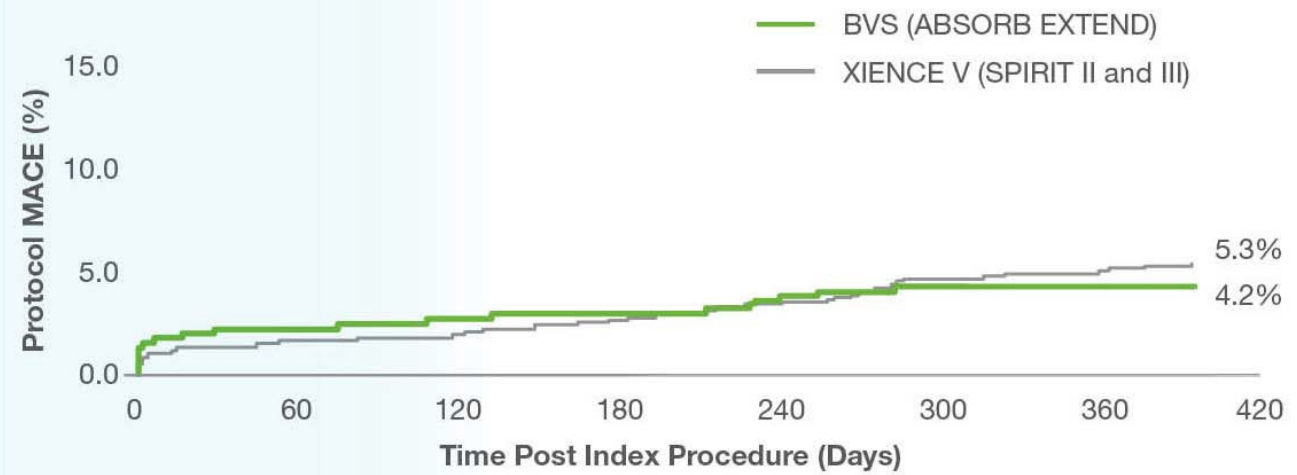
Time After Index Procedure (Days)	0	37	194	284	393	573	758	1123
Absorb BVS (B1+B2)	101	99	96	96	94	92	91	89
XIENCE V (3.0 x 18 mm subgroup, SPIRIT I/II/III)	227	224	219	211	204	202	191	182

Note: The datasets are from different trials, and displayed for descriptive purposes only.

Serruys PW, ABSORB Cohort B 3Year Data, Rotterdam EuroPCR Focus on BVS 2013

ABSORB EXTEND
Clinical Results – MACE at 12 Months

Intent to Treat (ITT) Analysis – Interim Snapshot



Number at Risk

Time After Index Procedure (Days)	0	37	194	393
Absorb BVS (ABSORB EXTEND)	450	439	436	429
XIENCE V (SPIRIT II and III)	892	877	857	814

The datasets are from different trials and displayed for descriptive purposed only. MACE: a composite of cardiac death, MI, and ischemia-driven TLR.

Chevalier. ABSORB EXTEND 12-month outcomes in the first 450 patient enrolled. Rotterdam EuroPCR Focus on BVS 2013

Absorb BVS (B+EXTEND) vs. XIENCE V (SPIRIT I, II, III)
Propensity Score Analysis at 1 Year – Adjusted Clinical Outcomes

Clinical Outcomes	Absorb (N=503)	XIENCE V (N=635)	P-value*
Myocardial Infarction, MI (%)	3.5	2.1	0.16
Ischemic-Driven Target Lesion Revascularization, ID-TLR (%)	1.6	3.1	0.089
MACE (%)	4.7	5.4	0.58
Target Vessel Failure, TVF (%)	4.9	8.5	0.017
Definite/Probable Scaffold/Stent Thrombosis, ST (%)	0.6	0.4	0.65

Absorb BVS Cohort: Pooled from ABSORB EXTEND and ABSORB Cohort B trials
XIENCE V Cohort: Pooled from XIENCE V arms of SPIRIT FIRST, II, and III trials.

*P-value: Weighted Chi-square test for dichotomous variables.
Analysis adjusted for patient baseline demographics, risk factors and lesion characteristics with Inverse Propensity Scores Weighted method. Study funded by Abbott Vascular.

A. Bartorelli, Most Recent Findings From ABSORB Clinical Trial Programme, EuroPCR 2013.

ABSORB EXTEND Compared to SPIRIT IV
Site-Reported Angina Outcomes at 1 Year Preliminary Observation

	Site-reported Angina Events Through 1 Year		
Population	Absorb BVS (EXTEND) (N=322)	XIENCE V (SPIRIT IV) (N=1999)	Unadjusted P-value
	16.5%	25.8%	0.0002

Site reported angina for the TAXUS arm (N=1005) in SPIRIT IV: 26.1%

Non-randomized data, analysis is not propensity-adjusted. Populations for Absorb Extend include the following geographies: EMEA, Japan, Australia, New Zealand, Latin America, Canada. Spirit IV was conducted in US.
P-values are descriptive and displayed for exploratory purposes only.
Study funded by Abbott Vascular.

A. Bartorelli, Most Recent Findings From ABSORB Clinical Trial Programme, EuroPCR 2013.

ABSORB FIRST:
An interim report on baseline characteristics, acute performance from the first ~800 patients from a prospective, multi-center, global registry

Eric Eeckhout , MD, Ph D
University Hospital CHUV
Lausanne - Switzeland
on behalf of the ABSORB FIRST Investigators

Background

- The safety and performance of the Absorb Bioresorbable Vascular Scaffold (Absorb BVS) (Abbott Vascular, Santa Clara, CA) has been previously established with clinical data up to 5 years (Cohort A), 3 years (Cohort B), 2 years (n=250, EXTEND), and 1 year (n>500, EXTEND). However, these trials treated patients with relatively simple lesions.
- ABSORB FIRST is designed to evaluate more complex lesions and patients in a post-approval, 'real world' setting.
- This first interim report presents results up to 30 days post PCI in the first 800 patients from this large, global study.

Study Design

Prospective, open-label, multi-center, single-arm registry real-world patient population → ABSORB BVS N ≥1800 At ≈ 90 sites

Study Objective:

- Post-market registry to evaluate safety and effectiveness of Absorb BVS

Clinical Endpoints:

- Death, MI, Revascularization, ST, TLF, MACE, etc.; Clinical endpoint events are independently adjudicated
- Device success and Procedural success

Scaffold Size: diameters at 2.5, 3.0, 3.5 mm; lengths at 28, 18, 12 mm

Product Training: according to the company's requirements

Safety Reporting: 100% reportable events are source verified

Lesion/vessel assessment : physicians visual assessment

# of patients enrolled by May 19, 2014: 1305

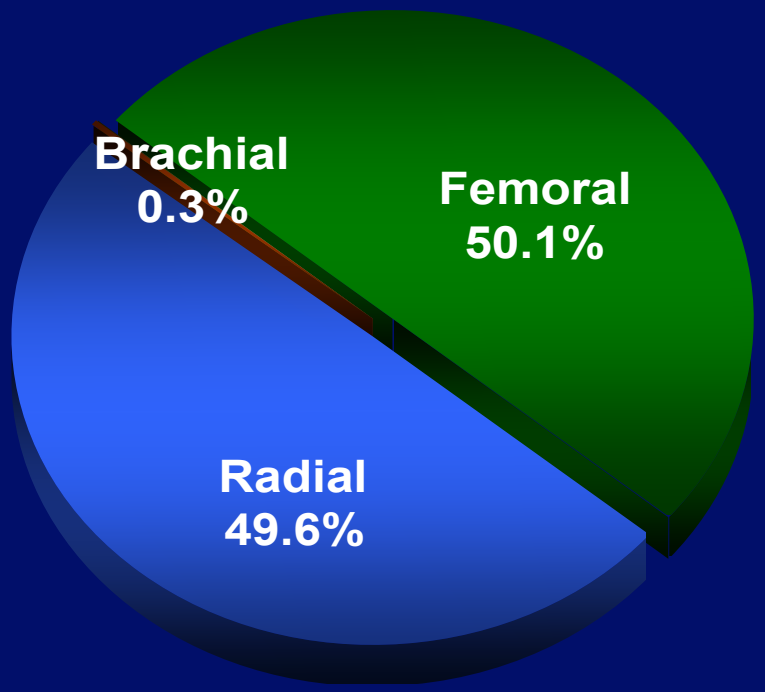
Lesion Preparation

Lesion Preparation (L=969)	Pre-Dilation	Post-Dilation
Any balloon angioplasty	94.3%	48.3%
Max Balloon Diameter (mm)	2.84 ± 1.74	3.27 ± 0.49
Max Balloon Length (mm)	15.4 ± 4.4	14.3 ± 4.8
Max Balloon Pressure (atm)	13.5 ± 3.4	16.5 ± 4.1
Focussed force Balloon	5.6%	NA
De-Calcification Techniques	0.2%	NA
Jailed side-branch	NA	4.7%
% DS	28.9 ± 23.12	3.3 ± 10.2 *

* post-procedure

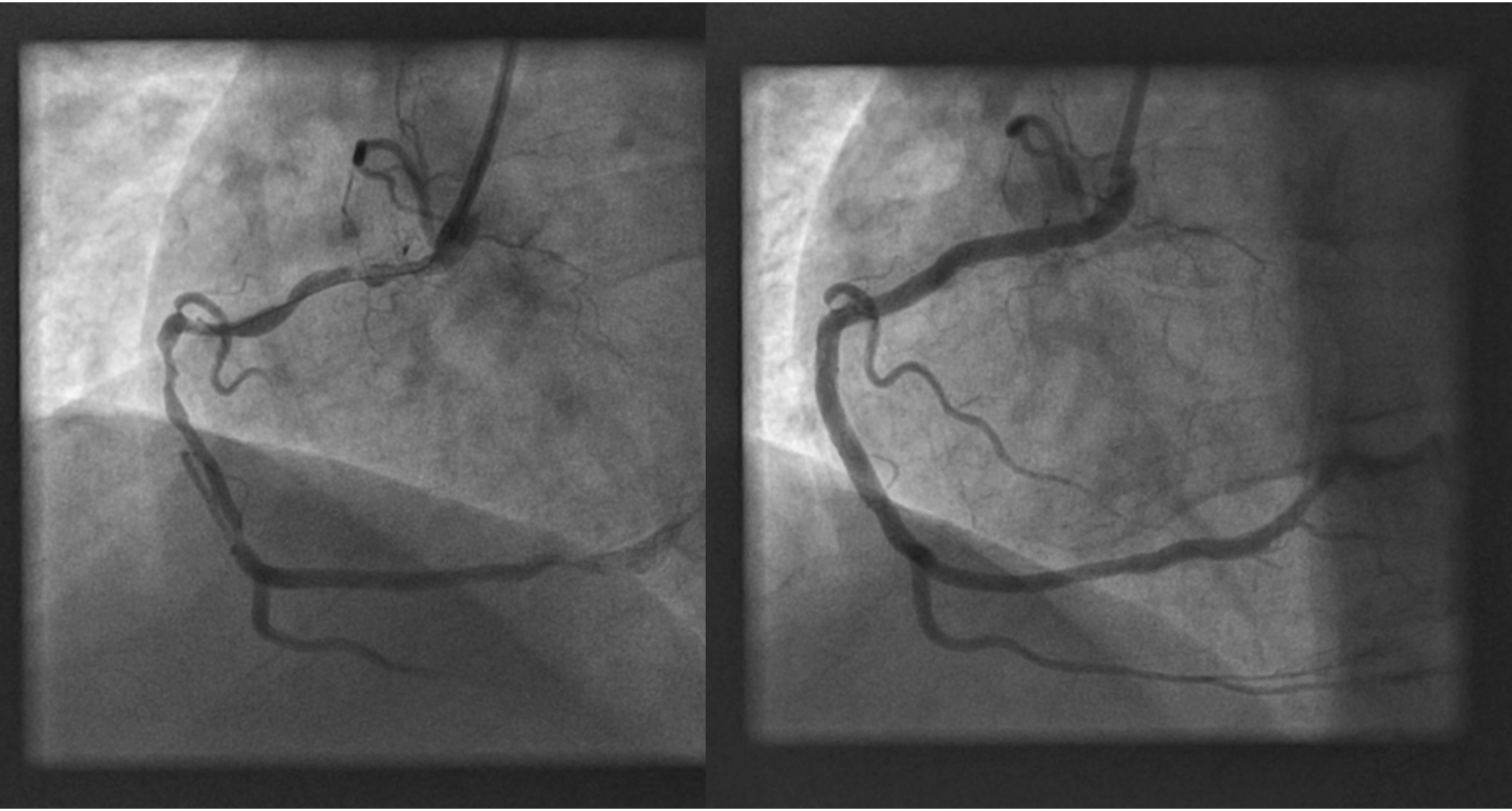
Vessel Treatment and Access Site

# of Lesions Treated	1.2 ± 0.6
≥ 2 Lesions Treated	19.5%
# of Vessels Treated	1.1 ± 0.3
≥ 2 Vessels Treated	9.3%
# of Scaffolds placed	1.4 ± 0.8
≥ 2 Scaffolds	27.1%

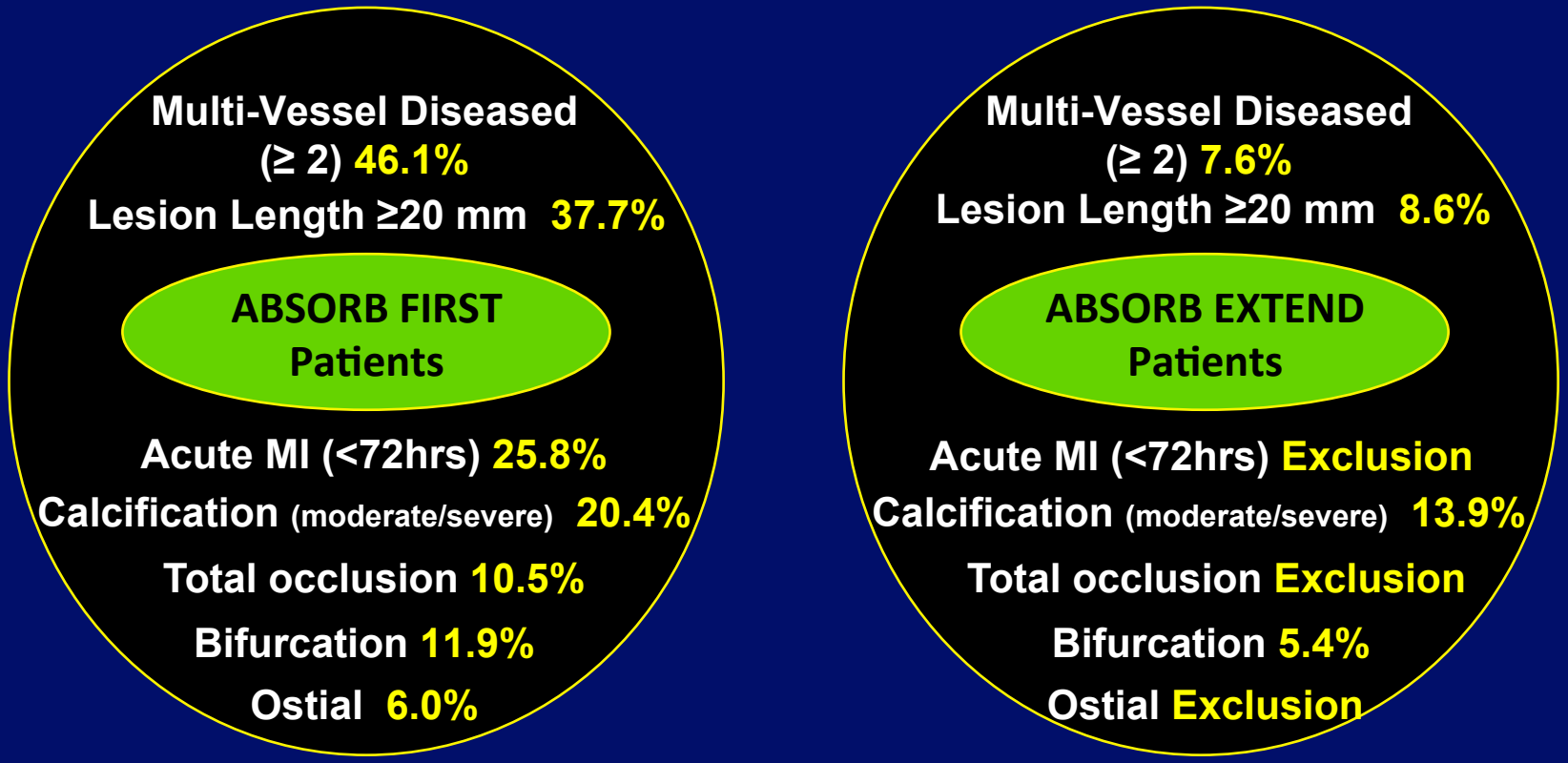


27.1% of patients had two or more scaffolds placed

Hirslandenklinik Aarau
RCA before and after PTCA/implantation of biodegradable Stents (Absorb)



ABSORB FIRST vs. EXTEND



98.9%	Device Success	98.9%
97.9%	Procedure Success	97.0%

Device success: Achievement of final in-scaffold residual %DS<50% without a device deficiency.

Procedure success: Achievement of final in-scaffold residual %DS <50% without cardiac death, target vessel MI and TLR within 3 days of the index procedure

Interim Clinical Outcomes within 30 Days

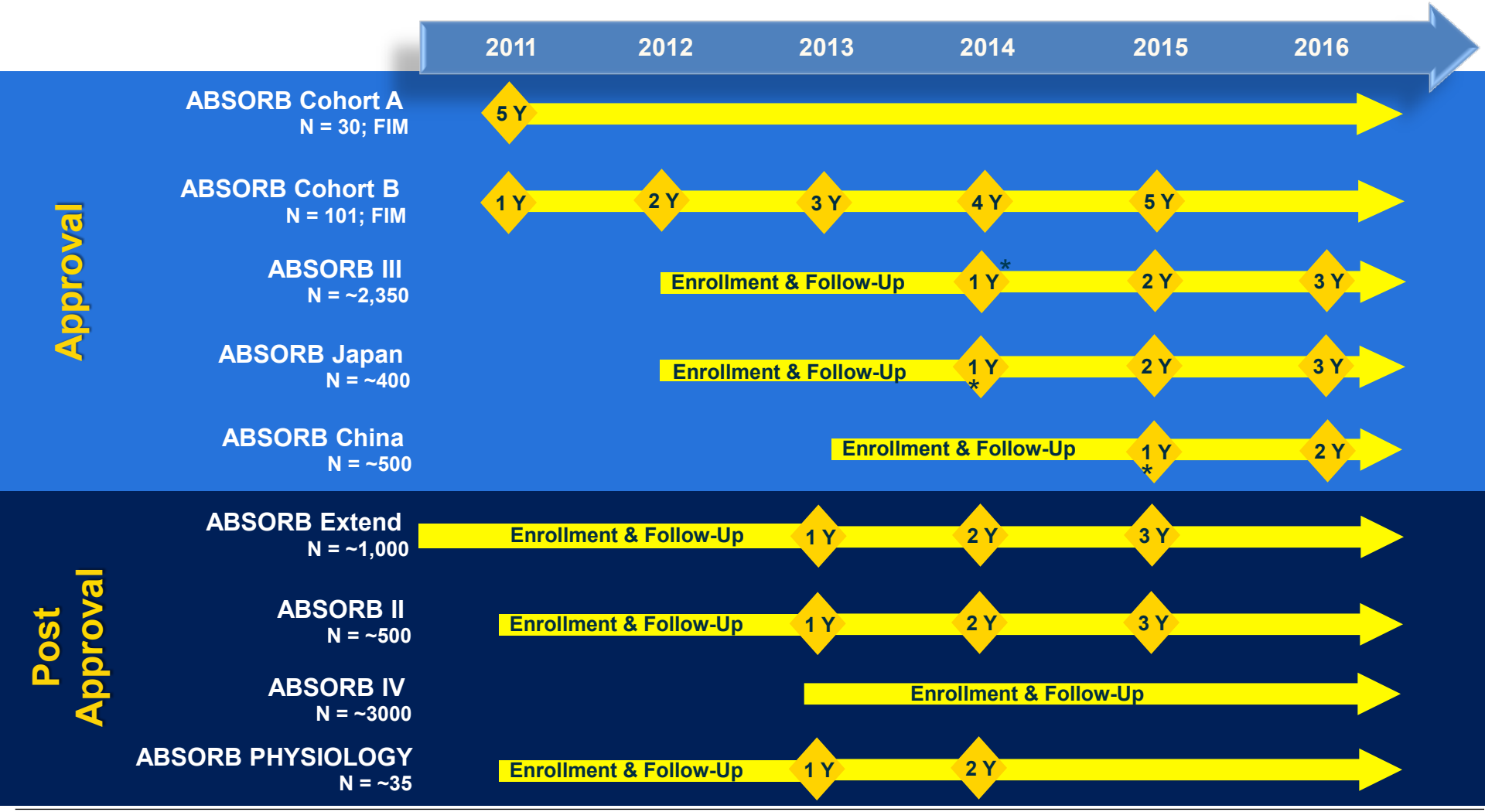
(Data snapshot as of May 6th, 2014)

Clinical Events	ABSORB FIRST (N=800)
All Death	0.0%
Cardiac Death	0.0%
Scaffold Thrombosis (Definite / Probable)	
Early (0-30 days)	0.3%
Acute (< 1 day)	0.0%
Sub-acute (1-30 days)	0.3%

Summary and Conclusion

- In this multi-center, real-world registry, Absorb BVS demonstrates excellent device success rate (98.9%) and procedure success rate (97.9%) from the 1st 800 patient data.
- Despite the complexity of this population (e.g. AMI: 25.8%, bifurcation:11.9%, total occlusion: 10.5%, ostial lesions: 6.0%), preliminary results show zero death and low rate of scaffold thrombosis (0.3%) up to 30 days post-PCI.
- These findings suggest the early safety and performance of Absorb BVS in complex, real-world patients in daily PCI use

ABSORB: Abbott Sponsored Studies



N = ~8,000

ABSORB: Randomisierte, prospektive Studien und Register (ca. 13000 Patienten)

Randomized Controlled Trials (2,764 Pts)

Study Title	Design	Number Patients	Primary Endpoint	Patient FU (yrs)
AIDA	All – comers RCT vs Xience	2194	2-Yr TVF	5
TROFI II	STEMI RCT vs XIENCE	190	6-Mo neo-intimal healing score	3
PROSPECT ABSORB	BVS vs GDMT in vulnerable plaque	300	2-Yr IVUS MLA	3
PROACTIVE	RCT vs XIENCE	20	Peri-Proc Platelet Reactivity	1
VANISH	RCT vs XIENCE	60	myocardial blood flow over time	3

Registries (10,030 Pts)

BVS EXPAND	All-comers (excl STEMI)	300	1 – Yr MACE	5
ASSURE	All-comers	180	Safety and Efficacy	3
ABSORB CTO	CTO	20	Safety and Performance	2
PABLOS	Bifurcations	30	Device, Procedural Success	2
IT-DISSAPEARS	MVD and long lesions	1000	Safety and Efficacy	5
GABI-R	All-comers	5000	Safety and Efficacy	5
REPARA	All-comers	1500	1- Yr MACE	1
POLAR ACS	ACS	100	Device and procedure success, in-hospital MACE	1
France ABSORB	De novo lesions	2000	1 – Yr MACE	1

Zusammenfassung
Vergängliche Stents

- Innovatives Konzept
- Erste Daten mit f/u bis zu 4 Jahren sehr positiv
- 6 Monate duale Plättchenhemmung ausreichend
- Zahlreiche Studien für ein breites portfolio an Indikationen ongoing
- Konkurrenzprodukte in den Startlöchern
- Sehr gute Erfahrung auch bei meinen Patienten, insbesonders bei komplexen Läsionen, insbesonders auch bei jungen Patienten/-innen

Merci beaucoup pour votre attention et bonne route!